DRUGS & MEDICINES OF NORTH AMERICA



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DRUGS AND MEDICINES OF NORTH AMERICA

A PUBLICATION

Devoted to the Historical and Scientific Discussion of the Botany, Pharmacy, Chemistry and Therapeutics

OF THE

MEDICINAL PLANTS OF NORTH AMERICA

THEIR CONSTITUENTS, PRODUCTS AND SOPHISTICATIONS

Vol. I.—Ranunculaceæ

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Commercial History, Chemistry and Pharmacy

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Botany and Botanical History

CINCINNATI
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PREFACE.

The reception with which this work has been favored forbids the editors to underrate its importance. From the date of its prospectus they have been encouraged, not only by the highest approval from those whose approval is of greatest value to them, but by assistance that has been indispensable to its success, from specialists in every branch of the undertaking. In returning our thanks for these signal favors, we desire to make our most cordial acknowledgment of the success they have enabled us to attain.

That an undertaking so new and so bold should have been generally approved by a profession so exacting, has seemed to us our best justification in making it. Yet not even the extraordinary preparation we had made for its execution would have sufficed, had not the profession made common cause with us, and aided in every way to give it completeness. And when we add that the plan of the work consists in its completeness, we need make no further acknowledgments.

It can not be denied that a plan so comprehensive has involved great expenses and difficulties. Nor can it well be doubted that this volume will be found of greater value year by year. Certainly, with the enthusiastic coöperation the work at present enjoys, of the most noted specialists in all the fields it covers, there is no occasion for anxiety regarding its future.

In this volume we have the record of all the American plants of the first natural order (Ranunculaceæ) that are known in medicine. We next take up the succeeding natural orders, and hope to continue until we have completed the subject.

To those who have assisted us by their subscriptions, we owe a heavy debt of thanks. The issue in periodical form has enabled us to enjoy every advantage both in the preparation and publication, for which we hope they will find a full equivalent in the resulting thoroughness of our work.

That "THE DRUGS AND MEDICINES OF NORTH AMERICA" may prove deserving of the reception it has met, and fill the place in medical science which such a work should occupy, is a hope almost too bold for us to express, yet one which the partiality of our friends permits us to indulge. In our attempts to realize it, we shall spare neither expense nor labor.

J. U. LLOYD.
C. G. LLOYD.

CINCINNATI, January, 1886.

LIST OF SPECIAL CONTRIBUTORS.

Prof. Roberts Bartholow, M. D., LL. D. (*Professor of Materia Medica, General Therapeutics and Hygiene, in the Jefferson Medical College, Philadelphia*). The Physiological Effects and Therapeutical Uses of Hydrastis, 156; Physiological Action of Aconitum uncinatum, 226; Physiological Action of Aconitum Fischeri, 229.

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Prof. Asa Gray. Permission to use figures from Gray's Genera.

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Mr. J. A. Knapp, Artist. Delineator of all the plates, and most of the figures of this volume.

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Prof. Robert Sattler, M. D. (*Assistant to the Chair of Ophthalmology, Lecturer on Otology, Miami Medical College, Cincinnati*). The Physiological Effects and Therapeutic Uses of Berberine and Hydrastine in Ophthalmic and Aural Practice, 171.

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PLATE I.



CLEMATIS VIRGINIANA.

(NATURAL SIZE, FLOWER

DRUGS AND MEDICINES OF NORTH AMERICA.

CLEMATIS VIRGINIANA.

VIRGIN'S BOWER.

PARTS USED.—The fresh leaves, flowers and stem of Clematis virginiana *Linn.*

Natural Order Ranunculaceæ, Tribe Clematideæ.

BOTANICAL ANALYSIS.—Stem, a woody, climbing vine. Leaves, opposite, ternate; the leafstalks winding around objects of support. Leaflets, ovate, acute, smooth, firm, veiny, more or less three-lobed; margins crenate-serrate. Flowers numerous, dicecious, in axillary clusters. Sepals four, white, petaloid, spreading. Petals, none. Stamens numerous, spreading, about as long as the petals. Fruit, an achene, with a feathery tail one to two inches long.

COMMON NAMES.—The name Virgin's Bower, applied to this species, is equally applicable to all the species of the genus. It is also called Ladies' Bower, Traveler's Ivy, and Love Vine, from reference to natural arbors which it forms. These names were originally applied to the English species, Clematis Vitalba, but have naturally been given to this and other species.

SPECIFIC DESCRIPTION.—Clematis virginiana is the most common native species. It is found in nearly every locality east of the Mississippi, extending north into British America, and west into Missouri and Kansas. It is very common in the mountains. The plant is a shrubby vine, climbing over fences and bushes by means of the leafstalks which coil around objects of support. The leaves are tri-foliolate and opposite. The flowers, which appear in mid-summer, are white and very numerous, and make the shrub a conspicuous object when in bloom, and on this account it is often cultivated. The fruits, which are produced in heads in the fall of the year, are achenes, with long, feathery tails. (See illustration opposite, Plate 1.)

GENERIC DESCRIPTION.—The genus Clematis is an extensive family, dispersed throughout the temperate regions of both hemispheres. It consists mostly of climbing shrubs, rarely erect, and more rarely with herbaceous stems. The flowers are very numerous and showy; hence different species are in cultivation as ornamental climbers. The properties of all the species, when fresh, are more or less acrid.

Plants of this genus can be readily distinguished from all other native climbing vines, by the peculiar habit they have of twining their leafstalks for support.



FIGURE 1.

Branch of Clematis crispa: 1, transverse section of the four sepals; 2, vertical section of the flower.

ALLIED SPECIES.—Clematis Viorna *Linn.*, Clematis Pitcheri *Torr. & Gray*, and Clematis crispa *Linn.*, are three closely related native species. The first is found from Pennsylvania south; the next, from Illinois west; and the last, in the Southern States. They belong to a natural section of the genus, which can be readily distinguished from Clematis virginiana by their large, solitary, nodding, bell-shaped flowers. The first two species, which are perhaps but varieties of the same, have four dull-purple, valvate sepals, of a very thick texture; hence they are often called Leather Flowers. Clematis crispa has purplish-blue sepals, with dilated thin margins. It is called in the Southern States Blue Jasmine, or Curled Virgin's Bower, and is probably our most acrid species. It is figured in Gray's Genera, vol. i., plate 2.

Clematis verticillaris *DC.* is a northern species and rather rare. It has large four-sepaled purple flowers, with thin, spreading sepals. It has small, petal-like bodies, resembling abortive stamens, and on this account the plant was formerly separated from the genus Clematis and named Atragene americana *Sims.*

It is called whorl-leaved Virgin's Bower, and figured in the Botanical Magazine, vol. xxiii, plate 887. Clematis alpina *Mill.*, is an analogous plant of the mountains of Southern Europe.

Clematis ligusticifolia *Nutt.*, of the Western States, takes the place of Clematis virginiana, which it closely resembles. We are informed by Dr. Louis Emmelheinz, of New Mexico, who forwarded us specimens for identification, that the roots of this plant are used as an alterative by the Indians, and called Wild Sarsaparilla.

Clematis Vitalba *Linn.*, is the most common species of Europe, and the only one found in England. It is called Virgin's Bower, Traveler's Joy, Love Vine, White Vine, Ladies' Bower, Old Man's Beard, Smoke Wood, Wild Vine, Bind-with, Hedge Vine, and Climbers.

Clematis recta (erecta) *Linn.*, is found in Middle and Southern Europe. It has an erect, herbaceous stem, about two feet high, and is probably the most acrid species of Europe. It is called Upright Virgin's Bower, and in old medical works, Flammula Jovis, and is figured in Woodville's Medical Botany, vol. iii, plate 171. This is the species that was first introduced into medicine.

Clematis Viticella *Linn.*, and Clematis Flammula *Linn.*, are climbing shrubs, native of France and other countries of Southern Europe. The former has blue flowers, and is known as Blue Clematis; the latter has white, fragrant flowers, and is called Sweet Scented Virgin's Bower; both are considerably cultivated.

Clematis dioica *Linn.*, of Jamaica, and Clematis mauritiana *Linn.*, of Madagascar, are used by the natives of those countries as rubefacients. The latter species is probably the most acrid of the entire genus.

DESCRIPTION OF DRUG.—The fresh leaves, flowers and stem of Clematis virginiana are the portions employed in our country in medicine. The leaves and flowers have been described in the botanical part of this paper.

The stem (Fig. 2) attains a diameter at the base of from one-half to one inch and has a spongy ligneous texture When recent, it is covered with a thin brown bark. The wood is coarsely divided into distinct medullary rays, between which, when the plant is recent, are deposited layers of a greenish substance, which contains the acrid principles of the plant.



FIGURE 2.
Stem of Clematis virginiana—natural size.

None of the species of Clematis are found in our market as commercial drugs.

MICROSCOPIC STRUCTURE.—(Written for this publication by Louisa Reed Stowell.)

Bark.—Beginning with the outside of the stem, we find there is present no epidermis. The *cork*, or outer layer of the bark, is composed of from five to twelve rows of thin-walled tabular cells of a brownish yellow color. The *green*, or *middle, layer of the bark*, is of nearly the same width, and composed of from five to twelve rows of oval parenchyma. Next to the green layer come large crescent-shaped masses of liber fibre. A cross and longitudinal view of a single liber fibre is seen in Plate II, fig. B, c 1 and c 2.

Just inside of this liber fibre is found a secondary formation of cork and the green layer of the bark, smaller and more delicate than the first. Embedded in this second green layer are masses of large stone-cells. These have rather thinner walls than the majority of stone-cells, still the walls are much thicker than all the other cells of the stem excepting the liber fibre. (See Plate II, h, figs. A and B.) Then come other slender, sharply pointed, crescent or horse-shoe shaped masses of liber fibre. The spaces inside of these inner masses of liber are filled up with hexagonal, thin-walled parenchyma. These masses of liber and the enclosed parenchyma form the *inner layer of the bark.*

The *cambium* separating the bark from the wood is composed of from three to six rows of tabular cells, clear white, and filled with protoplasm.

Wood.—The *medullary rays* are made up of from three to ten rows of thin-walled, white tabular cells. Between these medullary rays are the small, thick-walled, clear white cells of wood *prosenchyma*, resembling somewhat the liber fibre. With these are numerous large, open, pitted cells. The ends of these cells are seen in Plate II, fig. A, m; while in fig. B, m, the length of the cell is seen with the numerous pitted marks on its surface.

Two or three annular rings are generally to be seen in this stem.

Between the wood and the pith is the *medullary sheath*, composed of fine spiral vessels.

Pith.—Thin-walled, brownish, hexagonal cells of parenchyma make up the pith. Occasionally, pitted marks are found on the surface of the cells.

DESCRIPTION OF PLATE II.—Fig. A.—a and a′, cork; b and b′, the green layer of the bark; c, liber fibre; h, stone-cells; d, cambium; e, medullary rays; m, pitted cells; f, wood prosenchyma; i, parenchyma, or liber layer of the bark. Drawn with a 4-10 inch objective, and an "A" eye-piece.

Fig. B.—h, stone-cells; c, 1, cross section of liber fibre, c, 2, longitudinal view of the same; m, pitted cell of the wood, longitudinal section. Drawn with a camera lucida, with an ¼ inch objective, and an "A" eye-piece. (Figs. A and B reduced one-third.)

CONSTITUENTS.—The odor of freshly broken recent Clematis virginiana is peculiar and unpleasant. It imparts a rank taste, which, after prolonged chewing, becomes acrid and irritating, although at first it is only disagreeable. The descriptions in other works which we have consulted, would lead to the inference that all of the species of Clematis are possessed of an acrid principle resembling, in sensible properties, that of senega, or even of Indian turnip. This is not supported by our experience with Clematis virginiana, for there is no imme-

PLATE II.



FIG. B.

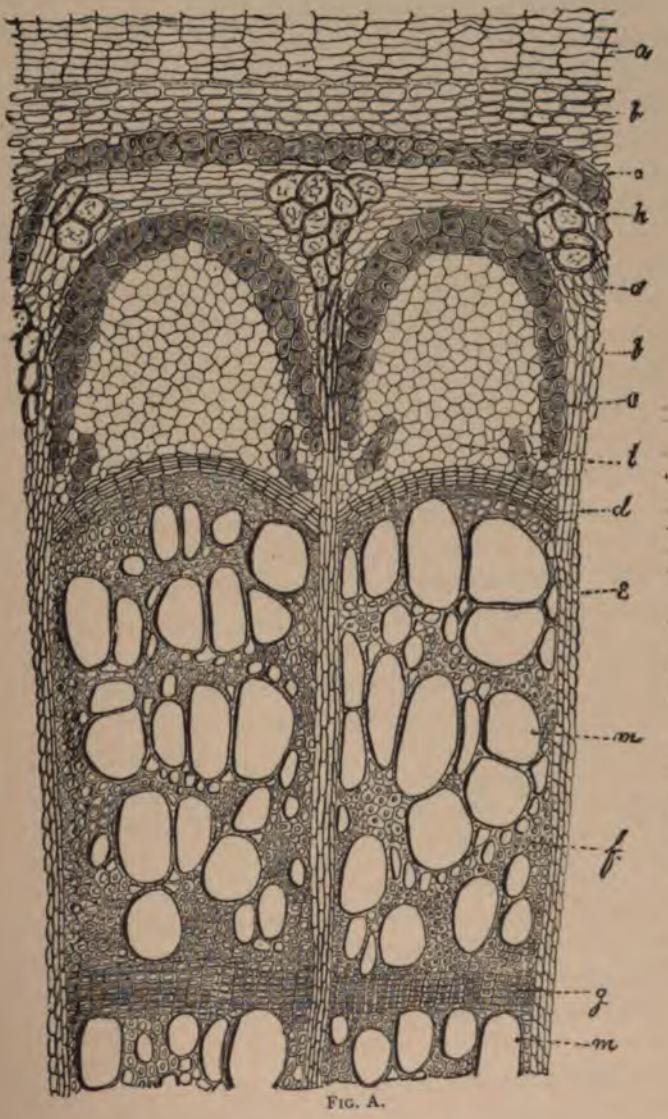


FIG. A.

MICROSCOPIC STRUCTURE OF STEM OF CLEMATIS VIRGINIANA.

Scanned with CamScanner

diately acrid sensation; and even prolonged chewing is not followed by pain, but rather by a dry, metallic-like roughness of the tongue and mouth. When the plant dries, its acrid nature disappears. The fresh juice is neutral to litmus paper. When recent Clematis virginiana is bruised, mixed with water, and distilled, the condensed liquid has an offensive odor, somewhat like skunk cabbage. This distillate is neutral, and does not contain an alkaloid, either when the plant is distilled with water or dilute solution of caustic potash. If the distillate be shaken with chloroform or benzol, the odorous principle is extracted from it, and dissolved by the chloroform or the benzol. Upon spontaneous evaporation of this solution, a colorless, oily substance remains, which is the characteristic principle of the plant, but which evaporates by exposure. If the vapor of the distillate be inhaled, it irritates the lungs, producing an after-effect similar to that which follows the inhalation of sulphurous acid gas, but not of a suffocating or immediately painful nature. Alcohol extracts all of the properties from recent Clematis, forming a green tincture, which changes to brown upon exposure to the light. The plant contains glucose and the usual constituents of plants, but our most careful examination failed to detect the presence of an alkaloid, either fixed or volatile.

Rafinesque (1830) states that the flowers of Clematis virginiana and Clematis Viorna hold a peculiar substance, clematin, similar to gluten. M. Gaube, of Europe (1869), claims to have obtained an alkaloid from Clematis Vitalba, and he named it clematine. He formed with it a salt, by means of sulphuric acid, which crystallized in hexagonal needles. In addition, he obtained an acrid volatile oil and the usual constituents of plants.

Medical History.—The European species of Clematis have been recognized in medicine since a very early day. The "*Histoire des Plantes*" (1762) gives rude figures of three species, viz.: recta, Flammula and Viticella, together with a fair medical notice, and refers to earlier publications. The properties are correctly stated as being acrid, and the uses are such as were attributed to the plants in after days.

Störck (1769) is the authority generally accredited with introducing Clematis to the medical profession, but we can not find that he notes much that had not been previously written.

Motherby (1775) says of Clematis recta: "The herb, with the flower, is caustic; the root, seed, bark, and all, if rubbed with the fingers, then held to the nostrils, strike them like lightning with a strong smell. It yields a water as hot as spirit of wine, but it does not seem safe to administer it internally." Boerhaave mentioned several species.

Clematis recta, generally under the name of Flammula Jovis, was recognized in a dozen or more of the local Pharmacopœias of Continental Europe from 1798 to 1840, and was mentioned in many old dispensatories and materia medicas.

No species of Clematis, however, had been inserted into the materia medica of any of the British colleges as late as 1803, and we fail to find it men-

tioned in the "New Dispensatory" between the dates of 1753 and 1818, or in Lewis' Materia Medica of 1761. It is not recognized by the Pharmacographia (1879), nor the recent editions of the German Pharmacopœia; and these facts, together with other testimony in our possession, are evidence that although Clematis recta was early introduced into European domestic medicine, and even into many pharmacopœias, it has generally failed to retain its position, excepting with homœopathic physicians. The first edition of Hooper's Medical Dictionary (1817, American reprint) stated that "More praises have been bestowed upon the virtues which the leaves of this plant are said to possess, when exhibited internally, as an antivenereal, by foreign physicians, than its trials in this country (England) can justify;" and this sentence is carried through the editions which followed.

The close relationship which exists between the properties of the American species of Clematis and those of Europe, has necessitated the foregoing remarks regarding the foreign species; and in considering our native species, we find that, like the European, they are but little valued in medicine at the present time; and they have never been favorites.

This is somewhat strange, when we consider the acrid, irritating properties of certain species, for in early therapeutics, and even at the present day, those substances which possessed disagreeable characteristics, especially if of a poisonous nature, were, as a rule, thought to be antagonistic to disease. Cutler (1783) mentions Clematis virginiana, but says nothing of its medicinal value. Barton considers Clematis Viorna and Clematis crispa in his Collections (1801), p. 30, and this note gave the plant a position in Coxe's American Dispensatory (1st edition, 1806); but the subject was thought so unimportant as to permit the passage remaining unchanged through nine subsequent editions of that work. The United States Dispensatory (1st edition, 1833) failed to mention any species of Clematis, an oversight which was corrected in the second edition (1834); but there has been little alteration in wording since, and it has always occupied a position in the appendix. Prof. John King, in the first edition of his Dispensatory (1852), gave Clematis virginiana and Clematis Viorna each a fair therapeutic notice; and this was carried through subsequent editions of that work. Prof. J. M. Maisch, in the National Dispensatory (1879), devotes to the different species of Clematis, foreign and native, as extensive a description as was necessary in a work of that description; and the therapeutical notice is equally satisfactory. Neither Thomson nor Beach refers to Clematis; and the other writers upon American medicinal plants have seldom mentioned it. Dunglison failed to introduce it into any edition of his New Remedies, or Materia Medica; Pereira omitted it from his Materia Medica; and Scudder, in his Specific Medication, simply speaks of Clematis virginiana as an agent that "deserves investigation." The Pharmacopœia of the United States has never recognized a species of Clematis. Our native species are occasionally used in domestic medicine, but physicians of all schools excepting the Homœopathic now neglect it altogether. The characteristics of the family are, however,

sufficiently pronounced to lead us to believe that, when properly investigated, some of the species will prove to be useful additions to our materia medica. The volatile nature of the active constituents, renders it necessary that a preparation of the fresh plant be employed; and this fact may have interfered with the general use of the plant as a medicine.

PHARMACEUTICAL PREPARATIONS.—The tincture is officinal in the Pharmacopœa Homœopathica Polyglottica (1872), and is made by pounding the fresh leaves of the Clematis recta, when the plant is flowering, into a pulp, and pressing out the juice, which is then mixed with an equal weight of alcohol. After standing in a dark, cool location for eight days, it is filtered. This tincture does not possess all of the properties of the plant, and a more accurate representation may be made as follows:

Take of the fresh stem, leaves and flowers of Clematis, one part; alcohol, two parts. Bruise the plant until reduced to an even pulp; add the alcohol; mix thoroughly, and allow the mixture to stand in a close vessel for ten days; then express the liquid, and filter it.

MEDICAL PROPERTIES.—We find it stated in the Histoire des Plantes (1762), that when the bark of Clematis Vitalba is boiled in oil, and verdigris and wax are added, an ointment is produced which is admirable in the treatment of tinea. This ointment has otherwise the same properties as the plant. It is also stated that the leaves of Clematis Viticella have caustic properties; that the seed, if bruised, and drank in sweetened water, will cause a discharge of bile and mucus from the bowels, and that the leaves, applied to the surface, cure the itch and leprosy. In speaking of Clematis recta, the same authority states that it is "hot and dry." Its leaves, flowers and seeds, like those of the third species of Clematis (Clematis Vitalba), have the same acrid taste. The very pungent, hot taste of the leaves gave this plant the name Flammula. It is asserted that water distilled over this plant is very effectual in quartan fevers; applied to the skin, its leaves produce sores; taken internally, it cures "cold diseases." To prepare the leaves for medicinal use, they were cut very fine, placed in a vessel, covered with fresh olive oil, and exposed to the sun for several days. This medicated oil is good for sciatic and gouty rheumatism, urinary troubles, stone and gravel. It can be used internally and applied externally. Störck (1769) used Clematis recta in secondary syphilis, cancerous affections, old ulcers, and headache. He used the powdered leaves as an external application, but for internal use he preferred an infusion of two or three drachms of the fresh leaves to a pint of water, of which infusion he gave to an adult four ounces three times daily. Störck considered that Clematis was a diuretic and diaphoretic, a claim that Prof. M. Sauveur (1866) sustained, for he reported the great relief, perhaps permanent cure, afforded in two cases of Bright's Disease where he administered an infusion of the drug. He states that it acted as a powerful diuretic, and we quote from Prof. King's translation of Sauveur's paper, as follows: "The effects of the remedy were quite prompt: a profuse diuresis, followed by a gradual diminution of albumen in the urine and a rapid

disappearance of the anasarca, and other symptoms." Motherby (1775) speaks of the caustic nature of Clematis recta. He does not advise its use as a remedy, stating that the plant "yields a water as hot as spirit of wine, but it does not seem safe to administer it internally."

Clematis Vitalba is used in Europe as an itch remedy. The leaves are first extracted with water, to remove some of the acrid principles, and then with hot oil. The resultant oil is applied to the affected parts, it is said, with perfect success.

Prof. Landerer, of Greece (1877), in speaking of the medicinal plants of the Orient, states that an intimate friend, subject for years to epileptic fits, and who had been through the line of regular medication without benefit, applied to a priest who had the reputation of curing the disease by means of a plant known only to himself. The result was a cure, or at least a complete suspension of the attacks. Prof. Landerer examined a part of this plant, and pronounced it to be a species of Clematis, either Clematis cirrhosa or Clematis sylvestris. He also supported the assertions of others, to the effect that the fresh leaves, if bruised, acted as a rubefacient, or even as a vesicant, when applied to the skin (New Remedies, 1877, p. 181).

Lindley (1838) is authority for the statement that in Jamaica an infusion of the bruised leaves and flowers is used to remove freckles, and that a decoction of the root in sea water acts as a powerful purge, and is used in dropsical cases. He also states that in the Isle of France the negroes use the Clematis mauritiana to blister the cheek, as a counter irritant when suffering from toothache.

Clematis virginiana, our common native species of Clematis, has properties similar to those of foreign countries. Rafinesque (1830) states that in small doses, Clematis virginiana and Clematis Viorna are diuretic and sudorific, and will cure chronic rheumatism, indolent ulcers, and palsy. Dr. Williams (Porcher, 1850) recommends these species of Clematis as valuable diuretics and sudorifics in chronic rheumatism. Prof. John King (1852) states that the solid extract of Clematis virginiana, in doses of from one to two grains, is a remedy for osteocopic pains; that the green leaves are bruised, and employed as a vesicant, and as an escharotic and detergent for venereal and other foul and indolent ulcers.

Dose.—(King) Of the solid extract of Clematis virginiana, from one to two grains; (Scudder) Of the tincture of the fresh plant, five to ten drops; of the infusion of the dried bark, a teaspoonful to a tablespoonful; (Störck) Of the distilled water of Clematis recta, four fluid ounces.

In searching the medical literature relative to the uses of our native Clematis, we failed to find a recognition of any species in the standard Homœopathic works. Knowing that the European Clematis recta is by no means unimportant, and that a tincture is imported, to a considerable extent, for the use of Homœopathic physicians, we consulted Prof. E. M. Hale, M. D.,* of Chicago,

* Prof. Hale has kindly consented to continue his contributions on the Homœopathic uses of the drugs considered by us.

who has devoted much attention to American drugs. Prof. Hale has contributed as follows:

HOMŒOPATHIC USES OF CLEMATIS VIRGINIANA.—This indigenous species of Clematis has not yet been formally introduced into the materia medica of our school. The writer is perhaps the only one who has made use of it to any extent. During my investigations into the comparative value of American, as compared with foreign species, of medicinal plants, I prepared a tincture of the green plant leaves and flowers, and prescribed it for the symptoms recorded in the provings of Clematis recta. I found it fully as active as its European congener, and equally as useful in *nervous erethism, sleeplessness, neuralgic* and *rheumatic headache and toothache.* It is particularly useful in the *reflex neurosis of women,* arising from irritation of the *ovaries and urinary organs;* also for the neurosis of men, when connected with painful affections of the *testicles and bladder.* It is useful in cystitis and urethritis; in *gonorrhœa* and *orchitis,* and in the *swelling of inguinal glands.* Many cases of poisoning by handling the plant have come under my observation. It causes a painful pustular eruption, which may be mistaken for eczema. I have known it to cause blebbs and bullae, which degenerated into small, painful ulcers. In this respect it resembles the Clematis recta. Prescribing it in accordance with the law of *similia,* I have found it curative in eczema, *herpes zoster,* and pustular eruptions on the scalp and face of children. Its pathological effects resemble closely other members of the family of *Ranunculaceæ*; namely, *Ranunculus, Pulsatilla, Delphinium,* and *Pæonia.*

PHARMACEUTICAL AND MEDICAL REFERENCES.

1762.—Histoire des Plantes, Vol. II., p. 561, 562, 563.
1775.—Motherby's Medical Dictionary (and other editions).
1783.—Cutler's Indigenous Vegetables. Memoirs Am. Arts and Sciences, 1785, p. 458.
1804.—Barton's Collections, p. 30.
1804.—Edinburg Dispensatory, p. 364.
1810.—Woodville's Medical Botany, p. 480
1817.—Hooper's Medical Dictionary, p. 208 (and other editions).
1825.—Cox's American Dispensatory, p. 200 (and other editions).
1830.—Rafinesque's Medical Botany, p. 211.
1834.—United States Dispensatory, p. 1078 (and subsequent editions).
1838.—Lindley's Flora Medica, p. 1.
1849.—Porcher's Medicinal Plants of South Carolina, Am. Med. Assoc. Rep., p. 683.
1852.—Dunglison's Medical Dictionary, p. 211.
1852.—King's American Dispensatory, p. 128 (and other editions).
1858.—Stearn's Medicinal Plants of Michigan, Am. Phar. Assoc. Proc., p. 254.
1861.—Journal of Materia Medica, p. 331.
1864.—Eclectic Medical Journal, p. 538.
1870.—Specific Medication, p. 116 (and other editions).
1870.—Eclectic Medical Journal, p. 13.
1871.—Featherman's Botanical Survey of Louisiana, p. 49.
1872.—Pharmacopœia Homœopathica Polyglottica, p. 92. 160.
1873.—Dictionary of Pharmaceutical Sciences, p. 129.
1877.—New Remedies, p. 181.
1877.—Pharmaceutical Journal and Transactions, p. 126.
1878.—Proceedings American Pharmaceutical Association, p. 250.
1879.—National Dispensatory, p. 428.
1880.—Supplement to American Dispensatory, p. 69.
1882.—Dictionary of Economic Plants, p. 432.
1883.—Merrell's Digest of Materia Medica.
Williams' Medical Botany of Massachusetts.

ACKNOWLEDGMENT OF CUTS AND PLATES.

Plate I.—Original—Drawn by J. A. Knapp.
Plate II.—Orginal—Drawn by Louisa R. Stowell.
Fig. 1.—Gray's Genera of Plants of the United States.
Fig. 2.—Original—From Photograph.

THALICTRUM DIOICUM.

MEADOW RUE.

PART USED.—The plant Thalictrum dioicum *Linn.*

Natural Order Ranunculaceæ, Tribe Anemoneæ.

BOTANICAL HISTORY.—This is a small herb, about a foot high, with alternate, tri-ternately compound, finely divided leaves, and small round crenate leaflets. The flowers appear early in spring, are inconspicuous, without petals, and the male and female are on different plants. The male plant, with numerous slender hanging stamens, is most likely to attract attention. The name, Meadow Rue, applied to this plant in common with all others of the genus, is derived from the finely divided, rue-shaped leaves, and has no reference to its medical properties.



FIG. 3.
Leaf of Thalictrum dioicum.

ALLIED SPECIES.—Thalictrum purpurascens *Linn.*, and Thalictrum Cornuti *Linn.*, are two other very similar but much larger indigenous plants, the stems growing from three to six feet high. They are both rather common, the former found in rocky places, the latter in damp situations.

MEDICAL HISTORY AND PROPERTIES.—These plants were not used by the American Indians; at least there is no record of that fact. The early writers on our indigenous remedies failed to notice them. The standard works, such as the Dispensatories, Medical Dictionaries, Catalogues of American Medical Plants, etc., omit them. Their near relatives, however, Thalictrum flavum *Linn.*, and other species, have been occasionally recognized in European medicine. According to Rafinesque (1830), the roots of certain of our native species of Thalictrum were used in Canada for the cure of snake-bites, and the leaves were sometimes employed as an ingredient of spruce beer; but the species referred to are not named. None of the American species of Thalictrum have been used by the Eclectic or the Botanic schools of medicine, nor have they ever been analyzed.

FOREIGN SPECIES OF THALICTRUM.—Some of these species have been used in Europe in domestic medicine, and formerly, to an extent, by the medical profession. The New Family Herbal (1790) gives Thalictrum flavum quite a notice, but the New Dispensatory, Lewis' Materia Medica, and other standard early English works ignore it. The supplement to the Pharmacopœia (Lon-

don, 1821) is authority for the statement that the roots of this species of Thalictrum were at that time used to adulterate rhubarb. The appearance of the two roots would forbid such admixture now, unless in form of powder. The root of Thalictrum majus, a native English species, according to the same authority, is "the best substitute for rhubarb, but requires a double dose." On this account the plant obtained the popular common name of Poor Man's Rhubarb. The first edition of Hooper's Medical Dictionary states (carried through the others) that the root of Thalictrum flavum is said to be "aperient and stomachic, and to come very near, in its virtues, to rhubarb, but is seldom used in this country (England)." Withering writes that a poultice of the leaves has been known to give ease in the sciatica; Hill, that the roots and young leaves are boiled in ale, and taken as a soup; Griffith (Medical Botany, 1847, p. 96) states that the root of Thalictrum flavum is used in Russia in treatment of hydrophobia, and that Thalictrum siense is demulcent and laxative, and is used in China in pectoral complaints. The species of Thalictrum which we have named as being used in England, viz.: Thalictrum flavum and Thalictrum majus, are known under the common names, Poor Man's Rhubarb, English Rhubarb, Spanish Meadow Rue, and Meadow Rue.

Taken together, the testimony is to the effect that some species of Thalictrum possess medicinal properties, and might be used in cases of necessity, but that other remedies are more certain and efficacious in the treatment of diseases to which they have been applied.

MEDICAL REFERENCES TO THALICTRUM.

1830.—Rafinesque's Medical Botany, p. 267.

1847.—Griffith's Medical Botany, p. 94.

THALICTRUM ANEMONOIDES.

RUE ANEMONE.

PARTS USED.—The tuberous roots and flowering herb of Thalictrum anemonoides *Michx.*

Natural Order Ranunculaceæ, Tribe Anemoneæ.

BOTANICAL ANALYSIS.—Roots consisting of a cluster of oblong tubers. Leaves radical, petiolate, tri-ternate; leaflets petiolulate, round, smooth, triple-veined, three to five obtusely lobed, cordate at the base. Stems erect, two or three from the same root-cluster; naked below, bearing a whorl of three to six floral leaves and a terminal cluster of flowers at the base. Floral leaves similar in shape and size to the leaflets of the radical leaves. Flowers perfect, peduncled. Sepals, five to twelve, generally about seven, white, petaloid, spreading, about a half an inch long. Petals, none. Stamens numerous, with slender filaments. Pistils, several in a head. Fruit, a head of sessile, round, acute, smooth, ribbed achenes.

COMMON NAMES.—The name, Rue Anemone, was given to this plant to indicate the relationship which it bears to both the Anemone family and the Meadow Rue. To conform to its now accepted botanical position, it should properly be called Anemone Rue.

Botanical Description.—This is a little herb from four to six inches high, very common in most sections of our country. The stem bears a cluster of fleshy, tuberous roots, and at its summit a whorl of floral leaves and an umbellate cluster of from three to six flowers, the central and first expanding one larger than the others. The flowers are white or pinkish, and appear in the first warm days of early spring. The leaves are all radical. The fruit is a head of a few dry achenes, which mature in a few weeks after flowering. The plant then dies to the roots, and in summer no trace of it can be seen.



Fig. 4.

Tuberous roots of Thalictrum anemonoides.



Fig. 5.

Fruit-head of Thalictrum anemonoides.

Botanical History.—This plant is a connecting link between the genera Anemone and Thalictrum, and has been ascribed to each by various botanists.

With the habit, involucre, and the flowers of an Anemone, it has the fruit and leaflets of a Thalictrum.

It was carried to England early in the last century, and grown in several botanic gardens, and was figured in the Botanical Magazine in 1805.

Linnæus (1753) named it Anemone thalictroides, which name was followed by the earlier botanists. Michaux (1803) transferred it to the genus Thalictrum, calling it Thalictrum anemonoides; and the name was adopted by De Candolle and most subsequent botanists. In 1832, Hoffmansegg proposed to establish a new genus to include this plant and the Thalictrum tuberosum *Linn.*, of Europe, calling it Syndesmon, and naming our species Syndesmon thalictroides. This change was also advocated by Spach (1839), who called it, however, Anemonella thalictroides; but neither name was ever adopted by other botanists.

Medical History and Properties.—Thalictrum anemonoides has never been recognized by any pharmacopœia. There is no record of its having been used by the aborigines. The standard early authorities do not mention it. It is omitted from Clapp's Catalogue of the Medicinal Plants of the United States, Porcher's Catalogue of the Medicinal Plants of South Carolina, Griffith's Medical Botany, Stearns' Catalogue of the Medicinal Plants of Michigan, etc. Dunglison mentions it in his Medical Dictionary, without, however, ascribing to it any medicinal properties. It was not recognized by any dispensatory, until the Supplement to the American Dispensatory appeared. In this work, Prof. John King writes: "Dr. S. E. Barber, of Consville, Mo., informs us that he has found it a valuable remedy in external and internal hemorrhoides, not accompanied with hemorrhage. The method of using it, is to simply eat three or four of the small root tubers three times a day. We have used some of

PLATE III.



THALICTRUM ANEMONOIDES.

(NATURAL SIZE.)

the tubers which he sent to us, in two cases of blind piles, and with apparent success."

PHARMACEUTICAL PREPARATIONS.—A tincture of recent tubers may be made, according to our process, for making tincture of Clematis.

MEDICAL REFERENCES.

1814.—Green's Catalogue of New York Plants, p. 97–132.
1852.—Dunglison's Med. Dict. (and other editions), p. 851.
1880.—Supplement to American Dispensatory, p. 149.

REFERENCES TO ILLUSTRATIONS OF THALICTRUM ANEMONOIDES.

Gray's Genera, Plants of the United States, Vol. I., plate 6 (good).
Botanical Magazine, Vol. XXII., plate 866 (good, colored).
Meehan's Wayside Flora, Vol. II., plate 30.
Barton's Flora of North America, Vol. II., plate 44 (good, colored).
Sweet British Flower Garden (second series), Vol. II., plate 150 (good, colored).
Lemaire, L'illustration Horticole (Ghent), **Vol. VI.**, plate 211.
Willdenow's Enumeratio Plantarum Horti Beroliensis, plate 44 (colored rather stiff).
Jussieu Annales du Musée, Vol. III., plate 21.
Loddiges' Botanical Cabinet, Vol. VIII., No. 770 (flowers double); also Vol. X., plate 964.
Hill's Vegetable System, Vol. XXV., plate 46, **Fig. 5.**
Plukenet's Almagestum Botanicum, plate 106, **Fig. 4.**

ACKNOWLEDGMENT OF PLATES AND CUTS.

Plate III.—Barton's Flora of North America, (corrected).
Fig. 4.—Gray's Genera, Plants of the United States.
Fig. 5.—Gray's Genera, Plants of the United States.

ANEMONE NEMOROSA.

WIND FLOWER.

PART USED.—The plant Anemone nemorosa *Linn.*

Natural Order Ranunculaceæ, Tribe Anemoneæ.

DESCRIPTION.—This is a graceful little plant, about four inches high, which blossoms in early spring, and is found in open woods. The root is a slender, horizontal root-stalk. The stem, which is produced from the extremity of the root-stalk, is simple, slender, erect, and leafless, except at the top, where it bears a whorl of three petiolate, three-parted floral leaves, and a solitary, small, peduncled, white or purplish flower. This little plant is of wide distribution in this country, and also in Europe. It is known as Wind Flower, Wood Anemone, and Wind Crowfoot.



FIG. 7. Fruit-head of Anemone virginiana.

ALLIED SPECIES.—There are several native species of Anemone having a very similar appearance, and distinguished most readily by the character of the fruit-heads.

Anemone virginiana *Linn.* is a tall herb, from two to three feet high, bearing in summer two to four small, greenish white flowers, on very long and unequal, erect peduncles. The calyx is silky, pubescent outside. The fruit is an oblong head of small densely woolly achenes. This plant, in addition to the names Wood Flower, Wind Flower, etc., applied to other species of Anemone, is also called in some works Thimble Weed (presumably from the shape of the fruit-heads), Huidweed, and Phenion. Anemone cylindrica *Gray,*



FIG. 8.
Fruit - head of Anemone dichotoma.

is a similar plant, but with cylindrical fruit-heads.

Anemone dichotoma *Linn.* (Bot. Syn. Anemone pennsylvanica *Linn.*) is a smaller plant, with larger white flowers on short peduncles, and heads of few, nearly smooth achenes.

CHARACTERISTICS.—Anemone nemorosa abounds in an acrid juice, which is particularly intense in the root. These properties disappear when the plant is dried, and hence only the recent plant, or preparations of the recent plant, are of value in medicine. In consequence of this fact, the dried plant is not a commercial drug, and doubtless, like others of this family, the uncertain nature of the plant when dry, has prevented it from becoming a recognized remedy.

CONSTITUENTS.—In common with several others of the natural order Ranunculaceæ, this plant contains anemonin. Its acrid nature depends upon this substance, which will be considered by us hereafter.

PREPARATIONS.—The tincture of the fresh root is the only reliable representation. Prepare it in accordance with our process for making tincture of Clematis virginiana.



FIG. 6.
Anemone nemorosa.

MEDICAL HISTORY.—Under the name Wind Flower, several species of Anemone have been used in domestic medicine, and they have occasionally been recognized by physicians. Culpepper (1720) states that the Wind Flower is a valuable remedy.*

Motherby (1775), speaking of the English species, remarks: "They are much admired in gardens, but rarely used in medicine." Meyrick (1799), in his Family Herbal, devotes nearly as much space to Anemone nemorosa as he does to aloes. This plant was introduced into the appendix of the Edinburgh Dispensatory (1804) as one of the "List of substances contained in some of the latest and most esteemed foreign Pharmacopœias, but not inserted in the materia medica of any of the British colleges." It was officinal in the Pharmacopœia of Russia (1803), of Sweden (1817), and of Turin (1833). Hooper gave it a position in the first edition of his Medical Dictionary (1817), which notice was carried unchanged through subsequent editions. We might cite

* In studying the history of some of our native plants, we must consider certain nearly related species of Europe and other countries. In these instances, however, we shall make only the references necessary to establish the connection between the plants botanically and medically, and refer to a few works that are ordinarily of easy access in our country.

other foreign references, both earlier and later, but enough have been given to affix to this plant a European medical history.

In America, some of the species of Anemone mentioned by us in our Botanical History have been used in domestic medicine, but only to a slight extent by our physicians. Hand (1820), in his House Physician, devotes considerable space to Anemone virginiana; and Rafinesque (1830), in his Medical Botany, recognizes only this species. The first edition of the United States Dispensatory (1833) neglected all of our native species of Anemone, but the second edition (1834) gave a short notice of Anemone nemorosa, and continued it through subsequent editions. Porcher (1849), Medicinal Plants of South Carolina; Clapp (1850), Medicinal Plants of the United States; Dunglison's Medical Dictionary (1852), and King's American Dispensatory (1852), each recognizes Anemone nemorosa as a native medicinal plant, but devotes very little space to its consideration. The plant was officinal (1872) in the "Pharmacopœa Homœopathica Polyglottica," and is now recognized by Hale's New Remedies, but not by Allen's Encyclopedia.

Medical Properties.—Culpepper (1725) considered a decoction of the Wind Flower to be valuable in suppressed menstruation; and he stated that the juice snuffed up the nostrils, or the root chewed, was considered useful in exciting the secretions, and that an ointment was of value in inflammation of the eyes or for malignant ulcers. Motherby (1775) states that the root of the scarlet Anemone is "detersive if bruised while fresh, and applied to ulcers, and on the skin it raises blisters." He states that the herb is used as an errhine, and as a collyrium. Meyrick (1790) writes that "the juice, if snuffed up the nose, or the root held in the mouth, excites a considerable discharge of cold, watery humors;" and he furthermore states that the bruised fresh leaves, applied to indolent ulcers or running sores, act as a stimulant, cleanse them, and induce them to heal. We are also informed by the same authority, that "some authors recommend it in suppression of the menses, but it is too acrid in its nature for internal use, and might be productive of fatal consequences." Hooper (1817) states that the bruised leaves and flowers applied externally, will cure tinea capitis; and he is also authority for the doubtful statement that the inhabitants of Kamschatka use the root of this plant to poison their arrows. Linnæus stated that when cattle feed upon the plant, it produces bloody urine and dysentery. The foregoing is the substance of European literature on the medical properties of this plant: and American writers, we find, have drawn largely from those we have cited. Hand (1820) gives us a more complete record of the diseases in which this plant was formerly applied than we find in any other American work. He adds that the fresh plant may be used for producing blisters; and, comparing it with cantharides, he reports that it is "more speedy, less painful, and equally serviceable." He also reports that the Anemone virginiana has properties similar to those of the Anemone nemorosa, but much more powerful. We quote from his paper on Anemone virginiana, as follows: "It is likewise of use internally in suppression of the monthly evacu-

ation in women, when dependent upon weakness exclusively, in blindness from obscurities of that part of the eye called the cornea, in venereal pains and tumors of the bones, and ulcers from rottenness, in indurated glands, in chronic creeping eruptions, in melancholy and palsies. The distilled water and extract are the only forms in which it is known to have been given. Half an ounce of the former and five or six grains of the latter, two or three times a day, is a customary dose. It generally produces some sickness and vomiting, and some increased pain in the seat of the local complaint for which it is given." It will be observed that Hand did not use the fresh plant internally, and doubtless the larger share of the acrid properties are destroyed in making the solid extract; but even then the remedy produced unpleasant results, and it is probable that he gave it too freely. Kalm states that the hairy seed of Anemone virginiana will relieve toothache, if dipped in alcohol and inserted in the cavity of the tooth. Porcher (1849) informs us that the juice of the plant will remove corns, and is vesicating, but that if properly applied the plant is a good remedy in fevers, gout, and rheumatism. Scudder (Specific Medication) states that "it influences the functions of waste and repair, but works directly upon the nervous system."

DOSE.—We find that, as usual, in early times physicians were accustomed to heavy doses. Hand gave five or six grains of solid extract at a time, and one-half ounce of the distilled water. These doses would scarcely be tolerated at the present time. Prof. Scudder advises the following: Mix ten drops of tincture of fresh Anemone nemorosa with four ounces of water, and administer of this a teaspoonful every two or four hours, gradually increasing the dose, if necessary.

HOMŒOPATHIC USES OF ANEMONE NEMOROSA.—In Prof. E. M. Hale's New Remedies (1875), we find a notice wherein Homœopathic physicians are requested to remember the near relationship which exists between this plant and pulsatilla. In continuation, Prof. Hale has written for our work as follows:

Anemone nemorosa has not been used by Homœopathic physicians. I have heard of several cases of poisoning, and the reported effects were very marked, resembling the toxic effects of pulsatilla, but much more severe. Among these effects were violent vomiting and purging, the discharges from the bowels being almost pure blood.

It is my impression that experiments on healthy individuals, and clinical experience in disease, would prove that Anemone nemorosa occupies a place between aconite and pulsatilla. I would advise that the tincture be made of the whole plant, collected after the flowering period, or when the seeds are ripening, for I believe that the seeds of this genus must possess the qualities of the plant.

(It must be remembered that Anemone nemorosa is of short life, and that it matures its seeds and dies to the ground in a month or so after flowering. Hence, should a demand arise for a preparation of it, collections must be made in early spring.)

SUMMARY.—The foregoing statements show that Anemone nemorosa and allied species have similar and active properties, and that from time to time these plants have been brought before the medical profession. They have not reached a prominent position however, not perhaps, in consequence of their worthlessness, but because they have not been investigated by the proper authorities. Their active natures indicate that they possess properties which may render them valuable in some skin diseases, and that perhaps they may otherwise enrich our materia medica. If prominent therapeutists will devote a series of investigations to these plants, using reliable preparations, the results may be fruitful. At this time, except with the Homœopathic profession, there is nothing written to indicate that our leading writers have any personal experience with them.

REFERENCES FOR ANEMONE NEMOROSA.

1725.—Culpepper's English Physician, p. 16.
1775.—Motherby's Dictionary (and other editions).
1783.—Cutler's Indigenous Vegetables.
1790.—Culpepper's English Physician, p. 62.
1802.—Quincy's Medical Dictionary, p. 43 (and other editions).
1804.—Edinburgh Dispensatory, p. 361 (and other editions).
1817.—Hooper's Medical Dictionary, p. 49, 679 (and other editions).
1820.—Hand's House Surgeon and Physician, p. 186, 187.
1830.—Rafinesque's Medical Botany, p. 192.
1834.—United States Dispensatory, second edition, p. 1070 (and subsequent editions).
1840.—Pharmacopée Universelle, p. 247.
1848.—Lee's Medicinal Plants of New York, p. 3.
1849.—Porcher's Medicinal Plants of South Carolina.
1850.—Clapp's Medicinal Plants of the United States (Am. Med. Assoc. Rep.), p. 717.
1852.—Dunglison's Medical Dictionary, p. 72 (and other editions).
1852.—King's American Dispensatory, p. 65 (and other editions).
1858.—Stearns' Medicinal Plants of Michigan (Am. Phar. Assoc. Proc.), p. 243.
1871.—Tilden's Journal of Materia Medica, p. 143.
1872.—Pharmacopœa Homœopathœa Polyglottica, p. 138.
1875.—Hale's New Remedies, Vol. II., p. 570.
1881.—Specific Medication, p. 73.

ACKNOWLEDGMENT OF FIGURES

FIG. 6.—Baillon's History of Plants. Vol. I.
FIG. 7.—Baillon's History of Plants. Vol. I.
FIG. 8.—Gray's Genera, Plants of United States.

ANEMONE PATENS.

AMERICAN PULSATILLA.

OFFICINAL PART.—The flowering herb of Anemone patens *Linn.*, var. Nuttalliana *Gray* (U. S. P., 1880).

Natural Order Ranunculaceæ, Tribe Anemone.

BOTANICAL ANALYSIS.—Root perennial; stem simple, upright, naked except the floral leaf, bearing a large terminal flower. Floral leaf cup-shape, surrounding the stem about an inch below the flower, divided into fifteen to twenty linear spreading divisions. Calyx of six petaloid thin sepals, purplish or white, covered externally with silky hairs. Petals represented by a few gland-like bodies, resembling stamens, but smaller. Stamens numerous. Pistils numerous, in a head. Fruit, consisting of many achenes, borne on an elongated stalk. Achenes bearing slender silky tails, about two inches long.

COMMON NAMES.—In botanical works the plant is called Pasque-flower, derived from the European species, which flowers at Easter.

If it comes into general use as a medicine, the name American Pulsatilla will most probably be that under which it will be known commercially.

BOTANICAL DESCRIPTION.—Anemone patens is a very conspicuous flower in early spring, found in prairie regions of Illinois, thence west to the Rocky Mountains, and northwest. The stem rises about four inches out of the ground, and is terminated by a large, erect, solitary, light bluish purple flower. Below the flower, encircling the stem, is a many-parted floral leaf, covered with silky hairs, as are all parts of the plant. The true leaves are not expanded at flowering time, but are afterwards developed from the root of the plant, and are palmately divided into many linear lobes.



FIG. 9.
An achene of Anemone patens var. Nuttalliana.

The fruit is a head of achenes, with long silky tails. It is borne on a stalk which is greatly elongated after the plant has flowered.

BOTANICAL HISTORY AND SYNONYMS.—The plant was first described as Clematis hirsutissima, by Pursh (1814), from a specimen collected by Lewis and Clark while on their Western expedition. Nuttall, in 1818, transferred it to the genus Anemone, where it properly belongs, and named it Anemone Ludoviciana, which name was changed by De Candolle, shortly afterwards, to Anemone Nuttalliana. The plant belongs to the section Pulsatilla of the genus Anemone, distinguished by having the achenes prolonged into hairy tails; and by many botanists this is considered a distinct genus. Sprengel adopted this view of the subject, and called the plant Pulsatilla Nuttalliana (1825).

Anemone patens (the typical species) is found in Siberia, and was discovered in British America by Hooker, and included in his Flora Boreali-Americana For some years the variety (Nuttalliana) was not distinguished from the plant collected by Hooker, and was accordingly called Anemone patens in Torrey and Gray's Flora, and Pulsatilla patens in Gray's Genera. It is only in late years that the plant has been recognized as a distinct variety, and it was named Anemone patens var. Nuttalliana, by Gray, in his Manual, fifth edition (1867).

ALLIED SPECIES.—Anemone alpina *Linn.* is the only other native species of the section Pulsatilla. It can be readily distinguished by the involucre consisting of three distinct, petioled leaves, in consequence of which it was considered a distinct section (Preonanthus) of the genus, by De Candolle.

It is found in the Rocky Mountains, extending north into British America, and is also found in many different varieties in the mountains of Europe.

CHARACTERISTICS.—All parts of fresh Anemone patens are acrid and very irritating. Dr. W. H. Miller informs us that his hands have been badly blistered, in consequence of the juice having spattered over them while pressing the plant. The vapors evolved from the fresh juice are of such an acrid nature as to have inflamed the eyes, and have closed them temporarily. For this

PLATE IV.



ANEMONE PATENS VAR. NUTTALLIANA.

(NATURAL SIZE, IN FRUIT AND FLOWER.)

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reason, persons refuse to work with the fresh herb, and botanists have been known to severely irritate their hands simply from contact with the recent plant.

COMMERCIAL HISTORY.—To Dr. W. H. Miller, of St. Paul, Minn., and his sons, is due the credit of having introduced American pulsatilla. The only demand for the plant, at present, is from Homœopathic physicians; and hence we find that pharmacists generally have no acquaintance with such a drug or its preparations. The wholesale druggists of St. Paul, Minn., and of Fon du Lac, Wis., inform us that they have have no demand for it. Since the Northwestern prairies must supply the plant, it is reasonable to suppose that the prominent houses of the cities we have named would receive orders for American pulsatilla, if it were in any way a commercial drug.

A prominent Homœopathic firm of New York write us that, in consequence of the readiness with which it decomposes, they have the plant carefully tinctured in their branch house of the Northwest. In Chicago, it can easily be obtained fresh from the adjacent prairies. The indications are that before long our American pulsatilla will be in demand, and doubtless replace the imported.

CONSTITUENTS.—All portions of fresh Anemone patens are very acrid, but the dried plant is scarely more than astringent, imparting, after being preserved a year, simply a tingling sensation, when chewed. Mr. A. W. Miller analyzed it (1862), and found that a hot infusion of the fresh plant gave off highly irritating vapors, thus supporting the theory of a volatile acrid principle. The aqueous distillate reacted upon blue litmus paper, showing the presence of some volatile acid principle. Upon agitating the aqueous distillate with chloroform, separating the chloroform and evaporating it spontaneously, a white substance remained. This possessed the acrid nature of the fresh plant, and was supposed to be anemonin, both in consequence of its characteristics, and from the close relationship of Anemone patens to other plants yielding anemonin. The amount obtained, however, was so small that it could not be positively identified. In 1873, Mr. F. B. Miller, brother of A. W. Miller, reëxamined Anemone patens, working with a mixture of five pounds each of the fresh and the dried plant. This mixture was placed in a still, covered with water, and one quart of distillate obtained. The distillate was agitated with chloroform, and the chloroformic solution evaporated, whereby a mass of feathery white crystals was obtained. These crystals were neutral at first, but assumed an acid reaction after a few days, and became colored. Some of the expressed juice of the plant, to which an amount of alcohol sufficient to preserve it had been added, was also distilled, and the distillate extracted in like manner with chloroform. The result was a colorless liquid, which became dark red as the chloroform evaporated, a mass of brown crystals, of an acid nature, remaining. Eight pounds of dried Anemone patens were then submitted to the foregoing manipulation, but none of the acrid substance was obtained, thus supporting the conclusion that the anemonin was destroyed by drying the plant.

In addition to anemonin, the Messrs. Miller found only the ordinary con-

stituents of plants, identifying glucose, a tannin, two resins, pectin, calcium compounds, magnesium compounds, and sulphates. Albumen was not found by either experimenter.

RESUME.—Our native species of Pulsatilla posseses the characteristics of the foreign Pulsatillas. Anemonin is the active principle, and it disappears when the plant is dried. Only preparations made without heat, and of the fresh plant, should be used in medicine. The United States Pharmacopœia states that the plant should not be kept longer than one year; but all of the testimony at our command, and our experience, is to the extent that even drying the plant renders it unreliable, and that preparations of the dried plant are almost, if not entirely, inert.

MEDICAL HISTORY.—Anemone patens was the chief medicinal plant of the Minnesota tribes of Indians. They considered it a "cure-all," and valued it highly, and it was by their recommendation that the plant was brought to the notice of Dr. W. H. Miller.

The first recorded recognition that we can find of American pulsatilla, is a note in Griffith's Medical Botany (1847), which was followed by a recommendation from Dr. Clapp, in his account of the medical plants of the United States (1850), and by Dr. John King, in his Dispensatory of 1852. These seem to have been only suppositions, drawn both from the relationships which exist between this plant and the European Pulsatillas, and their similar acrid properties. At any rate, these authors bring no evidence to indicate a personal experience with the plant, and produce no reference to show that others had employed it.

About the year 1854, Dr. W. H. Miller, of St. Paul, Minn., was induced to experiment with the plant by an Indian who informed Dr. Miller that it was the "great medicine" of the Northwestern tribes of Indians. At that time the plant grew in abundance over where is now the city of St. Paul, and Dr. Miller has used it in his practice from that date. In 1862, Dr. A. W. Miller, the son of Dr. W. H. Miller, presented a thesis to the Philadelphia College of Pharmacy (see p. 29), which was afterward published in the American Journal of Pharmacy. This paper introduced the plant to the authors of the United States Dispensatory, and in the twelfth edition (1865) it was briefly considered in that work under Nuttall's name, Anemone Ludoviciana, which was the term by which the plant was known to and recognized by the Messrs. Miller. Although Dr. Miller valued the plant highly, and was a member of the Regular school of medicine, we cannot find that others of that section have taken hold of it. However, these statements brought the plant before Prof. E. M. Hale, of Chicago, who experimented with it, and by means of a paper in the Medical Investigator brought it to the attention of Homœopathic physicians. Dr. Burt, of Lincoln, Ill., then "proved" the drug, and published the result of his observations in the United States Medical and Surgical Journal. Hale's New Remedies (1875), and Allen's Encyclopedia of Pure Materia Medica (1878), gave our American pulsatilla extended and favorable notices, thus bringing the plant

creditably before the Homœopathic section of the medical profession. Until 1882, the United States Pharmacopœia neglected all varieties of pulsatilla, but in the last revision introduced them, and recognized our American plant Anemone patens var. Nuttalliana, as one of the officinal species. There is no doubt that while this plant has been used successfully by one member of the Regular school of medicine, and by some Eclectic physicians, its recognition by our Pharmacopœia is due to the Homœopathic branch of the profession.

In reviewing this subject, we must admit that our Anemone patens var. Nuttalliana is so nearly like the foreign allied species that there is no reason that the future supply of "pulsatilla" should not be derived from our native plant. The European species that are collected for medicinal use, differ from each other as widely as from the variety of the species indigenous to America. Experience has shown that a tincture prepared from our fresh herb is perfectly reliable, and we would prefer such a preparation to the tincture of European commerce, made by persons over whom we have no control, and whose reputations are not at stake.

MEDICAL PROPERTIES.—The European pulsatillas have been used in medicine from very early times. Galen, Dioscorides, and others, have written about the different species of Anemone, but it seems to have been reserved for Baron Störck to have revived the application of pulsatilla. It is not our intention to review the entire history of the foreign plant, and we therefore refer the reader, if interested, to works which treat directly of those subjects. Griffith announced (1847) that the properties of our native variety of Anemone patens would prove to be similar to those of Anemone Pulsatilla; and this statement was supported (or accepted) by Clapp (1850). Prof. John King, in his Dispensatory (1852), states that it has been recommended in "amaurosis and other diseases of the eye, secondary syphilis, cutaneous diseases, and whooping cough. When applied to the head, it is said to be a speedy cure for tinea capitis. In the recent state, the leaves bruised and applied to the skin are rubefacient. In large doses, this article produces nausea, vomiting, looseness of the bowels, and bloody urine." Dr. W. H. Miller found it beneficial in certain eye diseases, and in ear-ache; but these names are indefinite expressions, and diseases such as "incipient blindness," may arise from different causes, so that, using the words of a prominent specialist, "to resort to any remedy for the relief of so important a symptom, without thoroughly investigating its cause, appears to me irrational." However, as the testimony is that under certain conditions it is a good remedy, the plant is worthy of a more detailed investigation in this direction. Dr. Miller also considers it a good pile remedy, writing us, "I have cured very bad cases in a comparatively short time;" and in this connection it might be well to note that the only ascribed value of the nearly related Thalictrum anemonoides (see p. 21), is that of a pile remedy. In the Regular section of medicine, however, there have been no investigations other than by Dr. Miller. In the Eclectic branch of the medical profession, Prof. J. M. Scudder has long been an active worker in favor of Pulsatilla. He has

stated, in his work "Specific Medication," the conditions in which he values this drug, and defined them more clearly than we have found elsewhere; and with his consent we reproduce, in part, as follows: "The principal use of pulsatilla is to relieve certain cerebral symptoms with difficulty relieved by other remedies. In some diseases of women, in spermatorrhœa and prostatorrhœa, in heart disease, and some chronic affections, we find certain *head* symptoms playing an important part, and giving a good deal of trouble. The patient is nervous, restless, has an active imagination for disease, a fear of impending danger, etc These symptoms are very unpleasant, and not unfrequently prevent the curative action of remedies. Pulsatilla reaches them, and gives prompt and certain relief."

"I would not treat some cases of spermatorrhœa without I could employ this remedy; for with the unnatural excitement of the mind, no remedy would exert a curative influence. So in some cases of heart disease, the head symptoms are the most prominent and unpleasant features. Relieve the unpleasant mental sensations and dread of danger, and we have removed a permanent cause of excitement."

"Though pulsatilla is the remedy for nervousness, it must not be given with any expectation of benefit where the excitement depends upon irritation and determination of blood. In this case it will either exert no influence, or it will be unfavorable. The pulsatilla exerts a marked influence upon the reproductive organs of both male and female. I regard it as decidedly the best emmenagogue, when the suppression is not the result of, or attended by, irritation and determination of blood; where there is simple suppression from atony or nervous shock, it may be used with confidence. In male or female it lessens sexual excitement. It does not diminish sexual power, but rather strengthens it, by lessening morbid excitement."

HOMŒOPATHIC USES.—(Written for this publication by Prof. E. M. Hale.) The uses of this plant in our school coincide nearly with the uses of the European variety introduced by Hahnemann. My provings and experiments show that the symptoms elicited are very similar. Those who have used it to any extent, declare it to be of great value in nervous erethism, especially when reflex, and due to disordered states of the sexual organs or the digestive tract. It is useful in chlorosis, with great nervousness, in neuralgia, characterized by its wandering, erratic character. We find it specific in catarrhal affections, especially in mucous diarrhœa and leucorrhœa. It causes venous congestion, and is useful in varicosis. It has cured urticaria, and itching papulæ. It is as useful in nervous or gastric sick headache, as is the pulsatilla of Europe. The pain commences in the nape of the neck, ascends to one side of the head and eye, and is attended by chilliness and vomiting. It has proved specific in conjunctivitis catarrhalis, ophthalmia tarsi, hordeolum, opacity of the cornea, pustules and granulations in the eyes. It is useful in otitis and otalgia from catarrh; in catarrhal angina, when the mucous surfaces are of a livid, purple hue, and covered with mucus. This light purple, or dark violet hue, attends all the local disor-

ders indicating pulsatilla. The indications for its use in gastric troubles are the same as for Pulsatilla *nig.* It has great curative power over disorders of menstruation, regulating irregular menses, restoring suppressed menses, and modifying painful or profuse menses. I have used it successfully in gonorrhœa and orchitis; as well as ovaritis due to suppression of the menses. It is well known that when a catarrhal flux from any organ is suddenly checked, a rheumatic affection of some muscle or joint may result. Here both species of pulsatilla act promptly curative, restoring the discharge and arresting the inflammation. I would advise its use for all the symptoms of Pulsatilla *nig.* It has the advantage of being indigenous, and obtainable pure, and in inexhaustible quantities.

PHARMACEUTICAL PREPARATIONS.—The fresh juice is mixed with one-half its bulk of alcohol (Dr Miller). A tincture is made by using one part of fresh crushed pulsatilla and two parts of alcohol, according to our method of making tincture of Clematis virginiana. The German Pharmacopœia recognizes a preparation (solid extract) made by heating the expressed juice of the flowering plant, filtering, evaporating the filtrate to a small bulk, adding alcohol, filtering again, and evaporating to the proper consistence.

DOSE.—King recommended from one to two grains of the fresh plant daily.

Dr. Miller writes us that he administers "ten drops of the juice of the fresh plant once a day, but for extreme cases, such as incipient blindness (see p. 31), or syphilis, I give from ten to twenty drops two or three times per day, until narcotic (*sic*) symptoms come, which consist of headache, watery eyes, and especially a sensation as if the patient was smelling strong mustard. Then I discontinue the medication for a few days, and afterwards resume with the same dose."

Prof. Scudder uses a mixture of from ten to thirty drops of fresh, strong tincture of pulsatilla, to four ounces of water, and administers of this a teaspoonful every four hours.*

MEDICAL AND PHARMACEUTICAL REFERENCES TO ANEMONE PATENS VAR. NUTTALLIANA.

1847.—Griffith's Medical Botany, p. 80.
1850.—Clapp's Synopsis of the Medicinal Plants of the United States (Am. Med. Assoc. Rep., p. 689).
1852.—Clapp's Synopsis of the Medicinal Plants of the United States, p. 33.
1852.—King's Eclectic Dispensatory, p. 65.
1862.—American Journal of Pharmacy, p. 300.
1862.—Proceedings American Pharmaceutical Association, p. 90.
1862.—Eclectic Medical Journal, p. 364.
1865.—United States Dispensatory, p. 1462 (and other editions).
1865.—Medical Investigator, May.
1865.—Medical Investigator, June.
1865.—United States Medical and Surgical Journal, October, p. 65.
1866.—United States Medical and Surgical Journal, January.
1867.—Transactions of American Institute of Homœopathy.
1870.—Tilden's Journal of Materia Medica, p. 367.
1871.—Tilden's Journal of Materia Medica, p. 143.
1873.—American Journal of Pharmacy, p. 298.
1874.—Proceedings of American Pharmaceutical Association, p. 127.
1875.—Hale's New Remedies, Vol. I., p. 539, and Vol. II., p. 566.
1878.—Allen's Encyclopedia of Pure Materia Medica, Vol. VIII., p. 242.
1879.—National Dispensatory, p. 1180.
1882.—Pharmacopœia of the United States, p. 271.
1884.—Companion to United States Pharmacopœia, p. 825.

*Prof. Scudder has used the imported tincture of fresh pulsatilla. We have stated that it is more than likely that there is no difference between the European and our native plant.

Botanical References to Anemone Patens Linn., var. Nuttalliana Gray.

1814.—Clematis hirsutissima—*Pursh.*, Flora Americæ Septentrionalis, Vol. II., p. 385.
1817.—Clematis hirsutissima *Pursh.*—Poiret, Encyclopédie Methodique Botanique, Vol. V., p. 623.
1818.—Anemone ludoviciana—*Nuttall*, Genera of North American Plants, Vol. II., p. 20.
1818.—Clematis hirsutissima *Pursh.*—De Candolle, Systema Naturale Regni Vegetabilis, Vol. I., p. 155.
1818.—Anemone Nuttalliana.—*De Candolle*, Systema Naturale Regni Vegetabilis, Vol. I., p. 155.
1823.—Anemone Nuttalliana *DC.*—Richardson, Botanical Appendix to Captain Franklin's Narrative of a Journey to the Shores of the Polar Sea, p. 12.*
1824.—Anemone Nuttalliana *DC.*—De Candolle, Prodromus Systematis Naturalis, Vol. I., p. 17.
1825.—Pulsatilla Nuttalliana.—*Sprengel*, Systema Vegetabilium, Vol. II., p. 663.
1825.—Anemone Nuttalliana *DC.*—Nuttall, Observations on a Species of Anemone of the Section Pulsatilla, in Journal of Philadelphia Academy of Natural Sciences, Series 1st., Vol. V., p. 158. Illustrated (Plate VIII.) with an engraving of the plant, but much too large and coarse.
1826.—Anemone ludoviciana *Nutt.*—Torrey, Account of Collection of Plants made by Edward P. James, during a journey to and from the Rocky Mountains, in Annals of Lyceum of Natural History of New York, Vol. II., p. 163* (published 1828).
1829.—Anemone ludoviciana *Nutt.*—Eaton, Manual of Botany for Northern and Middle States, 5th edition, p. 108; 6th edition, 1833, p. 21; 7th edition, 1836, p. —.
1831.—Anemone Nuttalliana *DC.*—Don, Dichlamydeous Plants, Vol. I., p. 16.
1834.—Anemone Nuttalliana *DC.*—Nuttall, Catalogue of Collection of Plants made by N. B. Wyeth, in the Valleys of the Rocky Mountains, in Journal of Philadelphia Academy of Natural Sciences, Series I., Vol. VII., p. 7.*
1838.—Anemone patens *Linn.*—Torrey and Gray, Flora of North America, Vol. I., p. 11.
1840.—Anemone patens *Willd.* (should be *Linn.*)—Eaton & Wright, North American Botany, p. 126.
1843.—Anemone patens *Linn.*—Torrey, in Nicollet's Report on the Upper Mississippi Basin, p. 144.
1843.—Anemone Nuttalliana *DC.*—Dietrich Synopsis Plantarum, Vol. III., p. 331.
1847.—Anemone patens *Linn.*—Wood, Class-Book of Botany, 2d edition, p. 140.
1848.—Pulsatilla patens *Mill.*—Gray, Manual of Botany of Northern United States, 1st edition, p. 5.
1848.—Pulsatilla patens *Mill.*—Gray, An account of the collection of plants made by A. Fendlei, in the vicinity of Santa Fé, New Mexico, p. 4.*
1849.—Pulsatilla patens *Mill.*—Gray, Genera of the Plants of the United States, Vol. I., p. 17. Illustrated with a lithograph (plate iii.) of a flowering plant, and dissections of the flower and fruit.
1852.—Pulsatilla patens *Mill.*—Parry, Catalogue of Plants of Wisconsin, Iowa and Minnesota, in Appendix to U. S. Geological Survey of these States under Owen, p. 608.
1856.—Pulsatilla Nuttalliana *Spreng.*—Gray, Manual of Botany of Northern United States, 2d edition, p. 4 (also same in 3d and 4th editions).
1860.—Pulsatilla patens *Mill.*—Gray, Catalogue of plants collected East of the Rocky Mountains, in Pacific Railroad Survey, Vol. XII., Part II., p. 40.*
1862.—Pulsatilla Nuttalliana *Spreng.*—Gray, Enumeration of Plants of Rocky Mountains, in American Journal of Science, Series II., Vol. XXXIII., p. 242* (not 410).
1863.—Pulsatilla Nuttalliana *Spreng.*—Gray, Enumeration of Plants collected by Drs. Parry, Hall and Harbour, in Proceedings of the Academy of Natural Sciences of Philadelphia, p. 55.
1867.—Anemone patens *Linn.* var. Nuttalliana.—*Gray*, Manual of Botany of Northern United States, 5th edition, p. 36.
1869.—Pulsatilla patens *Linn.*—Lawson, Ranunculaceæ of the Dominion of Canada, p. 22.
1870.—Anemone patens *Linn.* var. Nuttalliana *Gray.*—Porter, Catalogue of plants collected in Wyoming and contiguous Territories, on the Geological Survey under F. V. Hayden, p. 472.*
1870.—Anemone patens *Linn.* var. (β) Nuttalliana ——.—Wood, The American Botanist and Florist, p. 17.
1874.—Anemone patens *Linn.* var. Nuttalliana *Gray.*—Porter and Coulter, Synopsis of the Flora of Colorado, p. 2.
1878.—Anemone patens *Linn.* var. Nuttalliana *Gray.*—Rothrock, Report upon the Botanical Collections of the U. S. Geographical Surveys, page 55.*
1878.—Anemone patens *Linn.* var. Nuttalliana *Gray.*—Meehan, The Native Flowers and Ferns of the United States, Series I., Vol. I., p. 49, illustrated with a colored lithograph (plate 13) of the plant, showing a flowering plant with *full-grown leaves*, which is contrary to our knowledge of the plant.
1881.—Anemone patens *Linn.* var. Nuttalliana *Gray.*—Meehan, Wayside Flowers, Vol. I., p. 5. Illustrated with the same plate as The Native Flowers and Ferns of the United States.

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* Name and habitat only.

Note.—The recent valuable work by Prof. Sereno Watson, "The Bibliographical Index to North American Botany," contains such complete references, that little can be done more than to elaborate them. In arranging these references, however, by dates, we give at a glance the life history of the plant; and we have thought it best to give the titles of works in full.

PLATE V.



ANEMONE ACUTILOBA.

(NATURAL SIZE.)

TABLE SHOWING THE POSITION OF ANEMONE PATENS VAR. NUTTALLIANA, AS CLASSIFIED BY THE LEADING SYSTEMATIC BOTANISTS OF THE WORLD.

	SECTION.	GENUS.	TRIBE.	NATURAL ORDER.
Tournefort (1694)	....	Pulsatilla	.....	.....
Linnæus (1753)	Pulsatilla	Anemone	(Polyandria Polygnia)	.....
Adanson (1763)	.....	Pulsatilla	.....	Ranunculi
Jussieu (1789)	Pulsatilla	Anemone	.....	Ranunculaceæ
De Candolle (1824)	Pulsatilla	Anemone	Anemoneæ	Ranunculaceæ
Endlicher (1836)	Pulsatilla	Anemone	Anemoneæ	Ranunculaceæ
Gray (1838)	Pulsatilla	Anemone	Anemoneæ	Ranunculaceæ
Bentham & Hooker (1862)	Pulsatilla	Anemone	Anemoneæ	Ranunculaceæ
Baillon (1866)	Pulsatilla	Anemone	Ranunculeæ	Ranunculaceæ
LeMaout et Decaisne (1868)	Pulsatilla	Anemone	Anemoneæ	Ranunculaceæ

HEPATICA.

LIVER LEAF.

PARTS USED.—The dried plant of Anemone acutiloba *Lawson*, and Anemone Hepatica *Linn.*

Natural Order Ranunculaceæ, Tribe Anemoneæ.

BOTANICAL ANALYSIS.—Stem, none. Leaves radical, on petioles four to six inches long, broadly cordate, regularly three-lobed, coriaceous; margins entire. Flowers solitary, on hairy scapes about the length of the leaf-stalks. Involucre three-leaved, green, close to the flower, and resembling a calyx. Sepals six to nine, spreading, in two or three rows, resembling petals. Stamens numerous. Pistils, ten to twenty, in a head. Fruit, a sessile or short stipitate head of hairy achenes, tipped with persistent styles.

COMMON NAMES.—The plants are known as Liverwort in this country. This term properly belongs to a cryptogamic plant of the genus Marchantia, supposed to be good for diseases of the liver, and in Europe it is applied to the latter plant. We are informed by an importer who ordered "Liverwort" from Europe, that Marchantia was received. The name Liver Leaf, from the three lobes of the leaf resembling the three lobes of the liver, is a more appropriate and preferable name. It is also known as Noble Liverwort, Kidneywort, American Liver Leaf, Hepatica, Round Leaved Hepatica, Kidney Liver Leaf, Liver Weed, Trefoil, Golden Trefoil, Chrystalwort, and Herb Trinity. In some sections of the country the plants are known as May Flower.



FIG. 10.
Flower of Anemone acutiloba.

DESCRIPTION.—Liver leaf is one of the commonest and earliest vernal flowers, especially west of New England. It is a little stemless plant, about six inches high, growing in tufts. The flowers expand in the first warm days of spring, and are found in all shades of color, from dark blue to pure white. The leaves, which are the parts used in medicine, are regularly and equally three-lobed,* which gives them a fanciful resemblance to the shape of the liver; hence the common name. They are thick and coriaceous, smooth, of a mottled green color above, and when old, purplish underneath. They persist during the winter, apparently, however, having lost most of their vitality, and often lie procumbent on the ground; but they wither away in the spring,

* Abnormal specimens with five-lobed leaves are occasionally found.



FIG. 11.

a, Stamen (magnified); *b*, Petal (natural size); *c*, Achene (magnified) of Anemone acutiloba.

after the plant has flowered and the new leaves are partly unfolded. They are well represented in the accompanying plate (Plate No. V.), jagged and torn, as they usually are at flowering time. The leaf-stalks, flower-stalks, involucre and buds are covered with fine, soft hairs.

There are two species* growing in this country—Anemone acutiloba *Lawson*, and Anemone Hepatica *Linn.* They so closely resemble each other in everything except the shape of the leaves, that the foregoing description and botanical analysis are equally applicable to each. Anemone acutiloba has sharp leaf-lobes, and Anemone Hepatica blunt (see illustrations under the head of Commercial History of the Drug). A distinctive character between the two species has been observed by Chas. H. Peck, viz., when Anemone acutiloba is in flower, the young leaves have attained a considerable size, and are quite conspicuous; but when Anemone Hepatica is in flower, the young leaves have scarcely made their appearance, being yet closely packed away at the base of the scapes and old petioles.



FIG. 12.

Fruit of Anemone acutiloba.

That the involucre is not a calyx proper, is evident by its not being contiguous to the petals, as is shown in figure 10; and as this is the only structural character by which the sub-genus can be separated from Anemone, its botanical position, theoretically, is certainly with this genus. Yet there is such a marked difference in the general habits of the two sub-genera, and especially in the

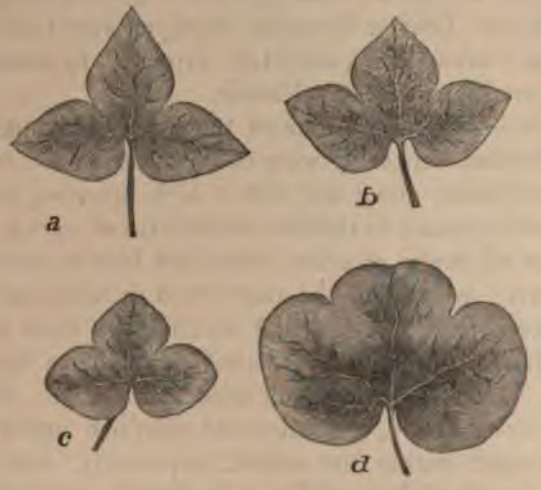


FIG 13.

Extreme forms of leaves. *a*, *b*, Anemone acutiloba; *c*, *d*, Anemone Hepatica.

*It is held by many good botanists that they are both varieties of the same species. Dr. Gattinger, of Nashville, Tenn., informs us that specimens with both forms of leaves from the same roots, are common in his State; and we regret very much that we have not obtained a specimen for the purpose of illustration. Prof. Babcock, in the Lens (Chicago, July, 1872), attempts to show, by a series of illustrations of leaves gathered at Mackinaw, that the two species merge into each other. We reproduce the extreme forms of each species, as shown by him. The original plate shows that the extremes of each species (*a* and *b*, *c* and *d*) are connected by all shades of intermediate forms; but the two leaves (*b* and *c*), which represent respectively the least acute of the acute-lobed species and the least blunt of the obtuse-lobed species, have, in our opinion, no connecting forms (Fig. 13).

medicinal and chemical properties, Hepaticas being mild mucilaginous plants, while Anemones are acrid and irritating, that we think the Hepatica will finally be considered as entitled to a distinct generic rank.*

The name, Hepatica, applied to this genus first by Dillenius (1718), is that by which the plant was known in old medical works. It is derived from the Greek *hepar*, liver, and was first applied to the cryptogamous Marchantia, but was later applied to this plant on account of its liver-shaped leaves, which, from the old doctrine of signatures, were supposed to be a remedy for liver troubles. To distinguish it from the true liverwort (Marchantia), known also as Hepatica, it was called Hepatica Nobilis.

Anemone Hepatica.—When Linnæus published his Species Plantarum (1753), he united this plant with the genus Anemone; and recognizing its old generic and medical name, called it Anemone Hepatica. Chaix† (1776) restored it to its generic rank, naming it Hepatica triloba; and this name was adopted by De Candolle and most other writers, until the appearance of Bentham and Hooker's Genera Plantarum (1862). These authors again placed it with Anemone; and their authority is now followed in the most recent American works. Salisbury (1796) applied the name Anemone præcox to the plant, without, however, any good reasons for the change, and this name is only considered a useless synonym.

The American plant was not considered distinct from the European by Walter or Michaux, who were the first to specifically describe it (1788 and 1803), although it is probable, from Michaux's description and the habitats which they cite, that they were both acquainted with the sharp-lobed form. Pursh (1814) was the first to note that there are two forms of the plant, both of which he considered varieties of the European species, calling the blunt-lobed form Hepatica triloba var. obtusa. His views were adopted by De Candolle, in his Natural System (1818). In the Botanical Register (1819) Ker figures the round-lobed form, and, considering it a distinct species, named it Hepatica americana; and De Candolle followed him in his Prodromus (1824). Although this name was adopted by but one other botanist (Miller), and has never been sanctioned by an American writer, yet it is given as the officinal name for the plant in each of the United States Pharmacopœias, where it has been officinal from 1830 to 1870, inclusive. Most of our botanists have considered the blunt-lobed form identical



FIG. 14. Abnormally developed flowers of Anemone acutiloba.

* The involucral character is clearly shown in an abnormal specimen which we found in the spring of 1884 (Fig. 14). In this specimen an axillary flower was developed from each leaf of the involucre, and the involucre leaves were lobed after the manner of Anemones. A specimen in the Gray Herbarium, Cambridge, has the stem branched above the involucre, and the involucral leaves are lobed.

† The characters of Hepatica triloba are given on page 336, in Vol. I. of the "Histoire des Plantes du Dauphine," of Villars, in a list of plants collected in the province of Dauphiny, by Dominique Chaix, and written by Chaix for that work. The herbarium formed by Chaix was destroyed in a fire which occurred at Toulouse a few years ago, and in it, probably, the type plant of Hepatica triloba perished.

with the European plant,* calling it Hepatica triloba, or very recently (first by Lawson, in his Ranunculaceæ of Canada, 1869) Anemone Hepatica.

Anemone Acutiloba.—The sharp-lobed form was first noted as a distinct form by Pursh (1814) as Hepatica triloba var. acuta, considering it a form of the European species. Bigelow, in the year 1824, called it Anemone Hepatica var. acuta. It is, however, now classed as a distinct species, called, first by De Candolle in Prodromus (1824), and by many subsequent writers, Hepatica acutiloba, which name was changed to Anemone acutiloba by Lawson, to make it accord with late views regarding the genus; and it is so adopted in Watson's Index.

Geographical Distribution.—The two Hepaticas are distributed over about one-half of the United States, extending from Missouri and Iowa east, but absent, as far as we can learn, west of these States.

The blunt-lobed species only is found along the Atlantic plain from Maine to the northern part of Florida, and in the Gulf States. It extends across New York, and is very abundant in the Lake Basin, and is connected by occasional stations along the Mississippi valley with its Gulf habitat. It is the lowland species, and is found in mountainous country only in the Southern States.

The sharp-lobed species is abundant in the mountainous portions of the Eastern States, and through the Allegheny ranges. It is also the exclusive species over most of Ohio, Indiana, Illinois, Iowa, and northern Missouri. In connection with the blunt form, it is common through central and lower New York, the Lake Basin, and the mountains of the Southern States.

DISTRIBUTION BY STATES.

Canada.—Both species abundant; the blunt common in Ontario and rare in western Quebec; absent from east Canada; the sharp common throughout the dominion.

Maine.—The blunt common along the coast plain; sharp, absent; no reports from northern part of State, but only sharp probably found.

New Hampshire.—The blunt extends up the Connecticut river valley in the western part of the State, and all over the southeastern portion, but in the central, the White Mountains, and the northeastern portion, the sharp only is found.

Vermont.—The blunt form is found in the Connecticut valley on the east, and in the immediate neighborhood of Lake Champlain on the west, but in the central and greater portion of the State, the Green Mountains and the hilly elevated country on both sides, it is replaced entirely by the sharp form.

Massachusetts.—The blunt form is common all over the State; the sharp found only in the northwestern part, where the spur of the Green Mountains extends into the State.

Connecticut and Rhode Island.—Blunt only found, but common.

New York.—Both forms are distributed over most of the entire State; the blunt form abundant in the Hudson valley; the sharp form more common in the central, northern and western sections, and the highlands of the eastern, and only absent in the extreme southeastern.

Pennsylvania.—Reports are meager from this State. In the extreme eastern part only the blunt form is found, but throughout the State generally both forms occur.

New Jersey, Delaware, and Eastern Maryland.—Only the blunt form grows. Both are absent from the New Jersey swamp section.

West Virginia, Virginia, and Western Maryland.—Sharp form found over all three. Reports are meager, but blunt grows most common probably in southern and eastern Virginia only.

North Carolina, South Carolina, Georgia, and Alabama.—Blunt in all sections. Sharp form reported very common in the western mountainous part of North Carolina and the northern part of Georgia, and probably found in the extreme western part of South Carolina and northern part of Alabama.

Mississippi.—No reports from this State, but blunt probably found in the eastern part of the State.

Louisiana.—No report, but both probably absent.

Arkansas.—Sharp found in northeastern section; blunt not reported, but probably occurs.

Texas, Indian Territory, Kansas, and Nebraska.—Both forms absent.

Missouri.—Sharp reported from St. Louis, and probably found over most of the State; blunt reported from the Ozark Mountains.

Iowa.—Sharp form common all over the State; blunt only reported from a few localities in the immediate neighborhood of the Mississippi.

*The specimens of Hepatica from Europe, in our herbarium, and the leaves of the commercial imported drug (see Fig. 17), are intermediate in shape between the two forms of the American plant, if anything more closely approaching the sharp than the blunt-lobed form. In our opinion, the blunt-lobed American form is entitled to the rank of a variety of the European species, if indeed it is not a distinct species.



MAP SHOWING THE DISTRIBUTION OF ANEMONE HEPATICA AND ANEMONE ACUTILOBA.

EXPLANATION OF MAP.

Stipple or Dotted Shading—Section of Country over which Anemone Hepatica (blunt-lobed Hepatica) is found.

Line Shading—Section of Country over which Anemone acutiloba (sharp-lobed Hepatica) is found.

Combined Shading—Section over which both grow.

For information to prepare this map, we have addressed botanists in all parts of the country; but in some sections reports were so few and scattered, that we do not claim positive information regarding the exact boundery of the two species. In all cases, however, where information was not furnished, we have taken the climate and character of the sections, and the different habits of the species, into consideration, in drawing our conclusions, and the map is, no doubt, substantially correct. The exact localities from which we have reports are indicated on the map, thus:

● Location where Anemone Hepatica is abundant.

▲ Location where Anemone acutiloba is abundant.

○ Location where Anemone Hepatica is reported, but not abundant.

△ Location where Anemone acutiloba is reported, but not abundant.

Where only one character is given on the map, the other species is not reported, and is presumably absent.

Document Control

Minnesota.—Reports meager. Both probably found over the State.

Wisconsin.—Both forms found in southern and eastern section; no report from northern part of State, but both forms probably found.

Michigan.—Both forms common throughout the State.

Illinois.—Sharp common all over the State; blunt only reported from the Lake basin in the northeast and the Wabash Valley in the southeast, and from an occasional station, but rare along the Mississippi.

Indiana and Ohio.—Sharp form found all over the States; blunt only in the immediate Lake regions.

Kentucky.—Sharp form all over the State; blunt rare on the cliffs of the Kentucky River, and also probably in the southern part of the State.

Tennessee.—Both forms common throughout the State.

DESCRIPTION OF THE DRUG.—Three varieties of liver leaf are found in commerce, corresponding to the three forms of the plant described under our botanical history.

The Sharp-lobed Domestic Drug.—This is derived from the Anemone acutiloba, and forms the great bulk of liver leaf collected in this country. We obtained thirteen specimens from collectors or dealers in widely separated sections of our country, and with but one exception they were of this form. The reason is obvious, for, while the blunt-lobed form is very common in some sections of the country, it is in the extreme South and the cultivated lands of the East, where few herb-collectors reside. The sharp-lobed form grows abundantly in the highlands, and especially in the mountains of the Southern States, which supply most of our native drugs. The shape of the leaves of this drug is accurately represented, natural size, in Fig. 15. The leaves are thinner than in either of the two other forms, and in mass the drug is of a darker green.



FIG. 15.
Sharp-lobed American Hepatica leaf, Anemone acutiloba.

The Blunt-lobed Domestic Drug.—This is derived from the Anemone Hepatica of American growth. It can be at once distinguished from either of the other varieties of the drug by the blunt lobes of the leaves, as shown in Fig. 16. It is very seldom seen in commerce, and we are satisfied does not form one fiftieth of the drug which is collected in this country. The only commercial specimen we could obtain during the past year came from St. Louis, and was collected in the southwestern part of Missouri. The texture of the leaves of this variety of the drug is thicker than in either of the other kinds; and in the specimen we examined the

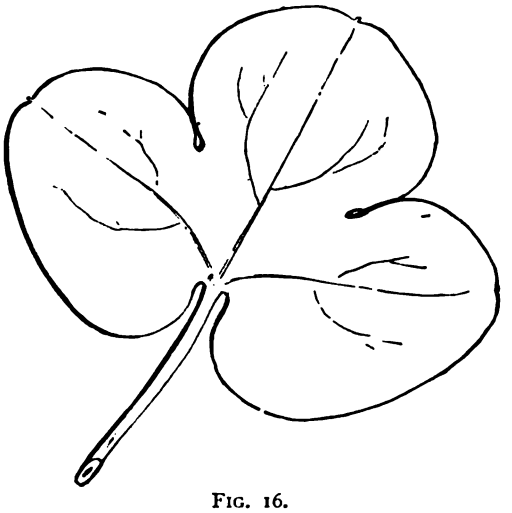


FIG. 16.
Blunt-lobed American Hepatica leaf, Anemone Hepatica.

leaves were of a brownish color, though that was on account of their having been collected late in the season. This variety of the drug is the only one that has ever been officinal, for the name given by the Pharmacopœia to the plant yielding the drug excludes both the sharp-lobed American drug and also the foreign.

The Foreign Drug.—This is derived from the Anemone Hepatica of European (mostly German) growth. In shape the leaf is intermediate between that of the two domestic drugs, but approaches much more closely the sharp-lobed form than the blunt-lobed form, as can be readily seen by the figures. The leaves and drug are of a much lighter green color than either of the domestic drugs. The foreign drug is that which is found now in most of the New York drug houses.

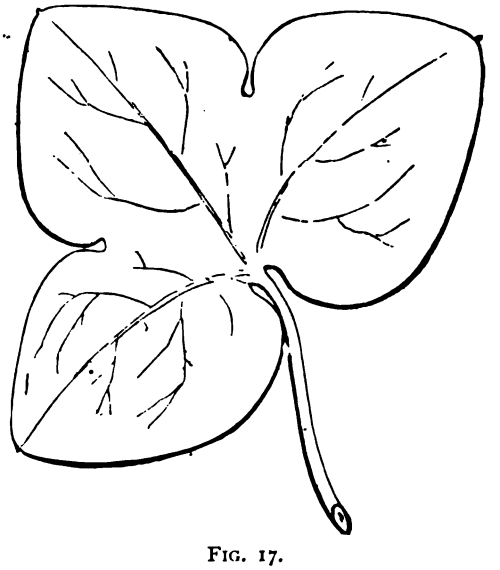


FIG. 17.
Imported Hepatica leaf, Anemone Hepatica.

In commerce, all three varieties of the drug appear in masses or in fragments. Sometimes portions of the roots are attached. Owing to the fact that the plant remains green during the winter, it might be supposed that it would sometimes be gathered in the early spring. If such is the case, we failed to find specimens of it; and examinations made by us of commercial hepatica show that such would be exceptional. The leaves preserve their green color extremely well in drying. When chewed, hepatica imparts a slightly astringent, herb-like taste, but it is devoid of any peculiarities by which its sensible properties can be prominently described.

MICROSCOPICAL STRUCTURE.—(Written for this publication by Louisa Reed Stowell.)

The minute structure of hepatica leaf is exceedingly simple. The cuticle upon the upper surface of the leaf is smooth, uniform, and about 1-6,000 part of an inch in thickness. It is thicker immediately over the midribs or prominent

veins, than over the fleshy part of the leaf. The epidermis on the upper side of the leaf is composed of large, open, round cells, having a uniformly thickened wall around each one. They are of a clear white appearance, containing nothing. The palisade cells found just beneath the epidermis on the upper side of the leaf, only slightly resemble the usual palisade cells of leaves. They are round or nearly square, instead of the usual shape. They have very thin walls, and are sometimes compressed into irregular shapes. In size they closely resemble the cells of the epidermis, being smaller than the cells of the rest of the leaf. Chlorophyll bodies are found in great abundance in these cells.

The loose parenchyma is found just beneath the palisade cells, and includes all the structure of the leaf between the palisade cells and the lower epidermis, excepting the veins. This structure easily divides into four or five layers of large loosely packed cells, having many open spaces between them. In these cells are scattered a few chlorophyll bodies, together with some small dried masses of protoplasm, and occasionally minute oil drops. The lower epidermis is easily separated from the loose parenchyma, and is composed of cells which are smaller, and with thinner walls, than the upper epidermis. The cuticle on the lower surface of the leaf is not so wide, and is more delicate than the cuticle on the upper surface of the leaf.

A few simple, unicellular hairs are found on the upper surface of the leaf. They are sharply pointed at one end, with a smooth wall, and are about 1-20 of an inch in length. On the lower surface of the leaf these hairs are more numerous, and are longer and more delicate. They are simple, unicellular hairs, from about 1-10 to 1-4 of an inch in length. Just at the edge of the leaf the same appearing hairs are more numerous yet, but shorter, and having quite thick walls, especially at their base. The stomates are very similar to the stomates of the average leaf, much more numerous on the lower surface than on the upper surface of the leaf, and average about 23,500 to the square inch on the lower side.

There is no marked microscopical difference between the leaves of the two species. The leaves of both are very liable to be visited by a vegetable parasite which we have observed in all the specimens we have examined.

COMMERCIAL HISTORY.—There was little demand in America for liver leaf preceding the year 1880, unless it were about 1830, during the little excitement regarding the use of this drug as a cough remedy. The records show that for a long period it burdened the pages of our pharmacopœia, an unused member of the materia medica. One of the most extensive collectors of American drugs informs us that just preceding 1880, by an error he sent one hundred and fifty pounds of liver leaf to a dealer who purchases quantities of all the American medicinal plants in use, and it was held as an unsalable overstock.* It is the experience of others, and ourselves, that few of the officinal drugs were in

* In domestic practice it is still somewhat employed as a constituent of cough syrups, but not sufficiently to create a demand. It seems to be an herb that is used in localities where it grows, and by those who can gather it for themselves.

less demand than liver leaf, until about 1880. At this time a demand suddenly sprung up, and the country was afterward scoured by the consumers or their agents. Circulars were scattered over the sections of our country where the plant was collected, urging gatherers of plants to give it special attention. Contracts were made for all that could be obtained from entire sections, or even States; and we have the statistics which show that one State alone supplied, during 1883, more than 30,000 pounds. The supply from America was insufficient, even under these circumstances, and the consumers were forced to turn their attention towards the Old World. Germany naturally was their field, and by means of circulars and agents, they obtained an enormous supply. This fact was soon recognized by Gehe & Co., of Dresden, Germany, for, in their Handelsbericht (September, 1882), attention was called to the fact that the price of hepatica had advanced in consequence of the large demand from America (New Remedies, 1882, p. 337). Persons who are not aware of the extent to which a drug may be consumed when it enters into a few well advertised specialties, must be astonished when the magnitude of the liver leaf trade is laid before them. We have statistics which show that there has been a continuous increase in the consumption since 1880; and collectors inform us that the plant is now becoming scarce over some sections of our country. From the importers of New York and the collectors of America we have statistics to show that in the aggregate 425,282 pounds of liver leaf were collected and imported to supply the demand during the year 1883. It is to be expected that some escaped our notice; and we think it can be safely said that during the year 1883 an aggregate of 450,000 pounds was imported and gathered for our home market. The demand is still on the increase, and probably this year will note a greater consumption.* .

PHARMACOPŒIAL HISTORY.—Hepatica was not recognized in the first edition of the Pharmacopœia of the United States (1820). It was introduced in the Philadelphia edition of the second issue (1830), but was omitted from the New York edition of the same date. It occupied a position in the secondary department of each revision from 1830 to 1880, at which latter date it was discarded. Neither the Pharmacopœia of the Massachusetts Medical Society (1808), nor Bigelow's Sequel to the Pharmacopœia of the United States (1822), gave it a position.

The officinal name has always been "Hepatica," and the plant recognized by De Candolle's name, Hepatica americana. In connection with the Pharmacopœial history of this plant, we note the following inconsistencies:

1st. That the plant should have been recognized by a name that was never adopted by an American botanist, as stated in our Botanical History.

* It will perhaps be questioned by some persons whether it is possible for such enormous amounts of a plant to be consumed, if it is inactive and of no medicinal value. We think that persons who study the history of drugs will scarcely doubt that such may be the case. This liver leaf is consumed in compounds, and even though itself inert, the associated substances may be active remedies; and certainly its presence will not interfere with their actions. If we were to venture an opinion, we would suggest that the real liverwort (Marchantia) was intended to be used, and that by a mistake liver leaf had been supplied. Marchantia has a record as a hepatic remedy, but liver leaf has none (see medical history and medical properties).

2d. That the species which supplies the bulk of the American drug should never have been recognized.

CONSTITUENTS.—Hepatica contains only the ordinary constituents of herbs. The description by Rafinesque, in 1828, is about as good as any that can be given now. He described it as "scentless and nearly insipid, not bitter; but a little astringent and mucilaginous. It contains tannin, mucilage, extractive, etc." We were unable to find the record of an analysis other than the brief statement of Rafinesque,* and therefore Mr. Harter and ourselves submitted the plant to an examination, the result of which was published as a thesis by Mr. Harter, in the Pharmaceutical Record, April 1st, 1884. Nothing of interest was discovered, the summing up being as follows: "It contains none of the classes of active constituents, found in medicinal plants, but consists of the usual constituents of plants, such as a tannin, gum, sugar, chlorophyl, and small amounts of a bland oleoresin." Of the substances named, none were in amount sufficient to render them conspicuous. It may be accepted that hepatica does not contain a single prominently marked constituent, and that few herbs present less decided peculiarities.

PHARMACEUTICAL PREPARATIONS.†—The Pharmacopœia of the United States has never recognized a preparation of hepatica.

The Pharmacopœa Homœopathica Polyglottica prepares an "essence" as follows: "The plant, or part of it, is pounded to a fine pulp, and weighed; then take double its weight of strong alcohol, and, adding first a sixth part of it to the pulp, rub well together; then add the rest of the alcohol, work up the whole well together and put in a well-corked bottle, and leave it standing for eight days in a dark, cool place; then pour off the essence and filter."

The only unofficinal preparation of which we have a record that contains hepatica, is Beache's "Vegetable Syrup," a preparation which is nearly or quite obsolete. Infusions or decoctions of liver leaf may be made by the usual processes. Fluid extract of liver leaf may be prepared by the officinal process for making fluid extract of digitalis, employing liver leaf instead of digitalis.

MEDICAL HISTORY.—The records show that at an early day a lichen of Europe (Marchantia) was used as a remedy in liver disorders, or what were supposed to be liver disorders, and that in consequence it received the vulgar name Liverwort. The shape of the leaf of hepatica somewhat resembled the three lobes of the liver, and hence this plant also was called Liver Leaf, or Liverwort.‡ Thus it came that two entirely distinct plants were known under the same name; and in order to distinguish them, one, a creeping plant, was called Liver-

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* Mr. Charles B. Smith, in a thesis presented to the New York College of Pharmacy, demonstrated the presence of a tannin in hepatica (see Druggists' Circular, 1863, p. 70).

† Cetraria islandica was once known as Iceland Liverwort. The Pharmacopœia of the Royal College of Physicians (London Pharmacopœia), 1809, 1824, and perhaps subsequent editions, recognized decoction of Cetraria islandica as "Decoction of Liverwort."

‡ The meaning of the word liverwort is liver weed.

wort (Marchantia), and the other, an upright plant, Noble Liverwort (hepatica). Some of the early medical works recognized both plants, but others, under the name liverwort only recognized Marchantia. As illustrations, we may refer to the New Dispensatory, 1753 (and other editions), wherein hepatica is named Noble Liverwort, a "gently restringent herb," and Marchantia is called Liverwort, and used in "obstructions of the liver, in jaundice, etc." This view is also taken by Culpepper's English Physician, 1725 (which only considers Marchantia); Lewis' Materia Medica, 1761; The Pharmacopœia Officinalis Extemporanea, or, A Complete English Dispensatory, by John Quincy, 1761; by Motherby's Medical Dictionary, 1775; and other standard European authorities which it is unnecessary to name. However, at even an earlier day some writers had included liver diseases among the many wherein "Noble Liverwort" could be used with benefit; and we may name Tournefort's Materia Medica, which was translated into English in 1708, and Salmon's English Herbal, in 1710, both of which ascribe hepatic properties to the plant. This view of the case seems, however, to have resulted from the theory of "Signatures,"* and few early writers that we have consulted recognized it in this light.

In 1817, Hooper's Medical Dictionary said of Marchantia, "so-called because it was thought to be useful in diseases of the liver," but to liver leaf the same work ascribed no hepatic value. There is no doubt, however, but that at that period both plants were used in domestic practice and with some members of the medical profession as hepatic remedies.

The earliest mention in American history that we can find of hepatica, occurs in Carver's Travels, 1778, but the plant was simply spoken of as Noble Liverwort, and no medicinal value was ascribed to it. David Schoepf, in his Materia Medica Americana, 1787, briefly mentions the plant as "inodorous, insipid." Barton omitted it in his "Collections for a Vegetable Materia Medica," 1798, 1801, and 1804, which is good evidence that at his day the plant was not valued, for Barton's tendency was to recommend all plants that were in the least medicinal, rather than to omit anything. Hand (1820) gave hepatica a passing notice in his "House Surgeon and Physician," but Rafinesque, in the first volume of his Medical Flora of the United States (1828), devoted considerable space to its consideration, and figured the plant.

In 1831, Geo. W. Carpenter, of Philadelphia, issued a work,† "Essays on

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* Formerly a plant was supposed to be of value in the diseases of an organ of the body which it resembled. This may possibly have assisted in introducing Hepatica for liver diseases. In connection with this subject, Dr. Charles Rice contributes as follows: "The Doctrine of Signatures, so broadly developed in later times, had its first beginning in certain philosophical speculations of Aristotle, who already maintained that internal qualities, character, etc., of living beings, could partly be traced or guessed by observing external signs. By a sort of peculiar metaphor, the idea became gradually developed that certain parts of plants or animals having a resemblance, or close relationship, to certain parts of the human body, exercised a peculiar influence over it, either for good or bad, when administered externally or internally. A regular system of treating diseases was gradually based on this doctrine. The chief exponent of it was Johannes Baptista Porta (died 1615), who wrote the well-known work, Phytognomica (often edited; with curious cuts)."

† This work was dedicated to the medical class of the University of Pennsylvania, and it will be observed as a coincidence in our Pharmacopœial history (p. 46), that hepatica was admitted to the Philadelphia edition of the U. S.

Some of the Most Important Articles of the Materia Medica," in which a "compound syrup of Liverwort, or Hepatica," was highly extolled.

The United States Dispensatory, 1833, 1st edition, introduced hepatica in the primary section of that work, owing to its being officinal in the Philadelphia edition of the Pharmacopœia, but the editors spoke lightly of it, saying: "It will probably ere long be forgotten." This paper, excepting the quotation we have made, was carried to the fifteenth edition (1883) of that work, at which time (the plant having been omitted from the U. S. P.) the paper on hepatica was transferred to the appendix.

Dunglison referred briefly to hepatica in the second (1843) edition of his Materia Medica; and in the third edition he added a copy of Rafinesque's figure of the plant, which, with the paper, was carried through the subsequent editions without further change.

Beach's American Practice (1847), Griffith's Medical Botany (1847), and Christison & Griffith's Dispensatory (1848), barely recognized hepatica, but the last named works reproduced Rafinesque's rude figure of the plant. King, in his Dispensatory (1852), gave it a short notice; Bartholow and Scudder ignored it; Stillé and Maisch placed no value on it.

SUMMARY.—In reviewing the medical history of Hepatica, we find that at an early day it reached an acknowledged but unearned position in medicine. It was introduced, through ignorance, for another plant, or in accordance with the illogical doctrine of signatures. Its worthlessness in the cure of diseases where it had stumbled into use, finally became apparent, and in the latter part of the 18th century it fell into disuse. Between the years 1825 and 1830 it was revived, by means of the advertisements of manufacturers of semi-proprietary preparations, and became somewhat prominent in the cure of a class of diseases in which it had scarcely been used previously. Hepatica now became officinal (1830), (see Pharmacopœial History, p. 46) remaining officinal until 1880, when it was discarded from the Pharmacopœia. However, very soon after the year 1830, it was again found to be unworthy, and was relegated into comparative obscurity, remaining in a nearly obsolete condition until about 1880. At this time a demand was created for it by manufacturers of prominent proprietary medicines; others imitated them; the demand increased immediately, and at the present day the consumption of liver leaf in North America is enormous. (See Commercial History, p. 46).

MEDICAL PROPERTIES.—"While the term 'hepatica,' or 'hepaticum,' belonged formerly to two different plants, one a cryptogam and the other a flower-

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P., 1830 (issued 1831), but was not recognized by the New York edition of the same date. The testimony at our command shows that the advertisements of Mr. Carpenter's "Cough Syrup" produced a demand, and that "imitations" of his syrup resulted, as we find him cautioning the "Faculty" against these imitations. Prominent physicians of that city, and throughout Virginia, used and recommended it, but others opposed it. Thus in Dr. Coxe's American Dispensatory (1831), we find that the only recognition of the plant is a sharp criticism, and we reproduce it as follows: "If half of what was said of liverwort be true, it ought never to have left the lists of the materia medica; but if the far greater portion of it be false, or founded in error, it ought never again to have been introduced among the already too crowded lists of remedies." Dr. W. P. C. Barton, in his "Prodome of a Work to Aid in Teaching the Vegetable Materia Medica" (1833), remarks: "Hepatica triloba has reputation, but I think undeservedly, in consumption."

ing herb, and much confusion arose from this afterwards, nevertheless liver leaf was used medicinally for a long time back. No mention appears to be made of it by any classical writers.

J. Bauhin states that it is chiefly used by recent surgeons (viz., living about the middle of the 16th century) for healing wounds, it being used both externally and internally; also, in decoction, as a gargle in inflamed throat; 'refrigerat enim, siccat et roborat.' He adds that the surgeons living at his time use it but rarely, and Parkinson says it has been found inert."—CHARLES RICE.

We find that in early English medicine "Noble Liverwort" was used as a "corroborant and restringent."* Thus, in the "New Dispensatory," 1753, (Quincy), the statement was made that "It is a cooling, gently restringent herb; and hence recommended in a lax state of the fibers as a corroborant." Lewis' Materia Medica (1761), and Motherby's Dictionary (1795), make, in substance, the same statement; and we find that during those times hepatica was scarcely recognized as a hepatic remedy. Meyrick (1790), in his New Family Herbal, stated that Noble Liverwort "is a good medicine in obstructions of the liver and other viscera," and that "if administered early in the disorder, it will frequently cure the jaundice." This was not accepted by others; and such an authority as Quincy, 1817 (Lexicon-Medicum), attributed to hepatica only the properties ascribed by the former works. Passing to 1820, we find in Hand's House Surgeon both views of the subject condensed into one, and the plant is said to be "moderately astringent and strengthening, and to have been supposed to be suited to cases of disordered stomach and liver;" but he added, "This article is, in reality, worth little." In summing up the attributed uses of liver leaf at that time, we can not do better than to quote from the supplement to the London Pharmacopœia (1821), as follows: "Aperitive, vulnery, useful in diabetes and dysentery; detergent in diseases of the skin, or in gargles."

We now come to the third period of unwarranted persecution that this innocent little herb has received at the hands of the medical profession. In our Medical History (p. 48) we stated that between the years 1825 and 1830 it was revived; and we find it then introduced as a remedy in bleeding of the lungs, coughs, and pulmonary affections generally. Rafinesque (1828), in his Medical Flora of the United States, called attention to this phase of the subject; but he added, "It has no effect upon the lungs beyond that of a mild demulcent astringent." Notwithstanding its worthlessness in these affections, advertisements from interested manufacturers of "Compound Liverwort Syrup," etc., which ascribed to it wonderful virtues, were thrust upon the medical profession

*This word seems to have been used by some of the writers upon English medicine of the last century, with a secondary meaning, somewhat as we use the word tonic. Regarding this subject, Dr. Charles Rice makes the following statement: "So far as I can ascertain, the term 'restringent' (which is never used by classic writers) was first employed by Harvey, and afterwards by a small number of English writers. It was not used on the Continent. Astringents (or restringents) were, to my knowledge, always understood to be remedies that 'contracted,' 'puckered' (the mouth, etc.), and the meaning *tonic* is only secondary, since many tonics are actually astringents."

of this country, and it came into a spasmodic demand. Like other substances, however, introduced in this manner, it naturally passed into oblivion as a cough remedy when the artificial support was withdrawn.*

From that time until 1880, hepatica was almost lost as a member of the materia medica, and it is not recognized by the medical profession of the present day. In making this statement, we must admit that authors sometimes briefly refer to hepatica; however, they find little, if anything, to say in its favor.

In connection with the medical history of liver leaf, we find that Homœopathic physicians scarcely use it. Prof. E. M. Hale has written the following for our publication, but he considers the plant unimportant:

HOMŒOPATHIC USES OF HEPATICA.—"This plant has been used by a few of our school in cough with bloody, sweet expectoration. Owing to the fact that we have only a fragmentary proving, we have but little clinical experience. My personal experience leads me to recommend it in catarrhal pharyngitis, laryngitis, or bronchitis, when sub-acute or chronic. It seems to be faintly analagous to Pulsatilla."

DOSE.—There is no dose. Infusions or decoctions may be given freely. If they are administered hot for coughs or colds, some beneficial effect may follow, for hot drinks are sometimes useful. If a compound syrup of liver leaf is employed, the dose will be in accordance with the dose of the associated ingredients.

SUMMARY. — We may compare the medical history of hepatica with the botanical, for in each instance much confusion has prevailed regarding it. We may say, to the credit of physicians, that it has never received the support of prominent men of the profession. The terms used by Quincy, Motherby, Dunglison, Wood, Bache, Stillé, King, Scudder, and others, are sarcastic or slighting. Barton, Pereira and Bartholow neglect to mention it. Every evidence points to the fact that hepatica is as inefficient a plant as we can find, and that the grass of the fields would prove as beneficial in the diseases to which it has been applied.† Distressed by the differences of botanists, who refuse even now to give it a clear title to a botanical home; persecuted by the medical world as it has been for some centuries, let us hope that when the present artificial demand has ceased, it may remain undisturbed our modest and charming early wild flower.

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*It was recommended and used mainly in the form of semi-proprietary syrups, which were accompanied by certificates from "reputable physicians." In a book before us (1830), dedicated to the medical class of the University of Pennsylvania, "Compound Syrup of Liverwort" is brought before the medical profession as a wonderful remedy, and the "*faculty*" are informed that each bottle of the writer's preparation will have his written signature, "without which none will be genuine."

†It may be argued that syrups containing hepatica, or infusions of liver leaf, have given relief in pulmonary affections; and that certain mixtures containing liver leaf have appeared to relieve diseases supposed to arise from disordered conditions of the liver. This we do not dispute, for sugar will often relieve a cough; and we have known simple syrup to prove valuable in colds. Besides, the substances with which the liver leaf is associated may be active remedies; and the maker of the once famous "Compound Syrup of Liverwort" called attention to the fact that where simple syrups of liver leaf failed to relieve, the Compound Syrup afterward effected a speedy cure. He neglected, however, to give the names of the other constituents of his syrup.

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*Should be Chaix.

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TABLE SHOWING THE POSITION OF THE SECTION HEPATICA, AS CLASSIFIED BY THE LEADING SYSTEMATIC BOTANISTS OF THE WORLD.

	SECTION.	GENUS.	TRIBE.	NATURAL ORDER.
Tournefort (1694)	....	Anemone	....	.....
Linnæus (1753)	Hepaticæ	Anemone	(Polyandria Polygnia)	.....
Adanson (1763)	.....	Anemone	.....	Ranunculi
Jussieu (1789)	.....	Anemone	.....	Ranunculaceæ
De Candolle (1824)	.....	Hepatica	Anemoneæ	Ranunculaceæ
Endlicher (1836)	.....	Hepatica	Anemoneæ	Ranunculaceæ
Gray (1838)	.....	Hepatica	Anemoneæ	Ranunculaceæ
Bentham & Hooker (1862)	Hepatica	Anemone	Anemoneæ	Ranunculaceæ
Baillon (1866)	Hepatica	Anemone	Ranunculeæ	Ranunculaceæ
LeMaout et Decaisne (1868)	Hepatica	Anemone	Anemoneæ	Ranunculaceæ

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1814.—Hepatica triloba —— var. (*a*) obtusa.—*Pursh*, Flora Americæ Septentrionalis, Vol. II., p. 391.
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1818.—Hepatica triloba ——.—Nuttall, Genera of North American Plants, Vol. II., p. 23.
1819.—Hepatica americana—*Ker*, Botanical Register, Vol. V., No. 387. Illustrated with a colored plate (No. 387) of a flowering plant (with *mature* leaves having *acute* sinuses).
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1824.—Hepatica americana *Ker.*—De Candolle, Prodromus Systematis Naturalis, Vol. I., p. 22.
1824.—Hepatica triloba ——.—Elliott, Sketch of the Botany of South Carolina and Georgia, Vol. II., p. 55.
1826.—Hepatica triloba *Ell.*†—Darlington, Flora Cestrica, 1st edition, p. 60.
1828.—Hepatica triloba ——.—Rafinesque, Medical Flora of North America, Vol. I., p. 238. Illustrated with a small cut (No. 48) of the plant.
1829.—Hepatica americana *DC.*‡—Eaton, Manual of Botany of Northern and Middle States, 5th edition, p. 241; 6th edition, 1833, Part II., p. 171; 7th edition, 1836, p. —.
1831.—Hepatica americana *Ker.*—Don, Dichlamydeous Plants, Vol. I., p. 22.
1837.—Hepatica triloba *Vill.*† var. obtusa ——.—Darlington, Flora Cestrica, 2d edition, p. —.
1838.—Hepatica triloba *Chaix* var. (a) obtusa *Pursh.*—Torrey and Gray, Flora of North America, Vol. I., p. 15.
1840.—Hepatica triloba —— var. (*a*).—Hooker, Flora Boreali-Americana, Vol. I., p. 9.
1840.—Hepatica americana *DC.*‡—Eaton and Wright, North American Botany, p. 267.
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1847.—Hepatica triloba *Chaix* var. (a) obtusa.—Wood, Class-Book of Botany, 2d edition, p. 141; —— edition, 1861, p. 204.

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* Name and habitat only.
† Should be Chaix.
‡ Should be Ker.

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RANUNCULUS BULBOSUS.

CROWFOOT.

PARTS USED.—The fresh bulbous base and flowering tops of Ranunculus bulbosus *Linn.*

Natural Order Ranunculaceæ, Tribe Ranunculeæ.

BOTANICAL ANALYSIS.—Roots, fleshy, fibrous. Stem erect from the bulbous base, branched, hairy. Leaves mostly radical, few cauline, petiolate, three-divided; divisions, lateral nearly sessile, terminal stalked, all more or less three-parted and incisely toothed and lobed; petioles, sulcate, grooved on the upper side, amplexical, the bases of those of the radical leaves fleshy and united, forming a bulbous base to the plant. Flowers terminal, slender pedunculate. Sepals, five, reflexed, hairy externally. Petals, five, orbicular, veiny, spreading, having a small nectariferous cavity on inner side at the base, covered with a small, wedge-shape, emarginate scale. Stamens numerous. Pistils numerous, in a head. Fruit, a globular head of achenes, tipped with short beaks.

COMMON NAMES.—The proper common name for all species of Ranunculus is Crowfoot,* from the shape of the leaves of some species which resembles that of a crow's foot. Ranunculus bulbosus should be properly designated as Bulbous Crowfoot.

This species, and others that have large yellow flowers, are popularly known as Buttercups† in this country. In England they are called also King-cups, Gold-cups, Gilt-cups, Gold-knobs.

They are occasionally called Yellow Weed and Meadow Bloom, from the yellow flowers; Blister Weed, from their acrid properties; and Burrwort because of the burr-like fruit, which, however, is not enough of a burr to justify the name.

Ranunculus bulbosus is sometimes called, in England, Saint Anthony's Turnip, or Saint Anthony's Rape, from the acrid bulbous base.

SPECIFIC DESCRIPTION.—Ranunculus bulbosus is an erect herbaceous plant, growing about a foot high. It is a native of Europe, but has been naturalized, and is very common in fields and in sandy soil in the Atlantic States, though rare in the interior of the country. In some places in the East it is a great pest to the farmers, and so common that when in bloom the fields present a mass of yellow. The characteristic of the plant is the bulbous base, which is well shown in our engraving (Plate VI.). This differs from the true bulbs of plants; it is really the bases of the leaves and stems, grown together and enlarged by the accumulation of nutritious juices. It is the storehouse of the plant, in

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* In this country the name Crowfoot is misapplied often to Geranium maculatum, which is known to many root diggers and dealers under this name.

† This name is not derived from *butter* and *cup*, but is a corruption of the old English Button-cop, meaning bachelor's buttons, which was given to the double, cultivated variety of the plant.—PRIOR.



RANUNCULUS BULBOSUS.

(NATURAL SIZE.)

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FIG. 18.
Ranunculus bulbosus. *a*, section of leafstalk; *b*, petal.

which is stored each summer the nutriment that the plant uses to grow and produce flowers next spring. The leaves are mostly radical, and are borne on succulent, grooved stalks. The flowers appear in May, and are about an inch in diameter, and of a deep glossy yellow. They terminate the stems and branches.

This species can readily be distinguished from the related species of Ranunculus by its bulbous base, by the stalked terminal division of the leaf (see Fig. 19), and by the early flowers.



FIG. 19.
Leaf of Ranunculus bulbosus.

ALLIED SPECIES.—The genus Ranunculus comprises about 150 species found in all countries, but most abundant in the temperate regions of the Northern Hemisphere. All possess more or less of the acrid properties.

Nearly 75 species and varieties are found in this country. In addition to Ranunculus bulbosus, only the following, however, deserve special mention.

Ranunculus Acris Linn.—Like Ranunculus bulbosus, this is also a foreigner which has established itself much too firmly in the Eastern States. The two species somewhat resemble each other in general appearance. The Ranunculus acris* can be readily distinguished by the following characters: The absence of the bulbous base; it is a taller plant, about two feet high; the flowers are on more slender stalks, and are of a lighter yellow color, and appear two months later, in July and August; the leaves are nearly orbicular, the divisions all sessile.



FIG. 20.
Leaf of Ranunculus acris.

Ranunculus Repens Linn.—This plant is also related to the two species previously described. It is a native of this country, though found in Europe. It grows in woodland pastures and along streams in most sections of the country. The stems are decumbent

*The plant is illustrated in Woodville's Medical Botany, Vol. III., p. 482, Plate 172, and in Stephenson and Churchill's Medical Botany, Vol. II., Plate 82.



FIG. 21.
Leaf of Ranunculus repens.

at the base. The flowers appear in the spring, and are of a glossy yellow color. After flowering, the plant sends out from its base creeping runners, whence the specific name. The leaves are three-parted, and the leaflets all stalked. Ranunculus repens possesses the acrid principle only in a mild degree. It is called Creeping Crowfoot.

Ranunculus sceleratus Linn.—This plant differs much in appearance from those previously described, and belongs to a separate section of the genus. The flowers are small and inconspicuous, and the fruit-heads are cylindrical. The stem is erect, smooth, succulent and hollow. The leaves are all three-parted, or three-lobed, with few-toothed lobes. This plant grows in wet situations, and is found also in Europe. It is probably the most acrid of our native species, and is called Cursed Crowfoot.



FIG. 22.
Flower of Ranunculus sceleratus (enlarged three diameters).

Ranunculus abortivus Linn.—This plant is a common weed in fields and around dwellings in most parts of the country.

It bears inconspicuous yellow flowers in spring, which are followed by small globular fruit-heads, and it withers away and dies in June, shortly after the fruit has ripened. There is a marked contrast in the shape of the leaves: the radical are round-cordate, crenate, and petiolate; the upper are sessile, three-parted, with linear, entire divisions; the intermediate leaves partake more or less of the character of both forms.

As this plant is common in most sections, and possesses in a marked degree the acrid principle* of the family, we introduce a cut by which it can be at once recognized. (See Fig. 23, next page.)

CHARACTERISTICS.—The entire plant of most species of Ranunculus is acrid, the full-grown, green fruit and the root being especially active. To the taste they are peppery and pungent, reminding us of mustard or horse-radish.

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*This is the species from which we derived the acrid principle for our experiments.

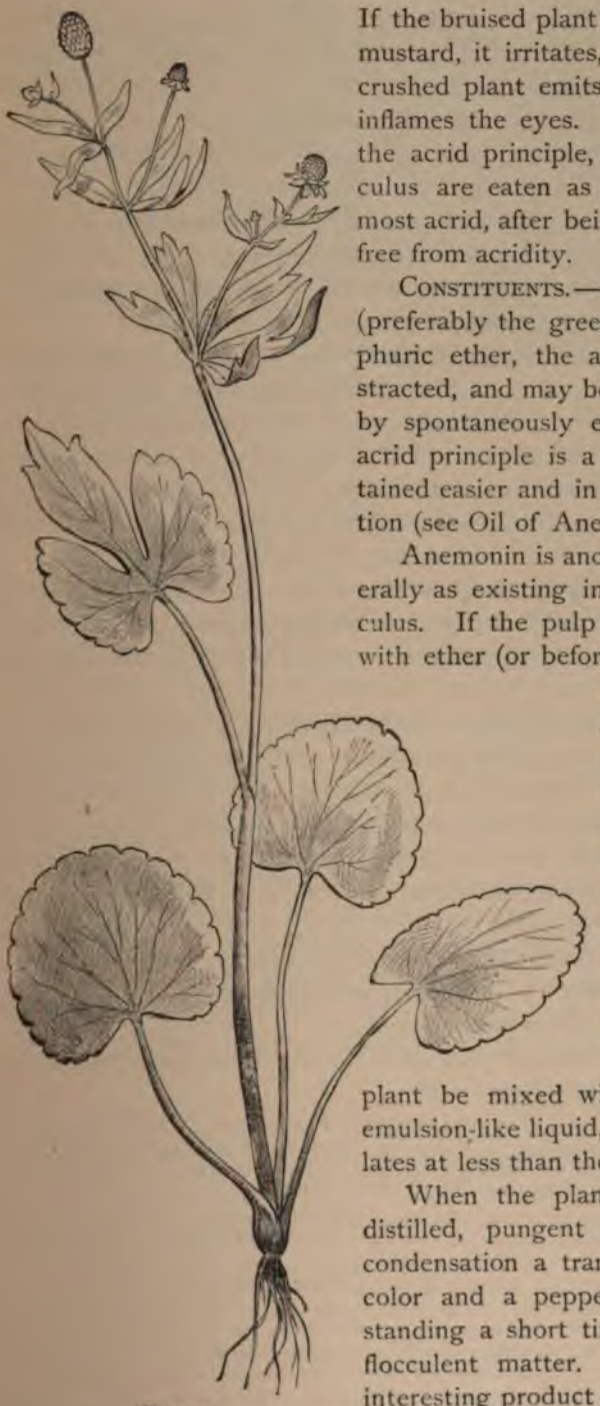


FIG. 23.
Ranunculus abortivus (plant naturai size).

If the bruised plant be bound upon the skin, like mustard, it irritates, inflames and blisters. The crushed plant emits a vapor which irritates and inflames the eyes. Boiling with water dissipates the acrid principle, and some species of Ranunculus are eaten as greens. The pulp of those most acrid, after being boiled by us, proved to be free from acridity.

CONSTITUENTS.—When the plant is bruised (preferably the green fruit), and treated with sulphuric ether, the acrid volatile principle is abstracted, and may be obtained in an impure form by spontaneously evaporating the ether. This acrid principle is a volatile oil, and may be obtained easier and in a purer condition by distillation (see Oil of Anemone).

Anemonin is another substance accepted generally as existing in the acrid species of Ranunculus. If the pulp of the plant, after extraction with ether (or before), be exhausted with chloroform and this chloroformic solution evaporated spontaneously, an oily residue remains, free from crystals of anemonin, and which refuses to react with Fehling's test solution for glucose. This leads us to believe that anemonin is a product of the action of boiling water on the plant rather than an educt.

If the bruised root of the plant be mixed with water, it forms a milky emulsion-like liquid, and, upon heating, it coagulates at less than the boiling point.

When the plant is covered with water and distilled, pungent acrid vapors escape. Upon condensation a transparent liquid of a pungent color and a peppery taste is obtained. After standing a short time, the liquid deposits white flocculent matter. This distilled water is the interesting product of the numerous plants yielding anemonin.*

* The following plants may be named as having been used in making

Examination of the Distillate.—Into a twenty-five gallon copper still,* thirty pounds of Ranunculus abortivus was placed, and covered with water. This was distilled, with the following result:

First gallon, colorless, clear, neutral, nearly tasteless.

Second gallon, colorless, neutral, pungent, acrid, with flocculent concrete substance throughout it.

Third, fourth, fifth and sixth gallon, corresponding to second in properties.

The odor of each fraction was herby as well as pungent. The last portion had a burnt odor. The amount of concrete flocculent matter that formed in the distillate rather increased as the process continued.

Chloroform† was then well shaken with the water, separated, and filtered. The water was now clear, and nearly tasteless. The chloroform was of a light straw color in bulk, transparent in small amounts. Small portions, by evaporation, left an acrid oil mixed with crystals. This chloroformic liquid was then cautiously distilled until it was concentrated to a small bulk. The residue was of a yellow color. The re-condensed chloroform did not contain the acrid volatile oil of anemone.

Upon permitting the chloroformic liquid within the retort to remain excluded from the air,‡ it deposited in twelve hours a flocculent substance of a drab color (impure anemonic acid), the liquid becoming colorless, but retaining its acridity unimpaired.

This liquid, by spontaneous evaporation, deposited a mass of crystals (anemonin), some amorphous material (anemonic acid), an acrid volatile oil which evaporated next after the chloroform, and a peculiar fragrant volatile oil which remained for some time after the acrid oil had vaporized.

If the chloroformic liquid be filtered, in a short time the deposit of anemonic acid again occurs, and will continue until most of the anemonin has perished.

Summary.—All parts of fresh Ranunculus yield, when bruised, a volatile principle that, from its resemblance to volatile oil of horse radish or mustard, may likely be identical with one of those substances.

Ether or chloroform will extract this oil from the fresh fruit, leaving an

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anemonin: Anemone nemorosa, Anemone pratensis, Anemone Pulsatilla, Anemone patens *Linn.* var. **Nuttalliana** *Gray*, Ranunculus bulbosus, Ranunculus Flammula, Ranunculus sceleratus. We have found it in Ranunculus recurvatus, and the plant used in this line of experiments, Ranunculus abortivus. Doubtless all the plants of the Ranunculaceæ containing a volatile acrid substance are of a like nature.

* Experiments on a small scale were unsatisfactory. The volatile oils were obtained in minute proportion, but the anemonin and anemonic acid were scarcely to be found. We made several batches on a large scale, with good results.

† Previous experiments had shown us that chloroform is the solvent for the principles contained in the distilled water. Sulphuric ether has been used by others, but, owing to the fact that water dissolves ether and thus forms a solvent for the volatile oil, those who use ether to separate the oil, labor under a disadvantage. Again, ether is an inferior solvent for anemonin, and hence is a poor agent to obtain that substance. These objections are overcome by chloroform, which extracts all of the volatile oils from the water as well as the anemonin and anemonic acid.

‡ Mr. O. L. Erdmann (see Am. Jour. of Pharm., 1859, p. 441) refers to the formation of this precipitate (anemonic acid), where a solution of anemonin is exposed to the air. He questions as to whether it is a product of oxidation, and will take place only in contact with water or air. Our experiments demonstrate that it is not necessary to admit the atmosphere in order that anemonin should disintegrate.

odorless pulp, which fails to produce the oil again upon moistening and exposure. Chloroform failed in our hands to extract anemonin or anemonic acid from any portion of the fresh plant, thus leading to the inference that these substances do not exist in the plant.*

Water distilled freshly from the plant is acrid, transparent, and free from flocculi. It does not react with Fehling's solution. In a few days it deposits a white substance which chloroform extracts from it. This substance is crystalline. The crystals react with Fehling's solution with an abundant deposit of cuprous oxide. This is anemonin. The indications then, are:

1st. That plants yielding oil of anemone produce it by the decomposition of proximate principles, after the manner of the production of oil of bitter almonds and volatile oil of mustard.†

2d. Anemonin and anemonic acid are products, and not educts.

ANEMONIN (C_{15} H_{12} O_6).—This substance has received attention from Heyer, Vauquelin and Robert, Schwarz, Rabenhorst, Löwig and Weidmann, Fehling, Müller, Erdmann, and perhaps others.

In 1771, Störk distilled a mixture of Anemone Pulsatilla and water. He noticed a flocculent substance in the condensed liquid, and called it Pulsatilla Camphor; and this substance was again noticed (1779) by Heyer. In our opinion, this is the earliest record of anemonin, for, together with the so-called anemonic acid, it partially separates from such a distillate.

Owing to the discordant reports from those who have experimented with anemonin, we must conclude that either different substances, or anemonin in an impure condition, was sometimes employed; and we are inclined to favor the latter opinion. Some persons may argue that, inasmuch as varying forms of crystals have been reported from Anemone nemorosa and Anemone Pulsatilla, it is probable that anemonin is not identical as obtained from different species of plants. This view we do not hold to be necessarily correct, since, according to our experiments, anemonin from Ranunculus abortivus may crystallize either in plates, in delicate acicular needles, or in clumps of grainy masses, varying in appearance and perfection of crystals, in accordance with the solvent and the impurities (see Fig. 24), although perhaps of the same fundamental form.



FIG. 24.
Different forms of Anemonin, as crystallized from chloroformic solutions.‡

* In endeavoring to extract proximate principles from fresh plants by means of chloroform, the operator must bear in mind the fact that chloroform will scarcely come in contact with these principles while the plant is saturated with water. If the substance to be obtained is insoluble in ether, wash the magma first with ether, then use the chloroform.

† It must be stated, however, that after drying the pulp and triturating it with emulsion of sweet almonds, the oil failed to be reproduced. With white mustard seed the experiment seemed to be more satisfactory, but owing to the fact that moistened pulp of white mustard emits a pungent vapor, we could not decide positively. The indications are that the ferment of Ranunculus is not identical with either of those we have named.

‡ These were both made from one solution, the difference resulting from depth of liquid and rapidity of evaporation.

In our paper on American pulsatilla (p. 30), and Anemone nemorosa (p. 22), we referred to anemonin as the important constituent of those plants, promising, however, to consider it later.* We will first give an arrangement of the properties of anemonin, as we find them recorded.†

Erdmann.—Anemonin results when by age the volatile oil of the Anemones decomposes. It is soluble in chloroform.

Vauquelin.—Anemonin volatilizes undecomposed when heated in a glass tube, condensing to an oil which concretes, a small amount of a brown resinous substance remaining. Anemonin is slightly soluble in cold water, more so in boiling water, crystallizing from the hot solution when it cools.

Heyer.—Anemonin yields, when heated, a colorless watery distillate of a peppery taste; a yellow empyreumatic sublimate, soluble in alcohol; and a charcoal residue. Anemonin burns in a flame without residue. It dissolves in hot oil of lavender and hot palm oil.

Heyer and Schwarz.—Anemonin is deposited with anemonic acid from the water which distills from Anemone Pulsatilla (Heyer) and Anemone nemorosa (Schwarz).

Heyer and Robert.—Anemonin is heavier than water, friable, inodorous; has a fatty taste when crystallized, but if melted is biting and burning, benumbing the tongue.

Grailich and Lang.—Colorless, mostly tabular shining prisms belonging to the right prismatic system; short rhombic prisms (Anemone pratensis); long prisms (Anemone nemorosa).

Löwig and Weidmann.—Anemonin dissolves without decomposition in sulphuric acid. Hydrochloric acid converts it into anemoninic acid. It dissolves in aqueous alkalies. Baryta water converts it, two molecules of water being taken up, into anemoninic acid (Fehling contra), which forms brown amorphous salts, of which the lead, mercury and silver salts are insoluble in water.

Fehling.—Anemonin is neutral. Softens at 15° C., giving off water and a pungent vapor, then turns yellow and decomposes above 300° C. Heated with nitric acid, it forms oxalic acid. Heated with dioxide of manganese and sulphuric acid, it forms formic acid. Solutions of the alkalies and baryta water dissolve it with a yellow color, and they are neutralized. Oxides of lead and silver form compounds with anemonin that crystallize on cooling, and which are sparingly soluble in cold alcohol, readily in boiling alcohol, crystallizing from the hot solution upon cooling. Anemonin is insoluble in cold ether and slightly in boiling. Sulphuric acid carbonizes it. If quickly heated in chlorine gas, hydrochloric acid and a volatile oil result. Anemonin is an acrid poison.

In reviewing the foregoing, it will be found that by mutual agreement, anemonin is considered as a crystalline solid obtained by distillation from several species of the Ranunculaceæ. It is also reported that an acrid volatile oil accompanies it; that, upon exposure to the atmosphere, anemonin decomposes, one of the products being a substance to which the name anemonic acid has been given. The only testimony concerning the theory of its production, is that of Erdmann, who states that the volatile oil decomposes by standing into anemonin and anemonic acid. In the main, our experiments agree with those of others; but the relationships of anemonin, anemonic acid and the volatile oil—all of which are obtained by distillation of the plant—have not been recorded as we view the subject. Erdmann approached the matter, but circumstances overlooked by him lead us to believe that anemonin and anemonic acid are not products of the decomposition of the volatile oil under the

*Owing to the early time of year, we could not then obtain the plants to prepare it.

†The experiments that have been made with anemonin were mostly instituted prior to the year 1864. Therefore Gmelin's Chemistry, Vol. XVI., may be consulted with advantage by those who are interested, for since that time there have been few additions.

influence of water or oxygen. Therefore we will bring forward our experiments, and venture to formulate an opinion regarding this problem.

1st. When the distillate is obtained it is transparent, acrid and pungent. In a short time it becomes cloudy, and finally fills with clots of white amorphous matter. Upon agitation with chloroform, this matter dissolves. Upon evaporation of the chloroform, it crystallizes. This is anemonin. However, the production of the anemonin does not seem to decrease the acridity of the liquid. The volatile oil does not disappear if the container be secured. Hence we doubt if anemonin results from decomposition of the oil.*

2d. If crude anemonin be exposed to the atmosphere, it decomposes, a substance remaining, which is insoluble in chloroform or other solvent of anemonin; and during this change there is a constant evolution of a pungent vapor and a volatile oil.

We are of the opinion that anemonin alone will not decompose to form oil by exposure. Our experiments indicate that some substance accompanies it, and induces the change. We have noticed that after prolonged exposure of a chloroformic solution, when nearly all of the odor of oil of anemone had disappeared, a small amount of anemonin remained. This refused to decompose, and we can only explain the fact by supposing that the ferment had been exhausted. Pure anemonin is permanent. It seems difficult to isolate each of these substances, as like solvents act upon them, but if crystals of anemonin be well washed with sulphuric ether, they are obtained pure, and are then permanent in dry air.

3d. If a clear, colorless chloroformic solution of anemonin, as obtained from the aqueous distillate, be permitted to stand a short time, it becomes cloudy, and in a day, or less time, the substance called anemonic acid commences to separate. Filtration of the mixture clarifies the liquid, but decomposition again takes place, and will continue until the anemonin has mostly perished.

If a chloroformic solution of anemonin, as obtained from the distillate of the plant, be exposed in an evaporating dish, the chloroform quickly evaporates; finally only a pungent liquid (oil of anemone) remains, which, however, is interspersed with crystals of anemonin. Gradually the oil evaporates and the anemonin disappears; the mass becomes acid and sour to the taste, assumes a yellowish color, becomes gummy (anemonic acid), and largely insoluble in the solvents for anemonin; and during this period there is a constant evolution of pungent vapors and of oils of anemone.

4th. If a chloroformic solution obtained from the distilled water of a plant which yields anemonin, be evaporated to dryness in a retort, the temperature of which can not rise above 82° C., the result will be as follows: First the chloroform distills; then the pungent substance, oil of anemone, with traces

* In exposing the chloroformic solution, after agitation of chloroform with distilled water of the plant, crystals of anemonin separate as the chloroform and oils evaporate. It would be quite natural to suppose that the oil decomposed to produce it, as Erdmann did.

of chloroform; then these substances, free from chloroform, but after the chloroform has evaporated, if the heat be continued the semi-crystalline mass within the retort decomposes, and finally a white, tough magma remains, which is insoluble in all solvents for anemonin. This is anemonic acid.

Summary.—Anemonin is the product of the action of boiling water on the fresh herb of various species of the Ranunculaceæ. It is associated with the volatile oils of anemone in the aqueous distillate obtained from these plants. It gradually separates from this distilled water in an amorphous condition, and when taken up by appropriate solvents may be crystallized. Anemonin, as associated with the substances accompanying it, is prone to decompose, one of the products being an insoluble amorphous body known as anemonic acid. This decomposition occurs either in contact with air and water, or excluded from it. Pure anemonin is stable.

To Prepare Anemonin.—Take any convenient quantity of the chloroformic liquid obtained (p. 60) by agitating chloroform with the distillate from a plant yielding anemonin. Place it in an evaporating dish, and by spontaneous evaporation, aiding the operation by gently fanning the liquid,* dissipate the chloroform. As soon as the odor of chloroform disappears, and crystals form, wash the crystals repeatedly with sulphuric ether, specific gravity 0.750. Then collect on a filter paper, and dry them by exposure to the atmosphere.

Description of Anemonin.—Anemonin is white, odorless, tasteless. It crystallizes in groups of acicular needles, or in tabular form. The crystals are transparent and shining, but if washed with ether become semi-opaque and white. (See Fig. 24, *a* and *b*, both of which were prepared from the same solution under different conditions.) They do not evaporate upon exposure.

Cold sulphuric acid does not discolor them, but dissolves them slowly, forming a colorless liquid. Heat changes this to yellow, then red, and finally brown, with evolution of pungent fumes. (This agrees with Löwig, Weidmann and Müller, but differs with Fehling, who states that sulphuric acid carbonizes anemonin.)

Hydrochloric acid (cold) does not affect anemonin, but boiling dissolves it. (Löwig and Weidmann state that hot hydrochloric acid forms anemoninic acid with anemonin.)

Nitric acid (cold) neither decomposes nor dissolves anemonin, but hot nitric acid dissolves it with decomposition and evolution of nitrous oxide, forming a colorless or straw-colored liquid. Ammonia changes this to yellow. (Fehling states that oxalic acid results as one of the products of this reaction.)

Ammonia water, cold or hot, refuses to affect it.

Heated in a retort, anemonin fuses with decomposition, turns yellow, then chars, a carbonaceous mass remaining. Pungent, irritating vapors are evolved during the operation, and upon condensation an oily liquid is obtained, which

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* Liquids of this nature should not be breathed upon to evaporate them. The moisture of the breath condenses in them, owing to the low temperature induced by the rapid evaporation. This water produces a milkiness, and after the chloroform, ether, benzol or carbon disulphide evaporates, the water remains, often to spoil a crop of crystals.

possesses the sensible properties of the acrid volatile oil of anemone, irritating the skin in like manner, and presenting the same odor.* It is neutral to litmus. Vauquelin and some others have stated, or accepted, that anemonin volatilizes. This is doubtless incorrect. Fehling states that heat softens and decomposes it, which is supported by our experiments; but we could not distill it. Heyer and Robert agree that if anemonin be fused, it is biting and burning to the taste, leaving a numbness on the tongue. We find that to even fuse anemonin is to partly dissociate it, one of the products being an intensely acrid, volatile, oily substance, which, in our opinion, produces the irritation.

If boiled with water, anemonin decomposes, a peppery, pungent, volatile oil distilling. This distillate is neutral, will not react with Fehling's solution, and is free from anemonin. It is a peppery, acrid liquid, and appears to depend for its properties upon the same volatile, oily substance that results from the dry destructive distillation of anemonin, showing rather positively that the destruction of anemonin under the action of prolonged boiling is similar to its decomposition by means of a quick, dry heat.†

Anemonin dissolves freely in chloroform, sparingly in cold alcohol and benzol, and scarcely at all in carbon disulphide and sulphuric ether. Cold water dissolves only traces; boiling water dissolves it sparingly, the anemonin separating when the solution cools. Anemonin burns like camphor, with a bright flame. If heated, and then inflamed, it flashes. Pure anemonin does not evolve volatile products by age. We have an old specimen in our possession, however, which has assumed a partly insoluble condition (in chloroform), and become opaque.

Crystallized anemonin rapidly reduces Fehling's test solution for glucose. We can find no record of this fact in the authorities at our command, and we do not recall a volatile glucoside. This non-volatile character of the substances that conform to the glucosidal reactions, would also seem to support the inference that anemonin is a product and not an educt. The experiments made by us (as before stated), in an endeavor to obtain anemonin from fresh plants that yield it by distillation, were failures. Suitable solvents of anemonin did not extract from the plant any substance that would react with the glucosidal reagents. In connection with this point, we will say that specimens of pure crystallized anemonin prepared by us were examined by Prof. Virgil Coblentz, who also reports that pure anemonin is permanent; and we quote from his letter as follows:

"Different glucosidal reagents were tried upon this compound, resulting with immediate reduction of Fehling's and Schsse's (Ag (ic) Cl, KI, KOH)

* We state (p. 64) that if a chloroformic solution of the volatile substances obtained from a plant yielding anemonin be distilled to dryness, the anemonin decomposes, crude anemonic acid resulting while oil of anemone distills. If this anemonic acid be heated under a direct flame, further decomposition follows, accompanied with the production of a substance like the afore named oil, which reminds us of acrolein, being not inferior to that substance in pungency and acridity.

† This might support the inference that anemonin exists in the plants, and decomposes to produce the volatile oil. We searched for it, and, as previously stated, failed to find it.

reagents. Böttger's, Schmidt's and Knapp's (Hg CN and Na OH) were only reduced after considerable boiling. Probably the slowness of reduction in these latter reagents was due to the insolubility of anemonin, while the rapidity of Fehling's might be on account of the solubility of the compound in the copper solution, as is the case with some organic compounds."

Dr. Fred. Hoffmann informs us that anemonin is still classed among the camphor-like bodies.* It is certainly a very interesting substance to the theoretical chemist, and a valuable contribution will be the systematic study of the products of the distillation of Ranunculus, and of the results of their subsequent reactions and decompositions. Our study of the literature and the experiments we have made, assure us that these reactions are quite intricate, and that under certain conditions products arise that may be absent under others.† These facts have doubtless led to the differences between some of the statements that have been made by those who certainly were careful investigators.‡

Crystalline Form.—Anemonin crystallizes readily, sometimes in long needles, and again, from the same solution, in short, imperfect prisms. (See Fig. 24, p. 61.) In either case the faces are broken. Upon magnifying the crystals, it is found that few are developed sufficiently to allow of classification. It is now generally accepted that they belong to the right prismatic system.

ANEMONIC ACID.—C_{15} H_{14} O_7 (Fehling). This formula would indicate that anemonin might change to anemonic acid by simply the taking up of a molecule of water, thus: C_{15} H_{12} O_6 + H_2 O=C_{15} H_{14} O_7. That anemonic acid can result from the action of heat on moist crude anemonin is evident (p. 63, 4th), but we doubt if the change is as simple as the above equation would suggest. The formulæ should be verified.

Preparation.—Expose to the atmosphere the chloroformic solution of the substances obtained from the distilled water of the acrid species of Ranunculus, occasionally adding a little water. Decompositions follow, and after some weeks a tough glutinous leathery substance remains. This contains impure anemonic acid, and is to be washed with chloroform (to separate anemonin), and

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*See also Pharmaceutische Rundschau, May, 1884, p. 98. One of, if not the, first names applied to this body (Störk, 1771), was Pulsatilla camphor.

†1st. If a chloroformic solution of the substances obtained from Ranunculus abortivus be exposed to the air, the residue crystallizes, turns slowly yellow, and becomes strongly acid. 2d. If it be securely sealed, an amorphous, pure white magma of anemonic acid is deposited: the solution still (eight weeks contains anemonin and the acrid oil, and is acid to litmus 3d. Upon mixing alcohol with the chloroformic solution, by spontaneous evaporation a tough, leathery, yellow, extremely acid mixture results, destitute of pungency.

‡We wish to call the reader's attention to the fact that our work, as recorded in July, pp. 60 to 64 inclusive, is not altogether supported by continued investigations in this number of the book. We find that a pure chloroformic solution of the principles obtained from the distillate has certainly become *less pungent*, and it is not unreasonable to suppose that greater time will note a complete destruction of this acrid principle. The liquid still contains an abundance of anemonin, a heavy and increasing deposit of white anemonic acid, and, when filtered, is of strong reaction to litmus, showing that the changes are somewhat complex. Time only can enable us to verify the supposition that the acrid principle will entirely disappear, to be replaced by the substances we have named, and thus practically support Erdmann. It will also be necessary to obtain fresh herb (next season), and estimate the proportions of these bodies and their compositions. At this writing we must say that, considering the unstable nature of the products of the distillation of this plant, and the uncertain and variable results of the subsequent changes, it is not to be wondered that investigators have disagreed. In the Addenda to Drugs and Medicines of North America, we shall continue the subject, but another season must pass before material can be obtained. It must not be forgotten that we are working with Ranunculus abortivus, a plant that others have not employed.

then repeatedly boiled with alcohol to separate associated products, one of which is an acid.

2d. Allow a chloroformic solution, as named above, to stand in a sealed vial. Gradually a pure white substance separates, and will continue to deposit for some time.* The chloroform becomes of acid reaction to litmus.†

The white precipitate, if washed with chloroform and then repeatedly treated with boiling alcohol, is the substance named anemonic (not anemoninic) acid.

Properties.—Anemonic acid is white, tasteless (slightly astringent before drying), odorless, of acid reaction to litmus if moist, non-crystalline, and insoluble in all menstruums tested by us excepting those that decompose it. It is insoluble in any of the following, either cold or boiling, viz.: water, anhydrous alcohol, chloroform, carbon disulphide, sulphuric ether, benzol, and spirit of nitrous ether (5 per cent.). When dried and chewed, it is glutinous, reminding of tapioca.

Rabenhorst states that anemonic acid unites with bases to form salts; Heyer, that it dissolves in liquor potassa; Schwarz, that it colors alkaline solutions yellow, a yellow powder remaining. According to our experiments, this substance dissolves but little in alkaline liquids, but changes, in accordance to its purity, to an orange or red color, and swells considerably, becoming transparent and gelatinous. This gelatinous material, if formed of fresh, pure, white anemonic acid, is so nearly transparent that it is sometimes necessary to decant the solution before it can be observed; then it will be found an undissolved jelly, occupying many times the bulk of the anemonic acid employed. If the anemonic acid is old, this jelly forms more slowly, and is not so transparent; if it is fresh, and a very dilute solution of the alkali is used, the result will be a mucilaginous liquid.‡

Rabenhorst states that nitric acid turns anemonic acid yellow, and then quietly dissolves it; and that this solution deposits flocculent matter upon the addition of water. Our experiments agree; and this precipitate we find to dissolve in alcohol or alkaline liquids.

Heyer states that sulphuric acid blackens it; and this is also supported by us, especially if the sulphuric acid is heated.

When heated in a tube, anemonic acid decomposes, a liquid condensing of a peppery taste. Vapor of this liquid is very irritating to the eyes. A carbonaceous mass remains.

Summary.—Anemonic acid is an amorphous body, formed by an unde-

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* Limit of time not yet determined by our experiments; and we have found no record from others.

† This liquid still contains an abundance of anemonin, and after two months' time appears to be less pungent. This would seem to support the theory that the pungent principle, by dissociation or reaction on other bodies, might produce anemonin and anemonic acid (see Wittstein's Organic Constituents of Plants, p. 13).

‡ In connection with this subject, we will say that Prof. Virgil Coblentz, to whom we sent a portion of purified anemonic acid, reports that it combines with alkalies, but that it is a very weak acid. He formed a lead and a soda salt, but the acid was nearly inactive.

termined reaction between certain volatile products of the distillation of fresh Ranunculus or of other plants that yield anemonin. The circumstances which give rise to it are such as yet demand considerable investigation.

It is a substance of feeble acid properties, but if fresh it will neutralize alkalies and form gelatinous substances which, in our experience, do not freely dissolve, but the jelly-like product is so nearly transparent as to often lead to the inference that it has formed a solution.

Anemonic acid is heavier than water. Many writers now seem to question the position of this substance; and Prof. Dragendorff, in his "Plant Analysis" (1884), omits it entirely.

ANEMONINIC ACID.—Löwig and Weidman boiled anemonin with excess of baryta water, and, as a decomposition product, obtained red flakes of a substance containing barium. This they named anemoninate of barium, calling the acid which gave rise to it anemoninic acid. Prof. Fehling afterward investigated this substance, and demonstrated that this precipitate only amounted to 7-10 the anemonin employed; and therefore "the acid can not be formed from anemonin by simply assumption of water."

There is no doubt that one of the substances produced under these conditions is of acid reaction, but chemists must have a clearer insight into the decomposition products of anemonin than at present, before a systematic connection can be formulated between anemonin and this acid. Acid products arise when anemonin decomposes under several conditions, but the explanation of the molecular changes has not yet been demonstrated.

ANEMONOL (Oil of Anemone).—This is familiar as the acrid principle, already often mentioned by us. Some writers have spoken of anemonin as being acrid, and we accepted that view when we employed the term on page 22, but now find that this oil of anemone is the principal acrid substance.

Preparation.—Place the ethereal liquid (obtained in preparing anemonin, p. 64) in a shallow vessel, and evaporate the ether by means of a current of cold air. When the odor of ether is no longer apparent, anemonol remains, but evaporates quickly by exposure.

Properties.—Anemonol is exceedingly pungent and irritating. The vapor will stifle a person who carelessly inhales it, and will inflame the eyes, and even close them, It reminds us of volatile oil of mustard, but, according to Erdmann, is free from sulphur. Those who experiment with oil of anemone in considerable amounts, must exercise care and avoid exposure. Some of the oil was accidentally spilled on the skin of the ball of the writer's thumb. It produced a deep inflammation, and in two days blistered the point of contact as effectually as could have followed the application of a hot iron.

In diluted form, it produced watery blisters when sprinkled over the skin. This is the oil recorded by Heyer, Schwarz, Müller, Erdmann, and noticed by others, and has been obtained by the distillation of Anemone Pulsatilla, Anemone nemorosa, Ranunculus Flammula, Ranunculus bulbosus,

and Ranunculus sceleratus. It is recorded as the substance that decomposes under certain conditions to form anemonin and anemonic acid.

OIL No. 2.—This seems to have escaped the notice of others. It is not as volatile as anemonol. It is obtained in small amount by cautiously evaporating anemonol from crystals of anemonin, as obtained from the crude chloroformic solution. After the anemonol has vaporized, this (No. 2) remains, and will adhere to the crude crystals of anemonin for days, and even weeks.

This second oil has a pleasant odor and a sharp taste. It exists in very small amount, unless it be that the intense pungency of the other oil (anemonol) overcomes it.

The second oil of anemone seems to be a product of chemical action after or during the condensation of the distilled water of the plant. At any rate, we failed to perceive it any part of the plant, or to obtain it direct from the herb.

Summary.—In conclusion, we sum the entire matter up as follows:

The peculiar acrid principle of many plants of the Ranunculaceæ is a volatile oil. This oil preëxists in the plant.

Anemonin is a crystalline product of the distillation of the plants with water. It is not acrid. As associated with the other substances obtained from the distillate, it will decompose upon exposure, especially if moist, several undetermined substances resulting from the reactions. One of these is a fragrant volatile oil; another a soluble acid; a third, the substance recognized as anemonic acid; and the probabilities are that other bodies arise. The connections between these various substances, and the changes which take place in their formation, are still obscure, and we now hesitate to do more than present the results of the work of others as recorded in the preceding pages, and add thereto our own experiences; and in thus temporarily closing the subject, we regret its very incomplete condition.*

PHARMACOPŒIAL HISTORY.—The second edition of the United States Pharmacopœia (1830, Philadelphia edition), recognized Ranunculus bulbosus in its secondary list. This position was retained through four revisions, the plant being discarded in 1880.

The New York edition of the Pharmacopœia (1830) refused Ranunculus a position, and it would have been more creditable had others been as conservative. As it is, we find that for more than half a century this plant has been a member of the Materia Medica, and recognized by the highest authority in American medicine, but has never, during all of this time, received the support of a single eminent practitioner of the medical profession that recog-

* We have arranged with a prominent worker in organic analysis, and by supplying him with materials of undoubted purity, shall enable him to enter systematically into the subject, but must await the coming season to obtain the fresh plant. The results will be announced in the Addenda to Drugs and Medicines of North America. It is certainly due the reader that we should state that, by an explosion and fire in our laboratory, the systematic work on this subject was interrupted, all the materials of this line of investigation being burned. Had we been permitted to follow the series to the end, we feel that more light would have been furnished on several obscure points.

nizes the Pharmacopœia.* There is no record to show that it was used by the regular medical profession at the time it became officinal, and there was no excuse for carrying it sixty years.

Part Used.—U. S. P., 1830 (Philadelphia), "The plant Ranunculus bulbosus."

1840, 1850, 1860, "The cormus and herb of Ranunculus bulbosus."

1870, "The corm and herb of Ranunculus bulbosus."

PREPARATIONS.—There are no preparations of Ranunculus in use excepting those of Homœopathic physicians. We therefore extract from the Pharmacopœa Homœopathica Polyglotta as follows:

Essence of Ranunculus bulbosus.—"The fresh flowering plant is gathered in the month of June, separated from the bulbs, and the juice pressed out. The bulbs are then pounded with some strong alcohol into a jelly, and likewise pressed out. The liquids, thus obtained, are mixed with equal parts by weight of strong alcohol. To the remains of the bulb-jelly add two parts of strong alcohol, macerate for three days, and press as before. The liquor, thus obtained, is mixed with the former liquids, macerated for eight days, and filtered."

MEDICAL HISTORY.—The several acrid species of Ranunculus have been mentioned in European medicine from an early day. They were more conspicuous members of the Materia Medica in times long past than at any recent period. Indeed, this seems natural, for the semi-barbarous treatment of former times induced physicians to eagerly accept a substance that could torture the patient like the acrid Ranunculus can, when heroically applied. Hence we find (1710) that Salmon's English Herbal devotes page after page to the plants of the Crowfoot tribe, enumerating and figuring eight different species. Following this work, we find that other European authors mention it, but with less respect; and at the present day the plant is on record as a vesicant and an acrid poison, unsupported by the friendship of a single prominent practitioner outside of the Homœopathic section, which would not use it in this manner. Prominent medical writers have given it a position, always seemingly under protest; and in this way we find it mentioned by modern authorities.

MEDICAL USES.—In early English medicine the acrid "Crowfoot" was recommended for a multitude of disorders. Salmon (1710) scarcely excepted an ailment to which the flesh is heir; and in reviewing his paper we are puzzled to discover the necessity for any other medicinal agent. Of Crowfoot, he writes:

"*The Liquid Juice.*—It is sharp and biting, good to bathe gently those parts of the skin which are effected with Scurvy, Morphew, Leprosie, Freckles, Spots, Yellowness, Roughness, etc. It is good also to drive away Scabs and Itch."

"*The Essence.*—It is good to waste away and consume Warts, Corns, hard Scabs of the Skin, Ruggedness of the Nails, and other like deformities of

*Our remarks under Medical History and Properties do not refer to the Homœopathic section of the medical profession. Ranunculus is recognized by them, as is shown by Prof. Hale's paper in this work.

the Cutis. The head being washed with it, it kills Worms at the roots of the hair, which eat the same and cause it to fall off. Neither juice nor essence, by reason of their violence, are ever used inwardly."

This strain is continued to ten times the amount of space quoted by us, and, included in the list, we find that crowfoot will cure ague, toothache, tumors, scrofula, itch, bleeding piles; is a diuretic, an emetic; will dissolve stone in the bladder; and finally, that it is a parturient. Meyrick (1790) quotes from Hill, that "all parts of these plants are exceeding acrid, and if bruised, act as a caustic." Cullen's Materia Medica (1802) classes the Ranunculus among the diuretics, stating, however, that "they have, as such, been hardly employed in practice: and that for the same reason I have given with respect to the Arum, that we have not yet learned how they can be introduced in such quantity into the stomach as to become powerful in the kidneys." Hand (1820), in his House Surgeon, states that crowfoot "produces a deep and thorough blister. Good where a lasting blister is wanted."* The Supplement to the Pharmacopœia (London, 1821) ascribes medical properties to the several acrid species of Ranunculus, stating that Ranunculus bulbosus will poison rats. And in 1865, we see it recorded in the Pharmaceutical Journal and Transactions that a child in England perished after eating the blossoms of crowfoot. Chapman's Therapeutics (1824) mentions crowfoot as a vesicant, saying, "and most promptly and powerfully does it operate." Chapman admits, however, that he has only seen it used to blister horses, and cautions his readers against the free use of crowfoot, in the following language: "By many means we raise a blister, and by some in much less time than with cantharides, yet there is none which precisely imitates their mode of action, or will do equal good in the cure of disease. Considering its (Ranunculus) great activity, I am inclined to suspect that we might make some beneficial application of it, though on this account alone it should not supercede the animal vesicatories." In 1858, Prof. Clarus, of Leipsic, instituted a line of physiological experiments with the acrid species of Ranunculus. He decided that anemonin was a narcotic, and the volatile oil an acrid irritant. Krapf, of Vienna, from a series of experiments with the acrid species of Ranunculus, found that no antidote experimented with could reduce the inflammation; and, indeed, that while water gave the best results, vinegar, honey, sugar, spirits, diluted mineral acids and solutions of alkalies increased the acrimony. In our recent experience, both our hands and mouth having been blistered, we exhausted the probable antidotes without relief.

Summary.—In the olden time the different acrid species of Ranunculus were used rather freely in medicine. As the practice of medicine inclined towards a humane system, physicians gradually substituted less virulent remedies; and in modern times we find that few who give large doses care

*"Lasting blister" is a good term. The writer applied the Ranunculus to a portion of his arm. It irritated, and caused watery blisters to form over several times the surface exposed. The blisters lasted for days, the irritation for weeks. The cuticle peeled off, and it was a decided success, if success can be valued in proportion to the "*lasting*" properties.

to use such agents as the Ranunculus plants, even externally. They produce painful, sometimes deep ulcers, and blister some persons very quickly. However, this action is not always certain; and sometimes we find subjects who seem not to blister under their influence, the result being a deep inflammation. The ulcers are slow to heal. In the opinion of the writer, a physician would hardly at this day be excused for resorting to such a barbarous agent, if used in concentrated form.

HOMŒOPATHIC USES OF RANUNCULUS BULBOSUS.—(Written for this publication by Prof. E. M. Hale.)

This species appears, from the experiments and practice of our school, to have a decided irritant action on the brain and spinal cord. It has been successfully used for neuralgia of the head, with vertigo and confusion of mind. A study of its symptomatology shows it to cause conditions which have been termed neuralgic rheumatism. Many of the pains closely resemble those of myalgia, or what has been known as muscular rheumatism. It appears to me to be a close analogue of cimicifuga. The latter, however, seems to affect by preference the large muscles, and particularly the belly of the muscles; but the former seems to attack the small, thin muscles, as those of the head and thorax. Both have an affinity for the sheaths of the nerves, rather than the axis. Pure neuralgia does not affect the sheaths of nerves, but the nerve itself; but rheumatic neuralgia affects the sheaths.

I have used it very successfully in rheumatic headache, aggravated by or brought on by change of weather from warm to cold and damp. These headaches closely resemble neuralgia, but will not be relieved by the purely neuralgic remedies. In rheumatic affections of the eyes it has been curative. It is an important remedy in rheumatic affections of the muscles of the abdomen, thorax and back. Nearly all the pains which indicate Ranunculus are stitching, with soreness, aggravated by motion. In the abdomen these pains are often mistaken for colic. When affecting the thorax, they are often mistaken for pleurisy. It is one of our best remedies in pleurodynia, intercostal rheumatism and myalgia. The thoracic pains extend to the back, and take the form of lumbago. All the muscles of the trunk seem to be affected with soreness, stiffness, stitches, etc., especially when first moving after sitting or lying. These symptoms will be recognized as those which are very common in a class of people exposed to changes of temperature, and who have an acquired or inherited rheumatic tendency.

The experiments with Ranunculus bulbosus have not been thorough enough to warrant us in recommending it for true spinal irritation, but, judging from analogy, we believe it to be capable of acting as an irritant to the spinal meninges. Most cases of so-called spinal irritation are either rheumatic or the result of anemia and debility. In the former Ranunculus will be specific; the latter will be most successfully treated with iron and hydrastis.

Ranunculus sceleratus and acris have an almost identical sphere of action, and are indicated by very similar symptoms.

The action of various species of Ranunculus on the skin is local, and caused by an acrid irritant in the juice of the plants. There is no proof that the internal administration of the drug has caused any eruptions; but the blood seems to be poisoned by the absorption of the secretions. The local affection takes the form of vesicles, blisters, or bullæ, and resembles pemphigus and some varieties of erysipelas.

Mezereum (Daphne Mezereum) has a similar local action, but in addition has actually caused, when taken internally, vesicles and bullæ, attended by violent stitching pains, such as precedes herper zoster. Ranunculus may be capable of similar action. If so, it will prove a remedy for herpes.

The secondary effects of this drug on the skin take the form of boils and obstinate ulcers, and even cutaneous abscesses. We observe the same effects from Rhus Toxicodendron.

In practice Ranunculus bulbosus and sceleratus have been used with good results (internally) for pemphigus, herpes on the hands and fingers.

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CALTHA PALUSTRIS.

MARSH MARIGOLD.

PART USED.—The fresh plant Caltha palustris *Linn.*

Natural Order Ranunculaceæ, Tribe Helleboreæ.

COMMON NAMES.—The proper common name for this plant is Marsh Marigold. In this country it is often called Cowslip (or corrupted into Cow's Lip), but improperly, as the name Cowslip belongs to the genus Primula, of Europe. The name American Cowslip is a decided improvement. The old English names for the plant are Mare-blobs,* or Mare-blebs, Water-blobs, Meadow Bouts,† Water Bouts. These names all refer to the yellow flowers and buds, which resemble buttons or knobs. The names Palsywort and Water Dragon, sometimes applied to this plant, are inappropriate. It is also called by some persons Colt's Foot‡ and Ground Ivy, which are names belonging to other plants.

DESCRIPTION.—Marsh Marigold is a very common plant in swamps, wet meadows and borders of streams in many parts of the United States. It is also found throughout Europe and part of Asia. The root consists of a bundle of fleshy fibrous rootlets. The stem is from six to twelve inches high, much branched, succulent furrowed and hollow. It bears in the spring numerous large, showy yellow flowers, which consist each of about six petaloid sepals, numerous stamens, and from five to ten pistils.



FIG. 25.
Fruit of Caltha palustris

The fruit pods, or follicles, are in a whorl of from five to ten in number, and contain several dark purple seeds.

The leaves are from two to four inches broad, the lower on slender leaf-stalks. They are alternate, crenate or entire, cordate or reniform. They vary much in shape in different sections of the country; hence there have been numerous varieties of the plant named.

An extreme northern form was formerly considered distinct, and called Caltha arctica *R. Brown;* and a simple, one-flowered form, known under a number of names, is now considered by Prof. Watson to be the same as the Caltha palustris var. sibirica *Regel.*

CONSTITUENTS.—Caltha palustris is somewhat acrid, faintly resembling the Ranunculus. It has no marked constituents other than this acrid substance, which exists in small proportion, and doubtless is identical with the acrid oil of ranunculus. We distilled several pounds of the fresh plant with water, but failed to obtain either the oil or anemonin.

PHARMACEUTICAL PREPARATIONS. — The Pharmacopœa Homœopathica

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*This name *mare*, marsh, and *blobs*, bladder, has been in some English localities corrupted into Horse-blobs, which has no meaning.

† *Bouts* means buttons, spelled also incorrectly Bowts.

‡ Since this paper has been written, we have received for identification a specimen of Caltha palustris from a physician, who states that the plant was brought from Canada by his wife, and called Colt's Foot. It is needless to state that it has no resemblance or affinities to the true Colt's Foot, Tussilago Farfara.



FIG. 26.
Caltha palustris, flowering top.

Polyglotta recognizes a tincture of Caltha palustris. This is the only pharmaceutical preparation recorded, and is made as follows:

The fresh plant, in time of flowering, is chopped, and well pounded to a fine pulp, and carefully pressed out in a piece of new linen. The expressed juice is then, by brisk agitation, mingled with an equal part by weight of strong alcohol. This mixture is let stand eight days in a well-stopped bottle in a dark, cool place, and then filtered.

MEDICAL HISTORY AND PROPERTIES.—Caltha palustris has been used in cough syrups (Lee's New York Medicinal Plants), but the remarks we make concerning liver leaf (page 51) will apply here. In times long passed it has been occasionally recommended, but has never received the support of a single reputable authority, to our knowledge. Salmon (1710) remarks: "For any of its medical virtues, nothing has yet been observed by experience;" and if Salmon failed to ascribe a medicinal use for a plant, others need scarcely attempt to honor it. Cattle and sheep refuse to eat the plant; and, according to Rafinesque, it inflames their stomachs if swallowed. Schoepf (1787) states that it is acrid, and that herds will not eat it. Caltha palustris is an excellent pot herb, and as it appears in the early spring time, it is extensively used for greens. The flower buds are sometimes pickled. This plant does not deserve a recognition in medicine.

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HYDRASTIS CANADENSIS.

GOLDEN SEAL.

PARTS USED.—The rhizome and rootlets of Hydrastis canadensis *Linn.*
Natural Order Ranunculaceæ, Tribe Helleboreæ.

BOTANICAL ANALYSIS.—Rhizome knotted, horizontal, with fibrous roots. Stem, from six to twelve inches high when in flower, about a foot high when mature; erect, round, sparingly hairy, with short, somewhat appressed hairs; surrounded at the base with two or three yellowish scales. Leaves, two, alternate, roundish-cordate, five or seven palmately lobed, veiny; margins, doubly serrate: Lower leaf, the larger, on a petiole one to two inches long; upper leaf, sessile. Flower solitary, erect, terminal, on a peduncle from a half to an inch long. Sepals from two to four, generally three, round, concave, greenish white, caducous. Petals none. Stamens numerous, spreading; filaments thickened upward, white; anthers adnate, dehiscing longitudinally. Pistils, ten to twenty, in a head; ovaries one-celled, two-ovuled. Fruit, a head of fleshy carpels, each containing one or two small, black, hard seeds.

COMMON NAMES.—The Pharmacopœia (1880) has adopted, and we think wisely, Golden Seal as the common name for this plant. In commerce the drug is known either as Golden Seal or Yellow Root. The name Golden Seal is very applicable to the plant, and has reference to the seal-like scars on the rhizome, and its golden or yellow color. The term was introduced by the Thompsonians, and is largely used by the drug trade, especially by Eclectic houses. Yellow Root is also applicable, and is also a common name for the plant in commerce. Unfortunately, however, it has been applied to several other plants: One of them, Xanthorrhiza apiifolia, is an article of commerce under the name. On this account it would be better if the name Yellow Root, as applied to Hydrastis, should be discontinued in favor of the Pharmacopœial name. In addition to these two names, a number of local names have been given the plant. In botanical works it is usually called Orange Root or Yellow Puccoon. When in fruit the plant resembles an herbaceous Rubus, and hence is called Ground Raspberry. It was formerly reputed valuable as an eye-wash, and in old works the name Eye-balm and Eye-root are given to it. From the yellow coloring matter, and the fact that it was used as a yellow stain by the Indians, it has received the names Indian Paint, Yellow Paint, Indian Dye, Golden Root, Indian Turmeric, Wild Turmeric, Curcuma, Ohio Curcuma, Wild Curcuma (spelled in old works Kurkuma), Jaundice Root and Yellow Eye.

BOTANICAL DESCRIPTION.—Hydrastis grows in patches in rich, open, hilly woods. The stem is produced from a terminal bud of the perennial rhizome. Its growth is very rapid: a week or ten days' continuance of warm weather in May is sufficient for it to grow six inches high and to expand its flower. At the base the stem is surrounded by a few yellow bud-scales, and the color of the underground portion of the stem, and for about an inch above the ground, is light yellow.

In a patch of Hydrastis will be found, in about an equal number, two kinds of stems, sterile and fertile. The sterile stems bear only a terminal peltate leaf. In reality these sterile stems are radical leaves, with the articulation at the base of the petiole.

PLATE VIII.



HYDRASTIS CANADENSIS.

Document Control

The fertile stem is from six inches to a foot high at flowering time, round, erect, and about an eighth of an inch in diameter. It is naked below, and at the top apparently forks, one branch bearing a leaf, the other a smaller leaf and a flower. In fact, the stem bears two alternate* leaves and a terminal flower, the lower leaf on a stalk about two inches long, and the upper leaf sessile at the base of the flower stem.

The leaves at flowering time are only partly developed: the lower is larger, measuring from two to three inches in diameter; the upper, which is about half as large, encloses the flower in the bud, and is generally but partially unfolded when the flower opens. After the plant has flowered, the leaves grow to be six to eight inches in diameter. In shape they are roundish cordate, and have five to seven palmate lobes. The veins are very prominent on the lower side of the leaf.



FIG. 27. Flower bud of Hydrastis canadensis.

The flowers are small, white, and last but a few days. A patch of Hydrastis will not remain in blossom longer than a week or ten days. The sepals are only seen in the bud, as they are caducous, falling away when the flower expands. The numerous stamens have white filaments, and they are the most conspicuous part of the flower.

The fruit ripens in July, turning from green to bright red. The color is of a very rich shade, and is that which is known to artists as crimson lake. It is borne on an erect stalk, about an inch long. In shape it resembles a large red raspberry, with coarse drupes. Botanically it is an etærio, viz.: a fruit consisting of several drupes aggregated together. Each fruit consists of from eight to twelve drupes. The drupes contain two, or, by abortion, one, round, black, shining seed, imbedded in a white pulp, which has a sweetish taste. Some of the drupes are generally entirely abortive, and some much more developed than others, giving the fruit an irregular appearance that is not sufficiently shown in our cut (Fig. 28), which was drawn from a very perfect fruit.

BOTANICAL HISTORY.—At the time Linnæus published the first edition of his Species Plantarum (1753), he was acquainted only with the leaves of the plant,† and from their resemblance to the leaves of Hydrophyllum, he supposed it to belong to this genus, and called it "Hydrophyllum verum canadense."

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*The alternate arrangement of the leaves is clearly indicated by the articulation. Plants are also occasionally found with three leaves, all alternate. A three-leaved specimen, sent us by R. H. Wildberger, has the two lower leaves of the usual size and position, the third a small, sessile leaf, placed about half way between the flower and middle leaf, and at an angle with both the other leaves.

†These specimens of Hydrastis leaves are still preserved in the Linnæan Herbarium. They were most likely given to Linnæus by Peter Kalm, the Swedish naturalist, who traveled three years (1849-51) in this country. On the sheet containing the specimens, Linnæus has written: "Hydrophyllum verum canadense, cujus flores non videt.—P. Kalm." In this connection it is a little singular that Kalm makes no mention of the plant in his works. He was an excellent observer, and had he known any economic use for the plant, would have no doubt recorded it. At Philadelphia, the only part of his journey where he could have met the plant, it is very rare, and was probably not brought direct to his attention.



FIG. 28.
Fruit of Hydrastis canadensis.

A flowering plant of Hydrastis* was obtained by Linnæus a few years later, and in 1759 he described the genus in Systema Naturale (Ed. 10, 1759), giving it the name Hydrastis,† and Ellis as authority for the name.

*This specimen, which in the Linnæan Herbarium has no mark to indicate from what source it was obtained, was probably given to Linnæus by John Ellis, who had many American correspondents. The specimen is a small flowering plant, broken off about three inches below the leaf, and is merely marked "Hydrastis," in Linnæus' handwriting. That Ellis was the donor of the specimen, we think is probable, because Linnæus gives the generic name, with Ellis as authority, though Ellis had never published any description of the plant.

†The derivation of this name is usually ascribed to the Greek words ὕδωρ, *water*, and δμάω, *to act*, in allusion to the medical action of the drug on the mucous membranes. This is, we think, an error, for probably neither Linnæus

PLATE IX.



MAP SHOWING THE DISTRIBUTION OF HYDRASTIS CANADENSIS.

EXPLANATION OF THE MAP.

The explanation of the different shades is as follows:

Section 1st, Heavy Shade. — Territory over which the plant grows abundantly in its natural habitats. This section furnishes all the drug of commerce.

Section 2nd, Much Lighter Shade.—Territory over which the plant can be usually found, but not abundantly. In many parts of this section the plant is extremely rare, but a diligent search in situations suited to its growth will generally result in its discovery.

Section 3rd, Very Light Shade.—Territory over which the plant is generally absent, but occasionally reported from a few localities.

Unshaded Section.—Plant entirely absent.

In the same year (1759), Miller published a good colored figure of the plant, stating, "This plant has been lately introduced from North America by the title of Yellow Root, and the character of its flower and fruit being different from those of all the established Genera of Plants, I have given it the name of Warneria,* in honor to Richard Warner, Esq., of Woodford, in Essex, who is a very curious botanist, and a great collector of rare plants."

The name Warneria, given to the plant by Miller, was only adopted, as far as we can learn, by Jussieu, who changed it to Warnera. That it should not have been generally adopted is, we think, a matter of regret, as it was published the same year as Linnæus' name, and was accompanied with a picture, and also a very accurate description of the plant.

GEOGRAPHICAL DISTRIBUTION.—The area of country over which Hydrastis grows abundantly enough to be a commercial source of the drug, is extremely limited. In but four States, Ohio, Indiana, Kentucky and West Virginia, can it be profitably collected. Cincinnati is nearly the geographical center of this area, and the supply of the drug once reached the market through this city. In extreme southern Illinois, southern Missouri, northern Arkansas and and central and western Tennessee, there are occasionally localities where the plant is common, but they are hardly of sufficient extent to yield any amount of the drug.

Throughout most of Illinois, northern Indiana, southern Michigan, the southern peninsula of Ontario, and near the base and along ravines of the Allegheny Mountains, the plant is found, but is scarce.

In Pennsylvania and western New York it is sometimes reported, but on every occasion as being extremely rare; and its discovery in most any section of these States is considered a matter of considerable botanical interest.

The plant grows in patches, generally on a hillside, in rich, open woods, where the leaf mould is abundant. It does not grow naturally in prairie countries, sterile soil, or swampy situations.†

Hydrastis has no power to adapt itself to altered conditions of growth. Cultivating the land is sure to exterminate it at once, and even cutting off the trees will cause it to disappear in a few years. It is the common report from all botanists that the plant is becoming scarcer every year. In many places where it formerly grew abundant, it is now reported rare.

DESCRIPTION OF THE RHIZOME.—The fresh, full-grown rhizome (see Plate VIII) is from one and a half to two and a half inches in length, and from one-fourth to three fourths of an inch in diameter. It usually subdivides when it reaches a length of from one and a half to two inches in length, and not

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nor Ellis was aware of its medical action. It is probable that Ellis gave this name from what he supposed was its natural situation, from ὕδρεια, an *imbibing of water*. Hydrastis is erroneously described as a bog plant in several old English works; and these statements are probably the cause of Prof. Wood, in as late a work as his Class-Book, giving its habitat as "bog meadows."

*This plate and name of Miller's was probably not seen by Linnæus until after the publication of the second edition of his Species Plantarum (1762). In Linnæus's private copy of this work, he has written on the interleaf opposite Hydrastis, "Warnera Mill. ic. 130, t. 285."

†The habitat in Wood's Class-Book, "bog meadows," is incorrect

unfrequently forms knotty clumps. When dry the diameter is from one-eighth to one-third of an inch. The color of the fresh rhizome, both internally and externally, is bright yellow, and the plant could be easily recognized by the bright color of the rhizome. The weight of the fresh rhizome, with attached roots, averages from eighty to one hundred and seventy-five grains, and we found that one hundred and sixty-six parts after drying gave forty-six parts. There is considerably more loss of weight by drying if the root is collected while the plant is succulent and growing, than there is after the fruit has ripened.



FIG. 29.
Dried rhizome of Hydrastis canadensis.

The dried rhizome is knotty, contorted, rough externally, of a dull brown color, and considerable soil usually adheres to that which appears in commerce. The young dried rhizome is usually marked by little ridge-like rings, from the sixteenth to the eighth of an inch apart. If it is gathered in the spring of the year, after the plant has commenced to grow, it shrivels in drying, and will be wrinkled longitudinally. Upon the upper side of the growing rhizome, near the stem, several cup-like projections are usually to be found, and these mark the positions occupied by former annual stems. These give the plant the name Golden Seal. The herbaceous stems are articulated to the rhizome, and easily broken off; hence remnants of the stems are seldom found attached to commercial hydrastis, and after the third or fourth year the scar (seal) often becomes indistinct. After four to six years' growth the rhizome gradually decays at one extremity as fast as it grows at the other, and hence a great age is not accompanied by a proportional increase of size.

The recent rhizome is thickly studded with fibrous roots which are sparingly distributed upon the upper surface, but abundantly upon the sides and lower part. These subdivide repeatedly, and when dry they vary in size from the twentieth to the fortieth of an inch, but when fresh are twice as large. The fresh fibers are from three to six inches in length, and are so brittle when dry that as found in commerce the rhizome is often nearly naked.

A transverse section of the rhizome shows that the central ligneous portion of the roots have their origin about one-third the distance from the surface of the rhizome. When fresh their structure is scarcely visible, but upon drying, the surrounding portions of the rhizome assume a hard, resinous appearance, and bright yellow aggregations are deposited upon the woody fibers.

The fresh rhizome contains an abundance of a bright yellow juice, which sometimes, in drying, assumes an orange-yellow color, and by concentration in certain places near the center of the root, occasionally imparts a reddish hue to the central part of the dried root. Usually, however, the fracture of a dry young root is golden or lemon yellow, and that of the old ones of a decided greenish yellow. When the dried rhizome is kept from season to season, it gradually changes internally to brown, or greenish-brown. This alteration com-

mences at the surface and creeps inward, until after some years, by this form of decay, the yellow principles will have nearly perished, and the drug will have become proportionately of less value.

If dried hydrastis is soaked in cold water, after some hours both the rhizome and roots resume near their natural size and fresh appearance. The freshly broken, dried drug presents a mealy appearance, and upon being magnified a few diameters this surface resembles broken yellow beeswax.

The odor of powdered or crushed hydrastis is peculiar and persistent, adhering for hours to the hands or the clothing of workmen who handle it in quantities.* All parts are bitter, and also impart, when chewed, a persistently acrid, irritating sensation, which is entirely distinct from true bitterness and the principle that produces the acridity occasions an abundant flow of saliva.

MICROSCOPICAL STRUCTURE.—(Written for this publication by Louisa Reed Stowell.)

Rhizome.—The cork upon the outside of the rhizome is composed of from four to eight rows of thin-walled, tabular cells, of a dark brown color, with broken and irregular walls, the outer edge of the cells frequently being darker than the inner. The green layer of the bark is composed of from twelve to fifteen rows of oval, clear white, thin-walled cells of parenchyma, loaded with starch grains, chlorophyll bodies, oil and protoplasm. The corners of these cells are thickened, leaving many little open spaces between the cells. The liber layer of the bark is very similar to the green layer, only that the cells are more compressed, fitting into each other so closely as to leave no intercellular spaces.

The cambium is composed of several rows of brick-shaped or tabular cells, separating the bark from the wood. They are clear white, with exceedingly thin walls, and contain only protoplasm.

The medullary rays are quite wide, and composed of a number of rows of parenchymatous cells, stronger and thicker walled than the cambium cells, and loaded with starch grains.

The pith has the usual appearance of large, hexagonal cells of parenchyma, loaded with starch grains.

The woody bundles between the medullary rays, the cambium and the pith, are not fully developed. There are a few small reticulated cells, with pointed ends, and surrounded with a small amount of prosenchyma and considerable parenchyma. The reticulated cells have quite thick walls, and are not parallel with the surface of the rhizome; so it is quite difficult to obtain a good longitudinal section of them. The prosenchyma is in clusters around the reticulated cells, and is of a bright yellow color.

Starch Grains.—Every part of the rhizome, excepting the cork and woody bundles, is loaded with minute starch grains. These are nearly round, with no

* Our experience is that after twelve hours have passed it will adhere to our clothing so noticeably as to be unpleasant to members of our family.

distinct rings or nucleus, and about 1-4000 of an inch in diameter. Occasionally they are found in groups of three, like the starch grains of sarsaparilla.

Root.—In the center of the root is the woody bundle. It is not perfectly developed, and often four clusters of reticulated cells are placed equal distances from each other. At the very center is found a small amount of wood parenchyma. The cells of prosenchyma found in the woody bundle are short and with thin walls. Surrounding the woody bundle is a single row of parenchymatous cells, with frequently the inner wall thickened like stone cells. This row is slightly tinged with yellow, and closely resembles the nucleus sheath of monocotyledonous roots.

The principle bulk of the root is found outside of the woody bundle, and is composed of simple parenchyma loaded with starch grains. This tissue occupies fully four-fifths of the entire root. On the outside of this parenchyma and surrounding the entire root, are two or three layers of dark brown, brittle, empty cells, closely resembling the cork cells of the rhizome.

All parts of the root, excepting the woody bundle and epidermal-like cells, are equally loaded with starch grains similar to those of the rhizome.

DESCRIPTION OF PLATES X. AND XI.

Fig. A. Cross section of the root of Hydrastis canadensis.—*a*, outer row of cells; *b*, parenchyma of the root; *c*, row of cells bordering the woody bundle; *d*, reticulated cells; *e*, central woody parenchyma; *f*, wood prosenchyma; *m*, root hair. (Magnified 75 diameters, and reduced ⅓.)

Fig. B. Longitudinal section of the root.—*a*, outer row of epidermal-like cells; *b*, parenchyma; *c*, border cells of the woody bundle; *d*, reticulated cells; *e*, wood parenchyma; *f*, wood prosenchyma. (Magnified 75 diameters, and reduced ⅓.)

Fig. C. Cross section of the rhizome of Hydrastis canadensis.—*a*, cork cells; *b*, green layer of the bark; *c*, liber layer of the bark; *d*, cells of the newly-formed cambium; *e*, medullary rays; *m*, woody bundle, with prosenchyma, parenchyma and reticulated cells; *g*, pith. (Magnified 75 diameters, and reduced ⅓.)

Fig. D. Cross section of the rhizome.—(Magnified 20 diameters, and reduced ⅓. For reference to parts, see Fig. C.)

COMMERCIAL HISTORY.—*The Early Record.*—Tradition teaches that hydrastis was valued by the North American Indians for a dye stuff, as well as in the treatment of disease. This is accepted by early American writers, and the rich color of its yellow juice renders the statement scarcely questionable, when we consider the value that our aborigines placed on bright colors. It is not always easy to establish authentic support for these accepted traditions, and we have therefore been to considerable trouble in searching the records, in order to discover a commercial value for hydrastis among the natives of America. This we are enabled to present as follows: Mr. Hugh Martin read a paper, October 4th, 1782, before the American Philosophical Society, entitled "An Account of some of the principal Dyes employed by the North American Indians." This paper was published in the transactions of the American Philosophical Society (1793, p. 224), from which we reproduce as follows:

"The Indians dye their *bright yellow* with the root of a plant which might very well be called *radix flava americana*. This root is generally

PLATE X.

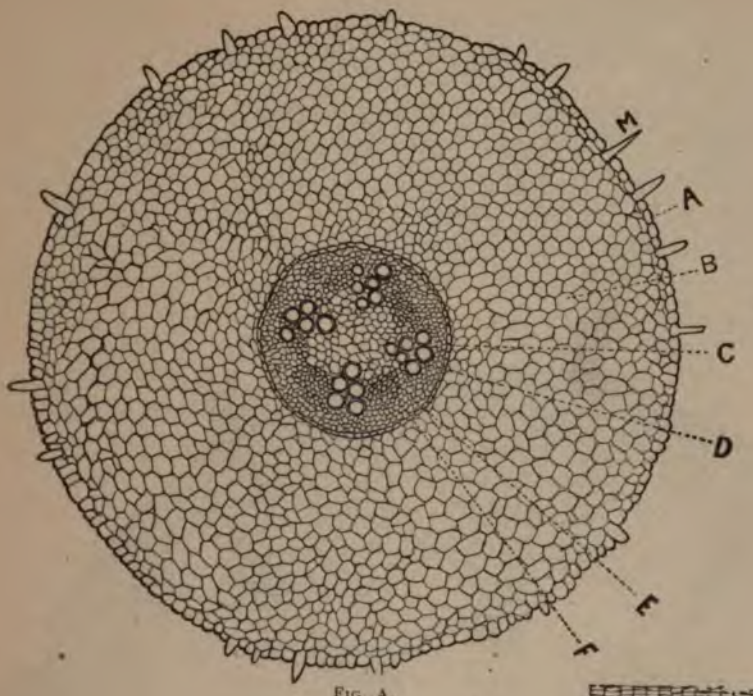


FIG. A.



FIG. C.



FIG. B.

MICROSCOPIC STRUCTURE OF THE ROOT AND RHIZOME OF HYDRASTIS CANADENSIS.

PLATE XI.

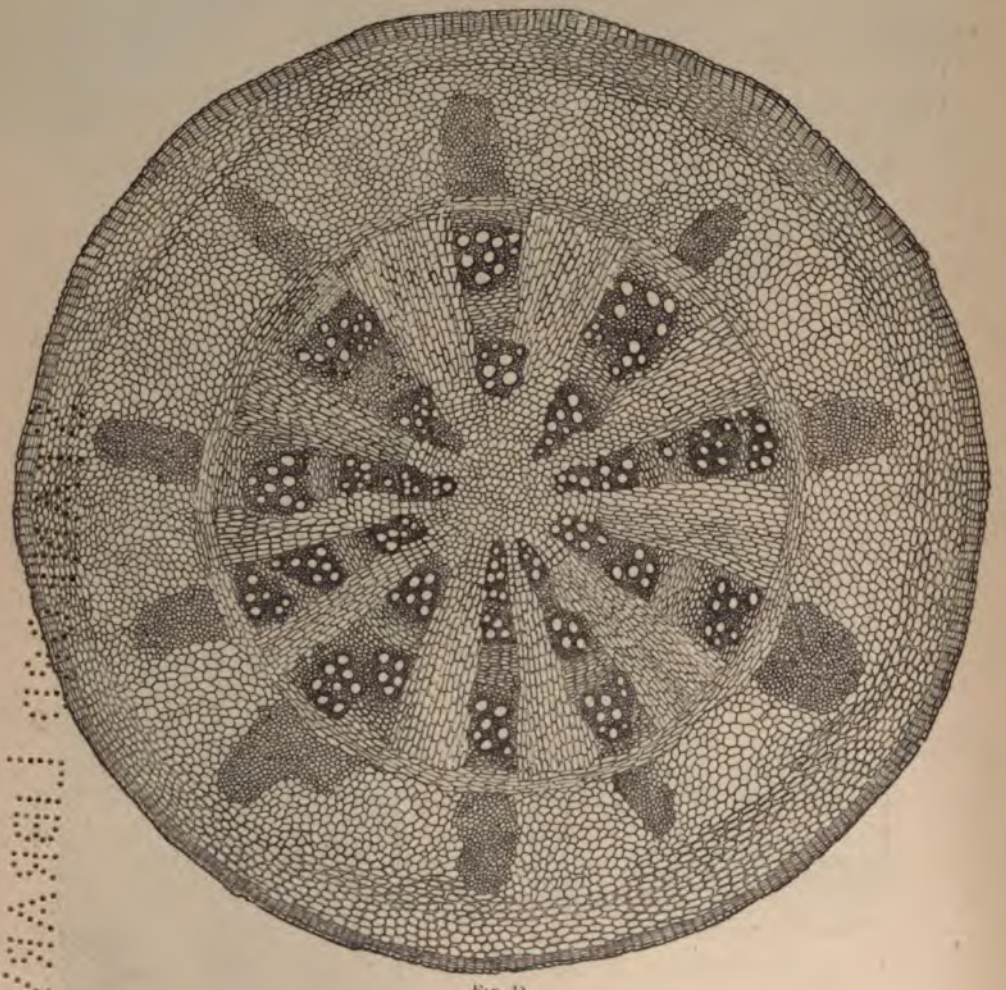


FIG. D.

MICROSCOPIC STRUCTURE OF A CROSS SECTION OF THE RHIZOME OF HYDRASTIS CANADENSIS.

from one to three inches long, and about one-half an inch in diameter, and sends out a great number of small filaments in every direction excepting upward; these filaments are as yellow as the body of the root itself. From the root there grows up a stalk about a foot from the ground, and at the top is one broad leaf.* A red berry, in shape and size resembling a raspberry, but of a deeper red, grows on the top of the leaf. This berry is ripe in July."

From the time of the Indians until a demand was created for hydrastis by the Eclectics, it was scarcely an article of commerce, but about 1847 (see Medical History and Uses) it became an important drug with those who supplied the medicines known as Eclectic remedies.

In viewing the commercial history of hydrastis, we find that it was scarcer and more expensive in its early day than afterward. The explanation is of interest, as other American drugs are usually found to have similar records. This was owing to the fact that botanists were few, and that there was comparatively little demand for American drugs. In consequence, it became necessary that a higher priced labor should procure the drug at that day than is engaged in its collection at present. Therefore, notwithstanding its abundance and the limited demand as compared with the present day, hydrastis was formerly more expensive than now.

Variation in Supply.—Cincinnati, at that day, was the source of supply for the country, as indeed it largely is at present. When crops are abundant and money plentiful, fewer persons engage in the collection of herbs than during seasons of a failure in produce, or in hard times. In consequence of this fact, the price of hydrastis tends to be greater when the commercial interests of the country are prospering, rather than when there is a depression in trade. This alone will not, however, account for the variation in price as witnessed during the past fifteen years. It is true of hydrastis as with many other of our indigenous drugs, that occasionally, and without any apparent reason, the supplies will be consumed at a season of the year when it is impossible to replace them. This creates an immediate increase in price, and an unwarranted valuation will be temporarily affixed to the drug by those who are compelled to have it. This fictitious price stimulates many persons to collect it who would not do so under other circumstances. The result is that after a few seasons the stock of the country is more than replaced, after which the market becomes glutted. It requires months to make this fact known to the root diggers, and as a consequence they often have a quantity of the drug left on their hands. This they must then dispose of on a market in which there is really no demand, and prices fall to less than the cost of collection. Then the collectors turn their attention to other substances, the hydrastis stocks of the country are gradually consumed, and prices are quiet and regular, until finally it is found that the supply is again exhausted, when "history repeats itself."

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*It is only the sterile stems that have solitary leaves. Those that bear fruit always have two leaves. Mr. Martin is a little confused in his statement.—L.

The foregoing record may be modified by circumstances of a local nature, such as the opening of a railroad through a new country; and in one case we know the market to have been temporarily (locally) glutted with hydrastis from this reason.

It will therefore be seen that with hydrastis the periods of abundance in market are not necessarily connected with the season's influence on the growth of the drug, although a long, wet autumn favors its collection. Indeed, this plant is of slow growth, and the question of its supply in market does not seem to be dependent on a favorable season.

Fluctuations in Price.—In arriving at the statistics herein tabulated, we must call attention to the fact that little dependence can be placed on old commercial prices currents.* Persons familiar with indigenous drugs will recognize the fact that list prices to the consumers of these drugs are not altered, unless some unusual reason exists for making a change.† Therefore we shall give this record from information furnished us by dealers in the drug and our own experience.

About 1844, Mr. Joseph West was a member of the Shaker village near Lebanon, Ohio. He distinctly recalls the early commercial history of the drug, and supports his evidence with figures that give the commercial value of hydrastis between the years 1844 and 1850 at $1.00 per pound. Dr. T. C. Thorp, of Cincinnati, an early dealer in indigenous drugs, corroborates him in these particulars; and we are thus enabled to show that at first hydrastis commanded a very much higher price than it has at any subsequent day.‡

The first demand was supplied at a price of $1.00 per pound, and from that the drug fell to forty cents, and afterward to twenty-five cents. It sold at $1.00 in 1849.§

In continuing the commercial history, we find that it declined in price until it reached this valuation of about twenty-five cents per pound, which may be said to have been the average price between the period of its fictitious valuation in the early day, and the close of the war.‖

After the war the depression in trade that followed caused hydrastis to further decline, until its ruling price was from twelve to fifteen cents, and finally the price paid to the collector was only about eight cents. This did not repay the labor of collection, even to the class of people who dig roots, and the drug

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*In the early days hydrastis was mostly in demand by physicians who carried their own drugs, and hence it was not named in regular drug lists.

†The writer has known some of these drugs to be sold for less than cost, rather than change the price temporarily.

‡There is little use to search elsewhere than about Cincinnati for a record of this drug from first hands at that period. Then Cincinnati was the headquarters for American drugs, and hydrastis especially came into market almost entirely from this city.

§Mr. West writes us, "Prior to 1846, we dug and sold golden seal root at $1.00 per pound."

‖Dr. Thorp states that during the war there was a market for all the hydrastis that came into Cincinnati at 25 cents. There was a scarcity in 1867 and 1868, the prices being 50 cents 1867 and 40 cents 1868, as shown by sales of Mr. West; but this was simply one of the periods of scarcity to which we refer elsewhere.

nearly ceased coming into market.* In the winter of 1867 and 1868 a general demand arose, for it was found that the stocks were exhausted and could not be replaced.† Then an advance followed, and collectors were paid as high as twenty-two cents for a limited period, and in some instances fifty cents (1867) and forty cents (1868).‡ Prices afterward gradually returned to their normal condition, and in 1879 the market was glutted and the warerooms were overflowing. At this period the price became so depressed that commission houses were glad to dispose of the drug for six and eight cents per pound; and we recall one lot of eight thousand pounds that sold in Cincinnati in 1880 at four cents.§

All collection of hydrastis had now ceased, and in 1881 many parties were found without a supply sufficient to carry them to the next season, and that year the memorable drouth that extended over the entire section of our hydrastis producing country rendered its replacement impossible.‖ During the winter of 1881 and 1882 hydrastis, in consequence of these combinations, advanced to a figure above anything that it has occupied since 1856, and the crude root sold in lots, when it was attainable, at from thirty-five to fifty cents per pound. The price in a small way was higher, and we recall several sales of from twenty-five to fifty pounds each of powdered hydrastis that commanded seventy-five cents.¶ One stock of twenty thousand pounds was entirely disposed of for not less than thirty cents. During this hydrastis famine consumers resorted to every available method to procure it. Advertisements were placed in the country papers, and even religious newspapers were used to reach the collectors; but of course there was no immediate return, because the drug could not be found and collected in the winter season. The collectors of 1882 received from twenty-two to twenty-five cents at first, but eventually the price

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* From 200 to 250 roots of dry hydrastis are required to make one pound, and after paying commissions it can bring but a trifle to the digger at six cents. In our pamphlet of 1878, entitled "Berberidaceæ of North America," we describe the people who gather the May-apple, and as the same class gathers hydrastis, we reproduce a portion of that description: "Large amounts from the mountainous and hilly parts of Kentucky and Virginia reach this (Cincinnati) market, from whence it is often shipped in quantities to eastern and other cities. It is gathered by the poorer classes, and regions of country not adapted to cultivation usually furnish the supply. The 'diggers' carry it to the nearest country store and exchange it for groceries and goods. The storekeeper in time accumulates a sufficient amount, sometimes several tons, and consigns the lot to a commission merchant or drug-broker, who disposes of it to manufacturing pharmacists or wholesale druggists. It is usually poorly washed, and is mixed with foreign substances such as trash, dirt, and varieties of other roots; large amounts are shriveled and worthless, being gathered out of season. Such a state of affairs results from the extremely low price of the article; and when we take into consideration the fact that it has paid two commissions and been transferred a hundred miles or more, we can not wonder that the poor digger is careless, or, that the 'root and herb gatherers' are the most distressed of our population."

† Hydrastis should not be gathered before the fruit turns red. After this occurs the plant quickly dies to the ground, especially during a dry season, and soon every vestige of it disappears. Thus it is that when the stock of the country is exhausted, it can not be replaced before the next season.

‡ The house with which the writer is connected was compelled to pay more than double their customary price for some thousands of pounds that had been sent from our city to New York, and we had to freight it back again.

§ This lot sold, in 1882, for thirty cents in New York, and part of it, we are informed, returned to Cincinnati at a higher figure.

‖ Members of the American Pharmaceutical Association will remember this drouth. It was the year the Association met at Kansas City, and the journey over the parched plains of what is usually a rich, verdant country will not soon be forgotten by those who made the trip.

¶ The question was not, What is it worth? but, Can you spare any? It must be remembered that the stocks in market really had cost but from six to eight cents, and a price of even twenty-five cents seemed exorbitant. However, these could not be replaced at the old figure for some time.

fell to fifteen and eighteen cents. Notwithstanding the stimulus of these figures, only an average supply was obtained, for with the entire stock of the country exhausted, it was impossible to more than replace it in one season, and the dealers in hydrastis were glad to get it in 1883.* Even now (1884) the price is firm at figures that really are higher than usual. However, the drug is freely coming into market, the small avenues of supply are running into the main channels, and it is not impossible that there will be another surfeit before many seasons.†

The Supply of Hydrastis.—By referring to our map (Plate IX.) it will be seen that comparatively a small section of country produces hydrastis in quantities sufficient for collection. Of this portion, a few narrow channels really produce all the drug of the market. The main source of supply is the country bordering on the Big Sandy river, and the adjacent mountainous portions of eastern Kentucky and West Virginia. Southeastern Ohio, where the country is hilly and broken, also contributes, but not as largely as the portions mentioned of Kentucky and West Virginia. It will be seen that these sections of country are tributary to the Ohio river, and naturally the drug collects in the country stores along the Ohio valley, and eventually much of it arrives in the Cincinnati market by shipment down the river, although some is retained in Wheeling, West Virginia.

Considerable amounts now reach the eastern cities via the Baltimore & Ohio Railway, and since the completion of the Chesapeake & Ohio Railroad through the mountains of eastern Kentucky and West Virginia, a portion of it passes to the seaboard by that line, which also, by means of its connections with the northeastern part of North Carolina, brings to that market a limited supply from the Allegheny Mountains, in the northeastern part of that State. It is estimated by Mr. George Merrell, that of the hydrastis which would ten years ago have all drifted to Cincinnati, but three-fifths now appears in this market, the remainder reaching eastern cities.

The Ohio & Mississippi Railway and the Ohio river carry the hydrastis from southern Indiana (yearly diminishing in amount) to either Cincinnati or St. Louis, although the latter city receives in all but little of the drug.

The sections of country that we have mentioned supply the hydrastis of the world. If the real collecting portions of these States could be placed together, we doubt if the space would occupy more room on our map than the size of the thumb nail. Of course limited amounts occasionally appear in other sections, but these are unimportant and spasmodic. We have consulted every prominent dealer or collector in American drugs in the hydrastis section of the country, and have corresponded with the wholesale druggists in each city

* It must be remembered that one season will not inform all the root diggers that a drug is in demand. Many of them live in mountainous countries, and it is not unusual for them to learn of a demand, then turn their attention to collecting the drug, and finally bring it to market when the demand is over.

† In this connection we must not overlook the fact that liberal advertisements of preparations of hydrastis have had a tendency to create an unusual demand during the past three years. There is no doubt that more hydrastis is now being consumed than ever before.

within and adjacent to the territory. We think that we have recognized every avenue that brings this drug to market, and every section that produces it for market.

The Past and Present Supply.—By consulting our map (Plate IX.), it will be seen that only a small area of country can yield the drug in amounts sufficient to repay collection at present prices, and of this section of country but a limited portion actually contributes any of it to the market. It does not necessarily follow, however, that the plant will not disappear over sections that have never yielded the drug. Hydrastis is so sensitive that even a partial destruction of the timber causes it to shrink away, and one turn of the soil by the plow blots it from existence. If it were like Podophyllum, and content to thrive in woodland pastures, the future would be brighter; as it is, each year witnesses a shrinkage in area and a loss to the world (without economic return) of this peculiarly interesting American plant. It has nearly vanished from the rich hillsides bordering the Ohio river, and is no longer found in quantity in the populated sections of our valley. The more inaccessible portions of broken hillsides must now be drawn upon, and in this view of the matter we find a second in Mr. George Merrell,* who writes us as follows:

"I think the root is becoming scarce, being gathered now, I am told, in small quantities, in isolated places here and there, where in former years it was found growing more like we have seen Podophyllum, in large patches."

In this particular we agree with Mr. Merrell, and from the foregoing view only of the matter we would readily decide that the drug would drop out of market in a moderately near period; however, there is another side of the case.

The mountainous sections of the States we have named can never be cultivated, and they are peopled by a class of inhabitants who barely exist, and who are perfectly content if they only exist. These persons have few expenses, and depend mainly upon the game of their forests and the ginseng and other marketable drugs of their hillsides. The game is becoming extinct, but the nearly inaccessible mountain sides are covered with the virgin forests, and excepting ginseng, with the original luxuriant vegetation and undergrowth. These people are doubtless now turning their attention more directly to our native drugs than ever before, and although the mountainous territory that yields hydrastis is small compared with the United States, it covers considerable area. Over this country these inhabitants and their descendants will ever wander and eke out their existence.† They may dig hydrastis for many decades without exhausting it, for to dig a patch is to leave enough to reproduce itself. They will not have the aid of the plowshare, as was the case when the drug disappeared from the now cultivated Ohio Valley hillsides; and unless some unusual

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* Mr. Merrell is a son of the late Wm. S. Merrell, who really introduced hydrastis as a drug into commerce. Mr. Merrell is now the moving spirit of the firm that is the heaviest consumers of hydrastis in the world, and his statistics are particularly valuable.

† Apparently in a miserable condition, in reality happy and contented. To pass through these sections of country is to have our sympathies excited, and unnecessarily. These people ask only to be left to themselves and their mountains.

demand springs up, it is not unreasonable to argue that hydrastis will continue in market as plentiful and as cheap as at present for a generation, perhaps generations to come. This argument is supported by the fact that since the introduction of the drug it has decreased steadily in price, and excepting the periodical scarcity we have mentioned (see Fluctuations in Price, p. 90), there has been an abundance of it. The fact that large lots were a drug on the market in 1879, and sold at less than cost of collection (we doubt if any instance preceding 1879 can be shown where as much as 20,000 pounds sold for from four to eight cents), would seem to indicate that the decrease in area is not necessarily accompanied by a decreased supply. The fact is, that the large territory once rich in hydrastis, and now depleted, furnished but a small amount of the drug. The timber was chopped and the underbrush cleared away, without any return. Only here and there did a "root digger" ply his vocation, and great, rich sections of our country, from which the plant is now nearly exterminated, have never furnished a pound of the drug.

Consumption of Hydrastis.—It is usually difficult to arrive at an exact statement regarding the consumption of a drug, but, thanks to dealers and the liberal spirit of manufacturing pharmacists, we are enabled to present statistics that are certainly not far from correct.

The total yearly production of hydrastis will not vary much from 140,000 or 150,000 pounds. We had estimated 140,000 pounds, from statistics furnished by first hands for the drug, and Mr. Geo. Merrell places it at near 150,000.

Of this amount, from 25,000 to 28,000 pounds are annually consumed in making the alkaloids, and the remainder is retailed, powdered, made into pharmaceutical preparations, and exported. It is used in some proprietary medicines, one notably consuming considerable amounts.

Export of Hydrastis.—There is some demand for hydrastis in Europe, although but few of our drug brokers have any European trade in it. From statistics kindly furnished us by exporters, we find that 15,000 pounds were exported in the fall of 1883, but that the foreign consumption is spasmodic. Some of our most prominent jobbers and brokers state that they have never had a call for it from Europe, while others report yearly shipments of from 200 to 1,000 pounds. The demand seems to chiefly come from manufacturing chemists, makers of proximate principles of plants, rather than from those who supply physicians, and we can not find that the drug has been long used in any amount as a remedy in European medicine. During the past year a few contributions to the medical press of Germany and other European countries have directed attention to hydrastis, but the demand that has followed it has, according to our record, mainly been for the fluid extract or proximate principles.

ADULTERATIONS.—The substances which usually contaminate our indigenous drugs, are to be found mixed with hydrastis. Fragments of foreign roots, such as serpentaria, cypripedium, senega, collinsonia, jeffersonia, trillium,*

* We once mentioned this fact, using the name beth root instead of trillium. As a consequence, we found it

etc., are common, and these admixtures usually result from carelessness of the collector. In a few (exceptional) cases, however, we have found them to constitute more than half the gross weight of several bales of the drug; and under these circumstances the admixtures were intentional.



FIG. 29.
Root of Stylophorum diphyllum (one-half natural size).

The root of Stylophorum diphyllum* resembles hydrastis in color when fresh, having a golden yellow juice, but it changes throughout to a dirty gray upon drying. Our attention was once called to a lot of one hundred pounds entirely made up of the root of this plant, which was thrown upon the market as an extra "Large Golden Seal." The appearace of this root will not permit of a confusion of it with the rhizome of hydrastis. (See Fig. 29). In our opinion, the color and peculiar odor of dried hydrastis will prevent any careful person from mistaking it for the root of any other plant known to us. However, very much inferior hydrastis is in commerce, some of it objectionable because of its having been gathered too early in the season, other portions because of dirt, mould, or admixtures. In consequence of these facts, much of it is unfit for use, and purchasers should exercise care in its selection.

PHARMACOPŒIAL HISTORY.—Hydrastis had never been recognized by any Pharmacopœia until it was made officinal in the Pharmacopœia of the United States, in 1860, as "the root of Hydrastis canadensis," and then no preparation of it was introduced.

The Pharmacopœia of 1870 continued it under the same name, and authorized the preparation of a fluid extract of hydrastis.

The revision of 1880 recognized it as "the rhizome and rootlets of Hydrastis canadensis." This revision continued the fluid extract, and introduced a tincture.

CONSTITUENTS.—*Berberine: History of the Name of this Alkaloid.*—In 1824, Huttenschmid discovered a substance in the bark of Geffroya inermis, and gave it the name jamaicine. This Wittstein (Organic Principles of Plants, p. 26) accepts as berberine.†

Chevallier and Pelletan discovered it in the bark of Xanthoxylum Clava Herculis (1826), and named it xanthopicrite, a name that could have been very appropriately applied to this rich, yellow alkaloid.

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copied into journals on each side of the Atlantic as *beet* root, a substance that could not well be used as an admixture with hydrastis.

*This plant is of interest, and will be considered by us in our publication in its proper place.

†Gmelin overlooked the work of Huttenschmid, and ascribed, in his Hand-Book of Chemistry, the discovery of berberine to Chevallier and Pelletan. Compare also the statements of J. Dyson Perrins, in the Journal of the Chemical Society (1863), and its reprint in the Pharmaceutical Journal and Transactions (1863), p. 464.

Rafinesque (1828) named the yellow coloring matter of Hydrastis canadensis hydrastine.*

Buchner and Herberger (1830) gave the name berberine to a purified extract of Berberis vulgaris, although Brandes previously (1825) may be said to have described a yellow coloring matter that he obtained from this plant.† He did not ascribe a name to it.

Thus it will be seen, accepting all of these substances to be identical, that the name berberine appeared last.

In reviewing the record, we are at a loss to determine why the names that were entitled to the precedence should have been displaced by the term berberine. It may be argued that the words jamaicine and xanthopicrite were not affixed to definite proximate principles, but since the name berberine was originally applied to a solid extract, we can not argue in its favor from that view. The word hydrastine, announced by Rafinesque in 1828, was overlooked by all writers, so that this term could not have entered the lists even had it been known at an early day that this substance was identical with berberine. Therefore the name least entitled to the honor from a chronological standpoint is the term berberine, which by common consent has been accepted.

History of the Alkaloid Berberine. — Authorities have recorded the history of this alkaloid in Europe. Since they overlooked the American history, or were not conversant with it, we shall introduce it, and in connection endeavor to review the entire matter, which can not but be of general interest.

As before stated, Huttenschmid (1824) gave us the name jamaicine; Chevallier and Pelletan (1826) gave us the name xanthopicrite; Rafinesque (1828) introduced the name hydrastine; and finally (1830) Buchner and Herberger announced berberine.

The fact that Rafinesque had entered the lists seems to have then been unknown, and we can find no recognition of him by subsequent investigators; and it seems to us an oversight in passing the work of this eccentric but talented scientist.‡ His "Medical Flora of the United States" (Vol. I.) was written between the years 1816 and 1828, being published at the latter date. In it (p. 253) he defined the yellow alkaloid of Hydrastis canadensis as "a peculiar principle *hydrastine*, of a yellow color." We fail to find a better description of this alkaloid until years afterward, for Rafinesque individualized hydrastine, and pointed to it as the prominent principle, by saying of hydrastis, "It contains amarine, extractive, several salts, and a peculiar principle *Hydrastine*§ of a yellow color."

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* Medical Flora of the United States, 1828, Vol. I., p 253.

† American Journal of Pharmacy, Vol. III., 1831, p. 173. Also Gmelin's Hand-Book of Chemistry, Vol. XVII., p. 186.

‡ It is true that Rafinesque took the broadest liberties with the sciences in which he wrote, and few will deny that he was very egotistical. However, he was a persistent student, and his works become more valued as the years pass. He entered the field as a writer in several branches of the Natural Science of his day, and it is now recognized that many of those works are among the most difficult to obtain. His "Medical Flora" is rare indeed, and his work upon Fishes is entirely out of market.

§ Italicized by Rafinesque.

We are thus careful in giving this record because the name hydrastine was accepted by a very considerable body of practitioners (Eclectic), and in American commerce it is now hydrastine. *

In continuing the history, we find that in 1830, when Buchner and Herberger announced the name berberine, it was applied to a purified extract of Berberis vulgaris. † The substance obtained by them was neither berberine nor a salt of berberine, and the berberine present in their extract could have only represented a small portion of the product. Their process will not admit of any other view of the subject, and the yield of berberine they report, seventeen per cent., can not be obtained from Berberis vulgaris. Hence the name berberine was not originally applied to an alkaloid.

In 1835, Prof. Buchner and son obtained, unknowingly, the hydrochlorate of berberine in crystalline form, but thought it a neutral principal, or a weak vegetable acid, and thus we may ascribe to the Messrs. Buchner the honor of really obtaining from Berberis vulgaris the first salt of berberine. ‡

Dr. George Kemp, in 1839, assigned berberine to a place among the alkaloids, producing a combination with picric acid. He recorded his experiments in Buchner's Reportorium, 1840; but this fact seems to have been overlooked. In 1841 he investigated the substance more thoroughly, producing a hydrochlorate, sulphate, acetate, and some other salts; but in consideration of a request from his friend Prof. Buchner, who wished his (Buchner's) son to re-examine the subject, Kemp withheld his paper from publication. §

Thus it occurred, that in 1847, Thomas Fleitman, unconscious of Kemp's work, published an essay on berberine and its salts, without recognition of Dr. Kemp's labors in the same field. He demonstrated that berberine was neither a neutral coloring matter, nor a weak acid, as the Messrs. Buchner had supposed, but a true alkaloid, and strongly basic. He even examined a portion of the substance made by the Messrs. Buchner in 1835, and supposed by them to be either a neutral principle or a vegetable acid, and found it to be hydrochlorate of berberine. And outside of Mr. Fleitman's report, the testimony from the Messrs. Buchner's description is, in our opinion, to the effect that they obtained hydrochlorate of berberine. They described their product as "A very light powder, composed of acicular crystals, of a bright lemon yellow color, very slightly soluble in cold water." This description will not apply to the alkaloid.

Hence we find that Thomas Fleitman gave to the world (1847) the first general intimation of the basic character of berberine, and he is, therefore,

* When it was shown by Mahla, 1862, that the substance employed by Electics was identical with berberine, they (Eclectics) would more readily have accepted the name berberine if it had quietly been announced. Considerable feeling once existed relative to this substance, and Eclectics were not willing to be driven into the use of a name that from their view came after the name hydrastine. But that feeling has passed, and the least said the better.

† Compare Am. Journ. Pharm., 1836, p. 368, from Journ. de Pharm., 1835.

‡ The date of its appearance is variously stated at 1830, 1832 and 1835. Dr. F. F. Mayer refers to Buchner's Report. xxxvi., p. 1, 1830, for the original paper (not at our command). See also Pharmaceutical Journal and Transactions, 1863, p. 517. We therefore accept 1830 as being well authenticated.

§ Chemical Gazette, 1847, p. 209.

accepted by most writers as having assigned it to a place among the alkaloids, although it is established that it had been known by Dr. Kemp to be an alkaloid from the year 1839. *

History of the Yellow Alkaloid (Berberine), as Obtained from Hydrastis Canadensis (1828), Originally Called Hydrastine. — We will again repeat, that in America the name hydrastine was originally given, by Prof. Rafinesque, to this alkaloid, which is the principal coloring matter of Hydrastis canadensis, and that he gave it before the name berberine appeared in Europe. By this name it was accepted when introduced into American medicine by the Eclectics (1847), Rafinesque's works being prominently recognized by this section of the medical fraternity. In our botanical history of Hydrastis (p. 83), we presume to regret that the appropriate name of Ellis (Warneria), was not continued to the plant, instead of the illogical name Hydrastis. We also think it unfortunate that, since the name Hydrastis was accepted by botanists, it was not followed by chemists in the naming of its prominent constituent, the yellow alkaloid.

No printed process for making the yellow alkaloid (berberine) appeared before 1851, and we must consider that Mr. Durand first announced a salt of berberine from Hydrastis canadensis, although he was unconscious that it was a salt. In the year 1850, he wrote a paper on Hydrastis, and published it in the American Journal of Pharmacy, April, 1851, in which he called attention to "a yellow coloring matter" made by precipitating an alcoholic tincture of the root of Hydrastis canadensis by means of a solution of bichloride of tin, describing it as "a most brilliant yellow precipitate." This substance Mr. Durand neglected to investigate, but suggested that it might "prove a useful pigment in oil and water painting." It was hydrochlorate of berberine, and thus he was the first to obtain a salt of this alkaloid from Hydrastis canadensis and record the fact.† At this time Eclectic physicians were using the substance as a remedy under the name Hydrastine, or Neutral Hydrastine, and hence it is that the hydrochlorate of the alkaloid was the first definite preparation supplied to the medical profession of America. ‡

Although Mr. Durand prepared the hydrochlorate of the alkaloid berberine, in 1850, from Hydrastis, and Pharmacists who made Eclectic medicines had supplied it to the medical profession in considerable quantities from before that period, neither had identified it as berberine, or as a salt of that alkaloid, although it was certainly known, by a few, to possess alkaloidal properties. §

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* Mr. Fleitman's paper may be found in the Chemical Gazette, 1847, p. 129, and following it in a subsequent number, p. 209, the statement from Dr. Kemp, that he Kemp had long known of the basic character of berberine, and had remained silent out of respect to the request of Prof. Buchner.

† By a coincidence, the first preparation of the alkaloid used in American medicine was also considered a neutral principle, and in reality was hydrochlorate of berberine. It was called Hydrastine Neutral, being made from Hydrastis canadensis.

‡ At first sight it may seem strange that the investigators, without exception, failed to ascribe to this substance alkaloidal properties. It was discovered independently in different plants, by several persons, as our history will show, and in no instance was it identified. Upon deliberation, however, it will be seen that in that early day the alkaloidal tests now so easily applied were unknown. Therefore an alkaloid, forming with hydrochloric acid an almost insoluble salt, was an exception to all known alkaloids, and consequently not likely to be compared with other organic basis.

§ See Grover Coe's work, positive Medicinal Agents, 1855. And we refer the reader to our historical introduction of hydrochlorate of berberine for some points in this connection.

Nothing appeard after Mr. Durand's work for a period of twelve years; but in 1862 the subject was taken up by Mr. F. Mahla, of Chicago, and in a paper contributed to the American Journal of Science and Arts, January, 1862, he clearly established the fact, that the Eclectic "Hydrastine" was the salt of an alkaloid, and that this was berberine. Therefore, to Mr. Mahla is due the credit of really identifying as berberine the alkaloid that had been discovered fifteen years previously in Hydrastis canadensis. * In this connection we must not forget to record the fact, that Mr. J. Dyson Perrins, of England, really discovered berberine in Hydrastis before Mr. Mahla identified it, but he neglected to announce the fact. He states in the Journal of the Chemical Society, 1863, that "sometime before the publication of Mahla's paper, I had noticed the occurrence of berberine in Hydrastis canadensis," and thus Mr. Perrins stands in comparatively the same position as Dr. Kemp, both having anticipated the work of the persons who made the announcements.

The Past and the Future Name of this Alkaloid. — It may seem that we overstep the line of prudence, and pass into a field that we should not presume to enter, when we even announce a heading such as the above. We trust, however, that our experience with this almost exclusively American drug, our aggravations commercially, and our endeavor to familiarize ourselves with its past record, will excuse us to the reader, if we cautiously consider the future.

There can be no doubt that the name berberine is applied to the alkaloid by a comparatively small number of American pharmacists and physicians, and that in America the recognized name is still Rafinesque's "Hydrastine." The endeavor to affix the term berberine to this yellow alkaloid of Hydrastis canadensis, has as yet proven a commercial failure. It is true, that with scientific men and many writers, berberine is acknowledged, but these men are few, compared with those who use the term hydrastine. The question that naturally presents itself is, are the men who prefer hydrastine entitled to consideration? Although we support the term berberine, we must acknowledge the justice of the name hydrastine from the following reasons:

1. The name hydrastine was applied before the name berberine, the one in America (hydrastine), the other in Europe (berberine).

2. This substance and its salts, under the name hydrastine, hydrastine muriate, etc., came into extensive use in America, and so generally, that at the present day we estimate that from 25,000 to 28,000 pounds of Hydrastis canadensis are annually consumed in making the alkaloid and its salts. They are scarcely used in Europe.

3. This name (hydrastine) has become so strongly fixed in the trade interests of our country, that for this reason alone we would even now acknowledge its claims for primary recognition, were *our* country only to be considered.

* We thus see that the American history coincides remarkably with the European, for in 1824 Huttenschmid discovered berberine, and fifteen years afterward Kemp identified it as an alkaloid, although between those periods it had been discovered independently, and examined by several good authorities.

However, even though the name hydrastine is chronologically entitled to preference, and though the amount of the alkaloid produced from Hydrastis canadensis for medicinal use, in America, is doubtless very much greater than that from all other sources the world over, we think that the fact of its being familiar to scientists of all countries as berberine, now entitles that word to preference.

Throughout America the name hydrastine is as firmly engrafted as before Mahla (1862) announced that hydrastine and berberine were identical. There is little indication that the term hydrastine will be supplanted by berberine at any immediate day, yet in common with others we have always given our assistance towards bringing about this result. All have failed, and the public seems to tenaciously insist that commercial precedence, and the source of the drug, shall have precedence in the recognition of a name. Hence, in America the name berberine is applied by a few, and hydrastine by the many.

It is not unlikely, however, that if the leaders in the various schools of medicine and in pharmacy will endeavor to bring about uniformity in expression, and will use the word berberine whenever it is possible, it can be made the name of the future. *

Processes Announced for the Preparation of Berberine.—It would be natural to suppose that a substance of the importance of berberine, and studied as this substance has been during a number of years, could now be readily prepared in a state of purity. We will venture to say, however, that according to our investigations, the production of this alkaloid, free from contaminations and decomposition products, is by no means an easy matter. A personal experience of some years on a manufacturing scale by means of the formulas suggested, and accepted by many authors as reliable, has not been at all satisfactory. It is therefore necessary for us to review the processes that have been named; and while we dislike to differ, even in the least, with such excellent authorities as have considered this subject, we must not neglect to add any light that may have been cast in this direction by our work. We find, also, that others have not been altogether satisfied; and investigators who are no less conspicuous in the literature of berberine than Mr. Perrins and Prof. Wm. Procter, have doubted the constitution of the substances produced as berberine. Thus Mr. Perrins states that "the pure alkaloid itself is equally unsuited for analysis. . . . Indeed, I find it not easily prepared in a state of purity." And that Mr. Perrins was uncertain of the substance known to others as berberine, is evidenced by the fact that his ultimate analyses were all made of the salts of berberine. Prof. Procter, in referring to this subject, has written:†

* Few realize the hold of the word hydrastine in America. When we consider that it is applied to a proximate principle that has been used extensively for twenty years, and that the name gives the origin of the drug, we can appreciate the fact that it will be displaced very slowly. There is another argument against the word berberine, and that is the resemblance to *beeberine*. These substances are often confused in commerce, and confounded by physicians, and that they so nearly resemble is unfortunate.

† American Journal of Pharmacy, 1864, p 10.

"Having occasion recently for information relative to the production of pure berberine in an uncombined state, a reference to all the authorities at my disposal, including nearly all the papers published within the last few years, I noticed with some surprise that these writers, in describing berberine, treated the substance obtained from Berberis vulgaris by the agency of neutral solvents, and which, as berberine is an alkaloid, must be a neutral salt of that alkaloid."

The substance originally called berberine having been found a mixture of berberine and extractive matters, led to the suggestion of several processes for freeing this alkaloid from its combinations. Mr. Fleitmann announced the following:* "Sulphate of berberine was made by decomposing the muriate with weak sulphuric acid; the salt then recrystallized, and dried at 212°F to expel all traces of muriatic acid. Baryta water was added to the solution until it became alkaline, when the liquid immediately assumed a dark red color. To remove the excess of baryta, carbonic acid was passed through the liquid, which was then boiled and filtered, upon which the dark red solution was evaporated nearly to dryness in the water bath, and dissolved in ordinary alcohol; the berberine was precipitated by ether, and recrystallized from water."

This is the process now adopted by most of the authorities we have consulted, but we regard the product as uncertain and by no means of uniform composition. He first directs the preparation of muriate of berberine, and this salt is then to be dried at a temperature of 212° F. This preliminary step introduces a possible impurity, for we are convinced that such a temperature can not be applied to the moist salts of berberine without risk of partially dissociating them. In this view we find that our experiments have also corroborated those of Mr. Perrins, who writes of muriate of berberine as follows: "I acquiesced in Fleitmann's formula, and even supposed that it was confirmed by my analysis of the hydrochlorate and by a platinum determination; but later experience has shown me that the hydrochlorate is not suited for ultimate analysis, as by pretty long exposure to a temperature of 100°C., or thereabouts, it undergoes some decomposition."

Next, we find that the addition of solution of caustic baryta until an alkaline reaction results, is a procedure that should be avoided if possible, and by no means should the alkali be added in great excess, for the equilibrium of this delicate alkaloid is likely to be disturbed by contact with excess of an alkali. Mr. J. Stenhouse noticed this dissociating power of the alkalies on berberine, and in the Journal of the Chemical Society, London, 1867, p. 187, he cautions us against their use, and considers caustic lime preferable to any of them as being less destructive.

Finally, the evaporation of the solution of berberine, after precipitation of excess of barium by a current of carbon dioxide, should not, in our opinion, be carried on at the temperature of a water bath, and most certainly not as Mr.

* Chemical Gazette, 1847, p. 129.

Fleitmann directs, "nearly to dryness." Such an application of heat, especially when continued in this manner, will decompose portions of the alkaloid.

Taking these factors together—and we doubt if many workers with this alkaloid will dissent concerning their several influences—we can not but accept that the product must be uncertain. Hence, while Mr. Fleitmann obtained a body which he found to possess certain characteristics, we are not surprised that others who have followed, and excellent authorities, differ both from him and from each other.

In 1862, Mr. Wm. S. Merrell stated that berberine might be prepared by decomposing sulphate of berberine by means of oxide of lead.* Acting on his suggestion, Prof. Wm. Procter elaborated a formula as follows:† Freshly precipitated oxide of lead, basic hydroxide, $Pb_2O(OH)_2$, was digested in excess with sulphate of berberine, which had been previously dissolved in boiling water, until a filtered portion of the solution failed to strike a precipitate with solution of acetate of lead or with baryta water. It was then filtered, evaporated and crystallized.

This process seems certainly to be free from some of the objectionable features of those that have preceded, and yet (admitting that berberine can be produced) as a necessity there must be a long-continued application of heat; and this should be avoided.

Again, in our hands the process has been a complete failure in other respects, because it abstracts only a part of the sulphuric acid; and in support of our view we give a synopsis of the following experiments that we have repeatedly made.

One part (480 grains) of nitrate of lead was dissolved in water and precipitated with excess of ammonia water. The basic hydroxide so produced was well washed, and added to a solution of one part (480 grains) of berberine bisulphate ($C_{20}H_{17}NO_4H_2SO_4$), in 32 parts of water. The mixture was digested at a temperature of 160° F. for forty-eight hours, with frequent stirring, the evaporated water being replaced, and was occasionally tested with solution of acetate of lead. ‡ The sulphuric acid was not withdrawn, the solution giving every evidence of being still a solution that contained a sulphate of berberine. If the liquid be evaporated to dryness, decomposition results; and upon re-solution a deep red liquid is produced, which still contains a sulphate of berberine after the lead is precipitated by means of sulphide of hydrogen. In this case, however, the sulphate conforms to the properties of the normal salt $(C_{20}H_{17}NO_4)_2H_2SO_4$.

Under the same circumstances lead monoxide, PbO, fails to withdraw the sulphuric acid from the bisulphate of berberine. We are convinced that Prof. Procter really obtained the soluble normal sulphate as we did with our

* American Journal of Pharmacy, 1862, p. 503.

† American Journal of Pharmacy, 1864, p. 10.

‡ Prof. Procter states that solution of caustic baryta can also be used to determine the absence of sulphate of berberine. We believe that the lead sulphate dissolves to a considerable extent in this solution of berberine; and hence we scarcely think that the barium test is reliable.

ammonia process, a compound that at that time was unknown. In this connection, we remember that Prof. Edward S. Wayne once informed us that in his hands the process was a failure.

In 1867, Mr. G. Stenhouse published in the Journal of the Chemical Society, London, a process in substance as follows:*

"One part of acetate of lead is dissolved in three parts of water, and to the boiling solution one part of very finely ground litharge is added in small portions, and heated until the whole forms a thick, pasty mass. This is then diluted with one hundred parts of water, and twenty parts of the finely ground wood is mixed with it and boiled about three hours, and strained. A little litharge is then added to the liquid, and it is evaporated to crystallization, when, 'on cooling, berberine crystallizes out in dark brown tufts of needles.'

"In order to purify the crude berberine obtained by the foregoing process, it is dissolved in boiling water, and subacetate of lead added as long as any precipitate is produced This solution, filtered while hot, almost solidifies on cooling to a mass of yellow needles, which, however, still contain lead and organic impurities. They are collected on a cloth filter, pressed, dissolved in boiling water, and sulphuretted hydrogen is passed through it. The hot solution, after filtration to separate the precipitated sulphide of lead which carries down some organic impurities, is acidulated with acetic acid and allowed to cool. The bright yellow needles of nearly pure berberine are collected, pressed, and dried at a gentle heat."

This process will not produce berberine, but an acetate of berberine. Even if the treatment with solution of basic acetate of lead yielded berberine, it would be impossible to finish the product by acidulating the solution with acetic acid, as Mr. Stenhouse directs, and avoid the formation of acetate of berberine, which is in reality the substance produced by the process. Hence those who employed this formula can not well agree in their description of the product with persons who used the process of Mr. Fleitmann.

Dr. T. L. A. Greve, of Cincinnati, suggested a process in the Eclectic Medical Journal, 1877,† whereby muriate of berberine is decomposed by means of oxide of silver. This process certainly produces chloride of silver, with the separation of the chlorine from the alkaloidal salt, and the formation of a substance that dissolves with a deep red color, and which forms salts with acids.

Dr. Greve's plan is to make a boiling solution of muriate of berberine, and add oxide of silver in amount sufficient to decompose it. The reaction we find to be rather violent if moderately large amounts are used, and is accompanied by the evolution of gas bubbles and a hissing noise, even in the small proportions of a few grains. When we consider the unstable nature of oxide of silver when in contact with organic substances, we can not but question the production of pure berberine by this process. The result in our hands seems

* Journal of the Chemical Society, London, 1867, p. 187.
† Eclectic Medical Journal, Cincinnati, 1877, p. 312.

quite conclusive that oxidation products arise from the action of this powerful oxidizer on the berberine, and that the reaction is not so simple as to be altogether explained by a double decomposition between the two substances.

Lastly, the writer suggested that berberine could be prepared as follows:* "Rub eight parts of sulphate of berberine in a wedgwood mortar, cautiously adding ammonia water until in slight excess. Pour the dark liquid into thirty-two parts of boiling alcohol, and allow the mixture to stand thirty minutes; then filter. Stir into the filtrate thirty-two parts of cold sulphuric ether, and cover tightly. Surround the vessel with ice, and allow it to stand from twelve to twenty-four hours; then separate the magma of minute crystals of berberine with a muslin strainer or filtering paper, and dry by exposure to the atmosphere."

This product is in reality a sulphate of berberine of the composition $(C_{20}\ H_{17}\ NO_4)_2.H_2\ SO_4$. At the time the process was announced, the writer considered the presence of sulphuric acid to be due to adhering sulphate of ammonium, but subsequent investigations have demonstrated that such is not the case; and the fact was announced in the American Druggist, 1884, Sep., p. 166.

After reviewing the published processes that have been brought to our attention, as announced in the foregoing pages, we must admit that this berberine subject is not in a satisfactory condition, and that the contradictory reports of those who have written on the properties of the alkaloid are doubtless mostly due to the variable condition of the product.

The Preparation of Berberine.—Our experiences with the processes that have been recorded having proved so unsatisfactory, and really in accord with the work of others, we have endeavored from time to time to obtain the alkaloid in a state of unquestionable purity. The most satisfactory process, but not by any means without objections, is based on that of Mr. Fleitmann—the decomposition of sulphate of herberine by means of solution of hydroxide of barium.† With the precautions that we suggest, a moderate proportion of a substance can be obtained that conforms to our description of berberine, and which we believe can be accepted as the pure alkaloid.

Make a saturated solution of sulphate of berberine $(C_{20}\ H_{17}\ NO_4)_2.H_2\ SO_4$‡ in distilled water, and at a temperature of 15.5° C. cautiously add solution of hydroxide of barium until in *very slight excess*. Pass a current of carbon dioxide at once through the product, until it ceases to afford a precipitate with a filtered portion of the liquid, and then filter it. Place this dark red solution of berberine in a shallow vessel, and expose it to dry air under a bell glass containing a vessel of sulphuric acid, chloride of calcium, or freshly burned

* J. U. Lloyd, in Proceedings of the American Pharmaceutical Association, 1878. See also American Journal of Pharmacy, 1879, p 11.

† If carbonate of barium would decompose sulphate of berberine completely, the action of an alkali would be obviated. However, it will not do so.

‡ The salt used by Fleitmann and others has been the bisulphate of berberine $C_{20}\ H_{17}\ NO_4\ H_2\ SO_4$. This is so nearly insoluble as to require heat. In order to evaporate the product, heat also is necessary in consequence of its dilute condition. We overcome this by making a cold, concentrated solution of the soluble sulphate.

lime. After the liquid has reached a syrupy consistence, a deep brown crust forms over its surface which is of rather uncertain composition, as it refuses to completely re-dissolve in water. However, deep garnet red, needle-like crystals form beneath it of considerable size, distinct and clearly defined. These bear no evidence of contamination, form salts to perfection, and in our opinion are pure berberine.

This process, it will be seen, presents the following advantages over others:

1st. A very soluble sulphate of berberine is employed, which enables us to obtain a cold, concentrated liquid.

2nd. By close attention the sulphuric acid can be all withdrawn with only a slight excess of caustic baryta, which must be immediately decomposed by means of a current of carbon dioxide.

3d. The final evaporation is without heat; and thus from the beginning to the close of the operation the temperature need not rise above 15.5° C.

Working with very small amounts has not been satisfactory. We prefer to employ not less than a pound of sulphate.

Identity of the Alkaloid (Berberine), as obtained from Hydrastis canadensis and Berberis vulgaris.—The differences in the description of berberine has led some persons to question the identity of the substance as derived from different sources. While it is true that processes that will separate certain salts of berberine from some plants, fail to do so with others, we are convinced that this is in consequence of the natural combination of the alkaloid or the influence of associated bodies. In our hands, after purification, the alkaloid known as berberine is identical in properties, whatever has been its origin. The sulphate, muriate, and other salts of berberine as obtained by us from Hydrastis, conform in character with the same substances made from Berberis vulgaris.

In the year 1862, Dr. F. Mahla, of Chicago, presented a paper* on the substance used by Eclectic physicians under the name Hydrastine.† From the reaction of its salts, and also by the support of an elementary analysis, he decided that it was the well known alkaloid berberine. He believed himself to have been the first to enter this field, for he wrote: "An organic elementary analysis of this substance‡ does not exist;" but at the same time Mr. Perrins, of London, England, was engaged in a similar investigation of the yellow alkaloid of Hydrastis.

Mr. Perrins, after enumerating a number of plants of different natural orders, accepted as indisputable the fact that they all contain the alkaloid berberine. He is undoubtedly our best authority on this subject. He included Hydrastis canadensis, and wrote as follows before entering into the elaborate analyses he made of the berberine salts:§ "It seems unnecessary to

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* American Journal of Science and Arts, Jan., 1862.

† See our history of the yellow alkaloid from Hydrastis canadensis.

‡ As made from Hydrastis canadensis.

§ Journal of the Chemical Society, London, 1862, Vol. XV., p. 343.

state in each case from which plant I have prepared the salt for analysis; suffice it to say that the whole of the sources now first announced are included."

Mr. Perrins did not advance his method of comparison; and although there can now be little, if any, doubt that his assertions were based on experimental proof, we feel that our paper would be less perfect were we to neglect the subject.

Therefore we forwarded specimens of perfectly pure and re-crystallized sulphate and bisulphate of berberine to Prof. F. B. Power and Prof. Virgil Coblentz, and to the latter gentleman a specimen of crystallized berberine, all from Hydrastis canadensis. These substances were analyzed by Prof. Coblentz, who, after several combustions, assigned to each alkaloid the formula C_{20} H_{17} NO_4. Prof. Power made combustions of the bisulphate only, and also reported the empirical formula C_{20} H_{17} NO_4. In view of these facts, we think it can be accepted beyond a doubt that the yellow alkaloid of Hydrastis canadensis is identical with that of Berberis vulgaris, and is berberine.

The Composition of Berberine (C_{20} H_{17} NO_4).—The history of the trials through which this alkaloid has passed must be continued to its chemistry. Indeed, it would seem strange if a substance that has gone through so many other vicissitudes should not have met with troubles in this department.

Prof. Buchner (1835) first assigned to berberine the formula C_{33} H_{18} NO_{12} (old notation).

In 1847, Thos. Fleitmann redetermined it from the analysis of berberine prepared by himself, the result being C_{42} H_{18} NO_9 (old notation).* He thought that the discrepancy between himself and Prof. Buchner probably resulted from the fact that Buchner examined an impure muriate of berberine. This paper led to a communication from Dr. George Kemp, † who, taking exception to Mr. Fleitmann's calculation, argued from Fleitmann's own analysis that the formula announced could not be correct. He therefore recalculated the formula from the figures of Mr. Fleitmann, and announced that C_{40} H_{17} NO_9 (old notation) more nearly agreed with the result of the analysis. ‡ However, from an analysis of the double chloride of berberine and platinum, he obtained the formula C_{42} H_{17} NO_7 (old notation).

Dr. Bödeker followed this with a communication to Liebig's Annalen, lxix., p. 37, in which, from an analysis of berberine made from Columbo, he agreed with Fleitmann that it is C_{42} H_{18} NO_9 (old notation).

Again, Dr. Hinterberger, 1852, from an analysis of the double chloride of berberine and mercury, and Kehl & Swoboda, 1853,§ from an analysis of a double salt of cyanide of mercury and muriate of berberine, both agree with Fleitmann's C_{42} H_{18} NO_9.

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* Chemical Gazette, 1847, p. 129.

† Chemical Gazette, 1847, p. 209.

‡ Gerhardt also noted the discrepancy in Mr. Fleitmann's formula, and proposed the formula C_{33} H_{19} NO_{10}. As shown by Mr. Perrins afterward, Mr. Fleitmann's formula was already too high in carbon.

§ Chemical Gazette, 1853, p. 70, from Ann. der Chem. & Pharm., lxxxiii., p. 339.

This was the unsettled condition of affairs when Mr. J. Dyson Perrins (1862) contributed his paper on the berberine question.* After reviewing the work of others, he very modestly states that "It is not without some hesitation that I allow myself to question the conclusions of chemists of the eminence of Fleitmann, Bödeker, and others; but my own results are so accordant with each other, the number of analyses I have made, and the variety of combinations I have examined are so considerable, that I feel not only justified in proposing an alteration of the formula, but, indeed, compelled to do so." He argues against Mr. Fleitmann's formula, as others had done, from his (Fleitmann's) own analysis, and says that "the numerical results . . . support the formula I propose rather than his own."

Mr. Perrins then presented the combustion of many salts of berberine, and ascribed to the alkaloid the formula C_{40} H_{17} NO_8 (old notation), which is accepted to-day; and we have C_{20} H_{17} NO_4 of the new notation.

That this formula is correct, has been settled beyond a doubt. Prof. Ernst Schmidt, of the University of Halle,† states that it is C_{20} H_{17} NO_4, as shown from numerous analyses, made of the pure base, the sulphate, hydrochlorate and nitrate; also from an examination of the hydroberberine. And lastly, we call attention to the combustions made by Prof. F. B. Powers and Prof. Virgil Coblentz (p. 105) of the berberine made by us from Hydrastis canadensis.

Properties.—‡Berberine crystallizes in tufts of dark brown-red needles, figure 31 representing the appearance of these crystals when slightly magnified. The crust that forms over the surface of the liquid is of a dark brown color. If a concentrated solution of berberine in alcohol be mixed with four parts of sulphuric ether a semi-crystalline magma of an orange yellow color is deposited. Micro-crystals of this are not so clearly defined and the salt is less soluble than the pure crystallized berberine. In connection with this subject we present (next page) figures 32 and 33, micro-drawings made by Mr. William J. Huck, under the personal supervision of Prof. F. B. Power, of the Department of Pharmacy, University of Wisconsin,§ from specimens of berberine prepared by us in the manner we have stated. Prof. Power contributes as follows:



FIG. 31.
Crystals of Berberine, slightly magnified.

"The alkaloid was presented in two forms, as a lemon yellow precipitate (made by precipitation with ether.—Ed.) without distinct crystalline structure, or as a reddish-brown crust, with a darker and somewhat crystalline exterior. Neither of these forms, however, admitted of exact representation, and the crystalline coating upon the crust, after being detached and brought under the

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* Journal of the Chemical Society, London, Vol. XV., 1862. p. 339.

† Berichte der Deutchen Chemischen Gesellschaft, 1883. No. 15, p. 2589.

‡ The berberine herein described was made according to our process and recrystallized from cold water over sulphuric acid. It responded to all tests for purity, was free from sulphuric acid, soluble in both water and alcohol.

§ Figures 32, 33, 34, 36, 37, and 38 are all the work of these gentlemen and prepared for our publication.



FIG. 32.
Crystals of Berberine (magnified 300 diameters).

microscope, showed such an imperfect aggregation that a drawing would be of little value. To obtain better crystals, both the yellow precipitate and a portion of the dark-colored crust were therefore dissolved in absolute alcohol, and the solutions allowed to evaporate directly upon an object glass.

"Fig. 32 represents the alkaloid berberine as precipitated from alcoholic solution by means of ether, crystallized upon an object glass, and magnified 300 diameters.

"Fig. 33 represents the reddish-brown crust of the alkaloid berberine as crystallized upon an object glass, and magnified 300 diameters.

"Neither of these show a definite crystalline form, while the crystals of Fig. 32 are especially irregular and much branched."

Berberine has a pure and lasting bitter taste and is odorless. It should dissolve without residue in both water and absolute alcohol.



FIG. 33.
Crystals of Berberine, (magnified 300 diameters).

Solubilities. — A reference to our history of the alkaloid berberine will render it unlikely that a name can be applied to so many different substances and these bodies have an accepted solubility. We find, therefore, that the solubility of berberine is stated to be all the way from one part in eighty of water, to one part in five hundred of water. According to our experience berberine varies in solubility in accordance with the proportion of the liquid to alkaloid and time of exposure, and we do not doubt that even with the same specimens different experiments will obtain discordant results. In presenting the following we will therefore say that a contact of one hundred hours was permitted in a closely-stopped bottle

between the liquid and an excess of one-eighth its weight of undissolved berberine at a temperature of 15.5° C. The mixture was shaken frequently, and after perfect subsidence of undissolved matter, the clear overlying solution was decanted, weighed, evaporated at an ordinary temperature by exposure to dry air, and the residue weighed and deducted from the weight of the solution. We used one ounce of berberine in each experiment.

Forty-five and one-fifth parts by weight of the solution of berberine in anhydrous alcohol yielded 6.7 parts of dry berberine.

Thirty-three and one-seventh parts of the solution of berberine in water yielded 1.9 parts of dry berberine. Consequently, one part of berberine dissolved in 6.79 parts of absolute alcohol and in 17.77 parts of water. It readily forms super-saturated solutions with both alcohol and water.

Berberine is practically insoluble in sulphuric ether, chloroform, carbon disulphide and benzol.

Decomposition Products of Berberine.—These are not of great interest to physicians or pharmacists, but we will briefly review the important features of the work that has been done in this direction. Fleitmann found that when berberine is heated from 160° to 200° C. vapors were evolved that condense to an oily liquid, which dissolves in alcohol and is precipitated from such solution by acetate of lead and by water. Hlasiwetz heated berberine in a sealed tube with water, and obtained a substance of a red color and a bronze-like luster by transmitted light, and a green color by reflected light. He added sodium amalgam to a boiling solution of berberine and produced a hydro-berberine of basic reaction of a yellow color and the formula $C_{20}\ H_{21}\ NO_4$. This formula has been confirmed (1884), by E. Schmidt,* who states that from its behavior with ethyl iodide, hydro-berberine must be a tertiary base. This author also formed berberine hydriodide by treating berberine with iodide of ethyl; and produced a dibasic acid $C_{10}\ H_{10}\ O_6 + 2H_2\ O$, by oxidizing berberine with an alkaline permanganate, which he considered identical with hemipinic acid.

Mr. O. Bernheimer† obtained as volatile products, ammonia and quinoline‡ by heating berberine in a retort with five times its weight of caustic potash. The residue was found to contain two acids which in properties agree with the acids announced first by Hlasiwetz and Gilm. One of these acids was supposed by H. and G. to be protocatechuic acid, and in this connection it is well to call attention to the fact that the alkaloid Hydrastine yielded protocatechuic acid when treated by Prof. B. F. Power with excess of caustic potash. Bernheimer obtained a yellow crystalline mass by heating hydro-berberine with methyl iodide in a closed tube which crystallized in the trimetric system from boiling methyl alcohol. This has the composition $C_{20}\ H_{21}\ NO_4$, Me I. and when suspended in water and treated with oxide of silver pro-

*Journal of the Chemical Society, 1884, March, p. 339.

‡Hlasiwetz and Gilm suggested that this substance was formed under these circumstances, and Bödeker had also previously announced that distilling berberine with either milk of lime or oxide of lead produced quinoline.

†Journal of the Chemical Society, March, 1884, p. 340 from "Gazzetta" 13, 342–347.

duced a crystalline hydroxide of the composition $C_{20} H_{21} NO_4$,Me HO + H_2 O. This is strongly basic, liberating ammonia from solution of ammonium chloride. The hydroxide decomposes when heated in a sealed tube, eliminating methyl alcohol. Mr. Bernheimer concluded that hydroberberine is a tertiary base.

The same author found that by heating berberine, mythyl iodide and mythyl alcohol together a methiodide $C_{20} H_{17} NO_4$,Me I, was produced. .

On treating this with silver oxide, the corresponding hydroxide was formed, similar in properties to the hydroberberine compound.

Fleitmann announced (1847) that a solution of sulphur in sulphide of ammonium ; mixed with a solution of hydrochlorate of berberine, produced a brown-red precipitate of a repulsive odor. This he washed and found still to contain sulphur, but he stated that it did not yield sulphide of hydrogen by treatment with hydrochloric acid. Mr. Bernheimer, upon the contrary, found this precipitate to be decomposed under these conditions with the evolution of sulphide of hydrogen, and the result proved to be hydrochlorate of berberine free from sulphur. He therefore assumes that the precipitate is probably a persulphide of berberine. Hydriodide of berberine ($C_{20} H_{17} NO_4$,HI) was produced by heating hydroberberine with iodine, both being in chloroformic solution. It is soluble in alcohol.

Salts of Berberine.—Berberine is a strong base and unites with acids, forming in many instances most beautiful crystalline salts. These salts of berberine are, as a rule, decomposed by the excess of an acid solution, especially if heated, and hence for example the muriate of berberine forms the sulphate when boiled with diluted sulphuric acid, although under like conditions the alkaloid has a stronger affinity for muriatic acid. It is obvious that the larger number of these compounds are not of interest to our readers, but a few are used in medicine and quite extensively. Some of these have interesting records, and in view of their positions in the history of the alkaloid berberine we were compelled several times to refer to them while considering that alkaloid. In this connection we will say that the early history and pharmacy of these substances has never to our knowledge been presented to the public, and we feel that in these pages it is accurately recorded for the first time.

MURIATE OR HYDROCHLORATE OF BERBERINE, $C_{20} H_{17} NO_4$. HCl. Crystallized, $C_{20} H_{17} NO_4$. HCl + 2 H_2 O.—The introduction into American medicine of the salts of berberine was an outgrowth of the introduction of the "concentrations" of early Eclecticism, and intimately connected with it. Therefore, we shall introduce muriate of berberine by the historical connection.

The preparation of podophyllin (Resin of Podophyllum, U. S. P.) in 1847* led to the preparation by similar processes of other materials from Cimicifuga racemosa, Veronica virginica, Sanguinaria canadensis, Cypripedium pubescens, and Hydrastis canadensis.* All of these substances were first

* See Eclectic Medical Journal, Cincinnati, January, 1849, p. 1, and compare statement of Wm. S. Merrell in American Journal of Pharmacy, 1862, p. 496.

made after the method employed in preparing podophyllin, by simply evaporating the alcohol from a tincture of the respective drug, and then pouring the creamy liquid into cold water. The precipitate, if it were capable of drying, was powdered and sold in that form; but if it was an oleoresin, it was distinguished as a "soft concentration." In an advertisement before us of August, 1852, we note, under the heading of "Concentrations":

"Powders.—Podophyllin, Leptandrin, Macrotin, Myricin, Sanguinarin, and Hydrastin. *

"Soft Concentrations.—Ptelein, Apocynin, Eupatorin, Asclepedin." †

Thus it happened that because podophyllum chanced to yield an active medicinal agent by this method, it was accepted that other similar substances would necessarily prove to be valuable, and Hydrastis was included. However, it was soon found that the precipitate, so-called Hydrastin, neither retained the sensible nor medicinal properties of Hydrastis. It is true that it had a yellow color, and was bitter; but the overlying liquid beyond a doubt contained the valuable constituents of the drug. These obvious facts led to experiments having for their object the separation of the real characteristic principles. After repeated trials, it was found that the addition of muriatic acid to the supernatant liquid (from which the so-called hydrastin had been precipitated) produced a brilliant yellow precipitate, that was very bitter, and seemed to possess the greater part of the sensible properties of the rhizome of Hydrastis. This was introduced into medicine as hydrastin neutral, to distinguish it from the former resinous substance known as hydrastin.‡

The introduction of this second substance inaugurated a confusion in nomenclature that, with the products of Hydrastis, has remained even to the present day. We find the two materials recorded in the prices current of the three principal manufacturers of those times, under three names, to-wit:

MAKER.	RESINOUS PRECIPITATE.	MURIATIC ACID PRECIPITATE.
No. 1.	Hydrastin.	Muriate of Hydrastin.
No. 2.	Hydrastin.	Hydrastin Neutral.
No. 3.	Hydrastin.	Hydra*stine*.

Thus it is that muriate of berberine was the first salt of the alkaloid used in American medicine, and was at first known by three names. Indeed, it was eventually known by four, because in a short time the resinous precipitate called hydrastin dropped from use, and the term hydrastin became affixed to this substance, muriate of berberine.

Eventually the name hydrastine neutral § was lost, and this muriate of

* These substances were mentioned by the late Wm. S. Merrell in the Eclectic Medical Journal, Cincinnati, July, 1852, p. 297. We have found no earlier record outside of the discovery of podophyllin by Prof. John King some years previously.

† Afterward the more appropriate term oleoresin was given to the "soft concentrations."

‡ See the first edition of the Eclectic Dispensatory, King & Newton, 1852, p. 214.

§ In those days this term was not so inappropriate. There was no known salt of muriatic acid and an alkaloid, of a practically insoluble nature, and consequently the salt was first thought to be an inactive chemical body which was thrown out of solution by the acid. We also call attention to the fact that Buchner and Herberger obtained the same substance, and regarded it as a weak acid or neutral principle.

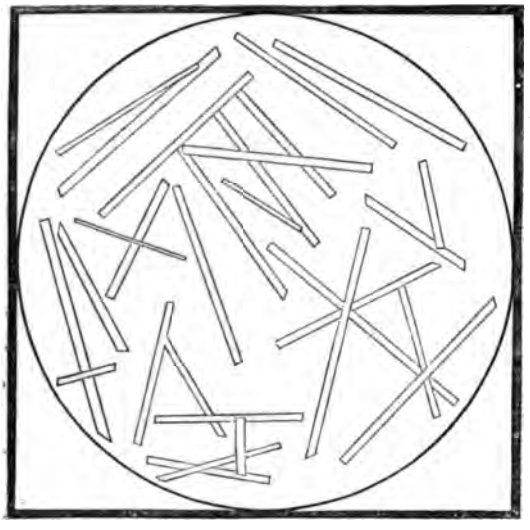


FIG. 34.
Crystals of Berberine Hydrochlorate, (magnified 60 diameters).

from dark-red to orange, the liquid will be transparent and syrupy. The liquid which results, mixes with alcohol, hydrochloric acid, nitric acid and officinal ether, but not with chloroform or benzol. With ammonia-water, it forms a dark-red liquid, and this will mix with water. Sulphuric acid also forms with it a dark-red solution, but this quickly changes to orange, with the evolution of gas bubbles. When diluted with water, an abundance of a yellow precipitate (*b*) results, which, when dry, presents the following characteristics: This precipitate is very bitter pulverulent at ordinary temperatures, but falls into a brittle mass when heated. It dissolves in officinal alcohol and ether, (but not in concentrated ether), forming in both instances orange-colored liquids, which stain organic matters yellow. Solutions of the hydroxides of potassium, sodium and ammonium, dissolve it, dark-red liquids resulting, which mix with water and alcohol in all proportions. The foregoing reactions would lead to the inference that this substance might be picric acid, but it is distinguished by the following properties: It is insoluble in chloroform and benzol. Its solutions do not precipitate with solution of ammonio-sulphate of copper, hydroxide of potassium, nor with solution of cinchonine in diluted sulphuric acid; and it gives no reaction with cyanide of potassium. Fleitmann calls it a yellow, difficultly soluble wax. Mr. H. Weidel has studied the oxidation products of berberine, and described berberonic acid, formed by the action of nitric acid on berberine, which can not be identical with this body, as he describes it as colorless, glassy crystals. *

Oxalic acid is another product of the action of hot nitric acid on hydrochlorate of berberine, and this is contained in the filtrate which passes when the precipitate (*b*) is separated. Both Henry and Buchner identified oxalic acid, and Buchner states that he obtained *only* oxalic acid as a result of the reaction. According to our experiments, the oxalic acid is in small amount, but if the proportions of the ingredients are varied, there might be a different result. In addition to the substances we have named, a yellow coloring matter results during the reaction between hot nitric acid and hydrochlorate of berberine, and this is soluble in water, alcohol, dilute acids and dilute alkalies. These decomposition products deserve further consideration.

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* We have access only to a summary of this paper, and therefore can not review it as we would like.

Sulphuric Acid, Action on Hydrochlorate of Berberine.—Sulphuric acid dissolves hydrochlorate of berberine with production of a lemon-yellow liquid, which, when heated, darkens, changes to a greenish brown, and finally to dark brown. When the solution of hydrochlorate of berberine in cold sulphuric acid is permitted to stand, it changes to yellowish-brown. There is a difference in statements concerning this reaction, for according to Buchner, the resultant solution is greenish-yellow; Chevallier and Pellatan, red-brown; and Polex, violet-red. Our experiments were made with the perfectly pure salt.

Hydrochlorate of berberine is dissociated when boiled with an excess of dilute sulphuric acid, bi-sulphate of berberine and hydrochloric acid resulting. This was part of Fleitmann's process for making the alkaloid (see page 101). If the amount of berberine hydrochlorate be great, a considerable proportion of the resultant bi-sulphate remains undissolved in consequence of the slight solubility of the salt in dilute sulphuric acid, even if hot. Ammonia water dissolves it immediately, the solution conforming to all the reactions of di-berberine sulphate.

Fleitmann states that the "reddish yellow" solution of hydrochlorate of berberine turns pale yellow on the addition of dilute sulphuric acid, and that the mixture, after a time, deposits delicate, pale, reddish-yellow needles. According to our investigations, a cold saturated solution of hydrochlorate of berberine is greenish-yellow, instead of "reddish-yellow," which latter color indicates the presence of impurities. When acidulated with sulphuric acid, it deposits minute lemon-yellow (instead of reddish-yellow) crystals, which dissolve at once when the liquid is rendered alkaline with ammonia water, thus showing that cold sulphuric acid in excess will decompose muriate of berberine with the production of a sulphate.

Hydrochloric Acid, Action on Hydrochlorate of Berberine.—Cold hydrochloric acid dissolves only traces of hydrochlorate of berberine, but, more freely upon boiling, forming a lemon-yellow liquid. The salt is not decomposed, and it crystallizes when the boiling solution cools.

Acetic Acid, Action on Hydrochlorate of Berberine.—Cold glacial acetic acid dissolves small amounts of hydrochlorate of berberine, and freely when boiling. A crystalline deposit forms when the hot liquid cools.

Hydroxide of Ammonium, Action on Hydrochlorate of Berberine.—Cold ammonia water dissolves small amounts of hydrochlorate of berberine apparently without decomposition, for the solution has the light yellow color of a solution of hydrochlorate of berberine. When boiled with an excess of ammonia water, an orange-colored liquid results, and upon further boiling a slight brownish precipitate is thrown down. It is apparent that the heated ammonia first liberates a small amount of berberine, which dissolves with the orange color, and is then partly decomposed, with production of the brownish substance. Upon cooling such a solution, an abundance of yellow crystals results, which, according to our examination, contain hydrochloric acid, and conform to the reactions of hydrochlorate of berberine. Schaffner states that warm ammonia

water forms a dark brown liquid with hydrochlorate of berberine, from which brown crystals are deposited upon cooling, a reaction we were unable to verify. Buchner and Schaffner supposed that ammonia combined with berberine under these circumstances, but we have not been successful in uniting them.

Hydroxide of Potassium or Sodium, Action on Hydrochlorate of Berberine.—Dilute boiling solutions of these alkalies dissolve hydrochlorate of berberine with liberation of berberine. This is shown by acidulating with sulphuric acid, whereby mono-berberine sulphate is produced. Concentrated hot solutions of these alkalies decompose the berberine, with production of a yellow resinous substance, almost insoluble in water. (See also decomposition products of berberine, p. 109). Hot dilute alcoholic solution of caustic potash acts like the aqueous solution of this alkali.

The carbonates of sodium and potassium, in dilute or concentrated solution, act like the alkalies.

Solubilities.—100 parts of distilled water, with one-eighth part of the undissolved salt, dissolved .204 parts of the hydrochlorate. Under the same conditions 100 parts of officinal alcohol dissolved .400 parts of the salt and 100 parts anhydrous alcohol dissolved .320 parts. It is practically insoluble in ether, chloroform or carbon disulphide.

Incompatibles.—The intense affinity that hot hydrochloric acid has for berberine renders this salt exceedingly stable, and, as we previous stated, led the discoverers to view it as a neutral body, or a weak acid. Consequently, it is not dissociated as easily as other alkaloidal salts. Boiling with excess of the mineral acids displaces the hydrochloric acid with the other. Solutions of the salts of silver decompose it immediately, and this is true of oxide and phosphate of silver, especially at high temperatures.

Hydrochlorate of berberine is mostly precipitated from aqueous solution by the addition of either hydrochloric or nitric acid, and largely, but less quickly, by sulphuric acid. Upon boiling with an excess of these acids, it is dissociated. Its aqueous solution is not precipitated by acetic acid, nor immediately by phosphoric acid (H_3PO_4). The solutions of many salts produce precipitates, among which may be named potassium cyanide (yellow), potassium ferrocyanide (dirty green), potassium chromate (yellow), and potassium iodide (yellow). It is not precipitated by either magnesium sulphate, copper sulphate, or ammonium oxalate.

Solution of picric acid and the soluble picrates precipitate the berberine completely from solution of hydrochlorate of berberine, with production of the insoluble picrate of berberine.

Mono-Berberine Sulphate—Bisulphate of Berberine $C_{20}H_{17}NO_4.H_2SO_4$.—This substance was introduced into medicine in America under the name Sulphate of Hydrastine. There are two sulphates of berberine (see di-berberine sulphate and phosphate of berberine), but as this is the one that has always been used under the name, it is the only sulphate recognized in commerce. Its medical value seems to be exactly that of muriate of berberine,

but owing to its more soluble nature, it has nearly displaced that salt from market. Sulphate of berberine has been a favorite with physicians ever since its introduction.

Owing to the fact that this substance can be purified without the application of heat, and that it readily forms a soluble di-berberine sulphate by the action of dilute alkalies, from which other salts are easily prepared, we prefer to make this sulphate, and from it produce the various combinations.

Preparation.—Moisten any convenient amount of powdered hydrastis with officinal alcohol, and pack the powder properly in a suitable percolator which has previously been prepared for percolation. Exhaust the powder with alcohol, conducting the operation until the percolate does not contain enough berberine to repay the expense of manipulation and the loss of alcohol.* Reduce the temperature of the percolate to 50° F. (10° C.), and then gradually stir into it a decided excess of sulphuric acid. The natural combination of the alkaloid will be overcome, and a magma of fine crystals of berberine sulphate will immediately result. Permit the vessel to remain in a cool location for twenty-four hours, and then collect the sulphate of berberine on a filter or strainer of muslin.† Reserve the filtrate for the preparation of the white alkaloid.

The sulphate of berberine at this stage of the operation is impure, being contaminated with free sulphuric acid, sulphate of calcium, a greenish oil which exists to a considerable extent in hydrastis, and with some other foreign substances.

Wash the sulphuric acid from the precipitate by means of cold alcohol; dry the precipitate, and mix it with sixteen times its weight of water; add ammonia water until in excess; allow the solution to stand a few hours, and then filter it. Add to the filtrate a slight excess of sulphuric acid, and collect the precipitated mono-berberine sulphate on a filter. Repeat this operation twice, and then dissolve the salt in boiling alcohol and crystallize it.

Description of Mono-Berberine Sulphate.—Excepting chromate of berberine, this sulphate of berberine is the darkest salt of the alkaloid known to us. When crystallized from a quickly cooled solution in boiling alcohol it forms beautiful groups of acicular crystals which, from their small size, have an orange yellow color. If the solution is less concentrated, and crystallization is conducted more slowly, the crystals are larger and of a deep orange color. When the crystals are of considerable size, an inch in length and an eighth of an inch in diameter, the natural color of the salt is that of a ruby, deeper than bichromate of potassium.

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* There can be no regular rule given for operations of this kind. The fineness of powder, packing of percolator, and temperature, influence the process to a considerable extent.

† When a concentrated aqueous extract of hydrastis in large amount is precipitated with excess of sulphuric acid, a finely divided, grainy precipitate of mono-berberine sulphate results. After this has subsided, white, needle-like crystals shoot out from the sides of the vessel and from the surface of the precipitate, which, when collected, washed with water, and dried, present a satin-like appearance. These are sulphate of calcium, and an examination of the precipitated sulphate of berberine, will show it to be largely contaminated with this substance which is also thrown down with it.

From what has been said it will be seen that the size of the crystals will alter the appearance of the salt. This may partly account for the discrepancy which exists in the writings of our authorities. In addition, the application of heat, as we have stated, will change the color, such action being undoubtedly accompanied by decomposition products. If an alcoholic solution be slowly cooled, crystallization commences with the formation of needle-like crystals, which, under certain conditions, will retain their characteristics until they cease to form. Under other circumstances, however, fan-like plates, resembling wasp wings, shoot out in most beautiful clumps, and, finally, perhaps another class of crystals will appear, consisting of granular nodules. These various forms are all sulphate of berberine, modified in appearance by different conditions of the solution and they are not different alkaloidal salts, a supposition once entertained by the writer. Upon separating them from each other, and severally dissolving them, all the modifications may crystallize from each solution, or the needle-like crystals may grow into the fan shape.

Figure 35 represents the micro-crystals of mono-berberine sulphate, prepared by us, and drawn for this publication by Mr. W. J. Huck, under the supervision of Prof. F. B. Power, of the Wisconsin University. They were mounted in glycerine, and were in the form of distinct acicular prisms.

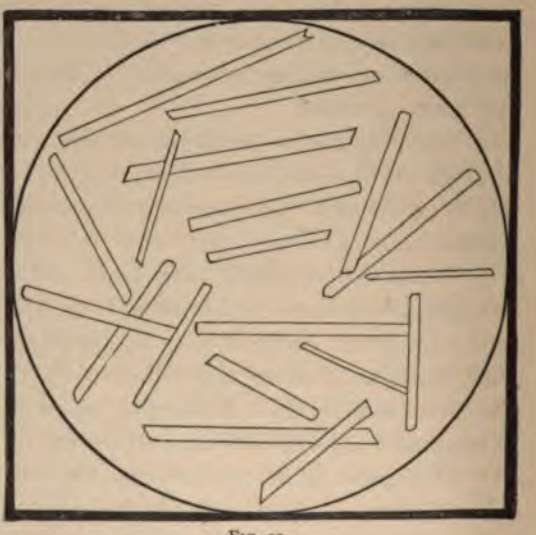


FIG. 35.
Crystals of mono-berberine sulphate (magnified 300 diameters).

Mono-berberine sulphate is odorless, and imparts to the taste a pure, persistent bitterness, which is devoid of the nauseating properties of such substances as quassia or aloes. When the fine orange-yellow crystals are gently heated, they darken and change to a deep orange, but resume their original hue when the salt is cooled. It dissolves freely in ammonia water, and from this solution the mineral and some other acids in excess throw down precipitates of a salt of berberine and the acid employed. We take advantage of this fact in making other salts of berberine, as before remarked, for it is usually easier and more economical to prepare this sulphate and decompose it, than to prepare the other salts direct from the percolate.

Mono-berberine sulphate crystallizes from both water and alcohol in an anhydrous form. An exposure of eight hours to a temperature of 100° C. does not result in loss of weight. A higher temperature fuses and then decomposes it, a carbonaceous mass remaining.

Action of Reagents on Mono-Berberine Sulphate.—Dilute sulphuric acid,

when boiled with mono-sulphate of berberine, does not immediately produce a red liquid. Cold concentrated sulphuric acid dissolves it, forming at first a greenish yellow, then a brownish, and finally a dark, almost black, liquid. Hot sulphuric acid dissolves it immediately with the production of a black liquid.

Cold hydrochloric acid dissolves a small portion of mono-berberine sulphate, forming a greenish-yellow liquid, which does not change upon boiling. If hydrochloric acid, or nitric, is added to an aqueous solution of mono-berberine sulphate, a flocculent mass of crystals of hydrochlorate of berberine, or nitrate of berberine, results. These do not dissolve upon the addition of an excess of ammonia water.

Hot glacial acetic acid freely dissolves sulphate of berberine, forming an orange liquid from which, upon cooling, a mass of fine crystals separate. These are freely soluble in ammonia water, from which solution either hydrochloric acid or nitric acid produce precipitates; sulphuric acid, however, under like circumstances, forms a dark brown liquid.

Hydroxide of ammonium dissolves mono-berberine sulphate freely and immediately, sulphate of ammonium and the di-berberine sulphate resulting. If to such a solution an excess of the ordinary acids be added, combinations of these acids and berberine results, with displacement of the sulphuric acid with crystallization of the berberine salt. Advantage may be taken of this fact to prepare other salts of berberine.

Carbonate of Potassium or Sodium solutions, if dilute, freely dissolve mono-berberine sulphate. Concentrated solutions of these substances decompose it, as with hydrochlorate of berberine.

In other respects, the remarks which we have applied to hydrochlorate of berberine may be applied to this sulphate.

Solubilities.—Mono-berberine sulphate dissolves slowly in water. After agitating one part of the salt for four days with seven parts of water, it was found that 100 parts of the solution contained 1.33 parts of the salt. If a mixture of mono-berberine sulphate and water be heated, however, it rapidly dissolves, forming a supersaturated liquid, which has a dark red color, and stains glass a deep orange. It can be filtered, and sometimes permitted to remain for some days in a cool situation, without other change than the deposition of aggregations of small grainy crystals. If a little sulphuric acid be added to this supersaturated liquid (sometimes only in minute amount to a portion of it), it immediately precipitates a magma of minute crystals of mono-berberine sulphate throughout the entire liquid, and the color of the supernatant liquid changes from red to yellow.

If mono-berberine sulphate be added to a ten per cent. solution of sulphuric acid in water, until an excess of one-eighth of undissolved sulphate is present, and the mixture be heated, the sulphate will entirely dissolve, and if the solution is permitted to cool, it will form a fine magma of minute crystals. If one part of mono-berberine sulphate be quickly dissolved in twenty parts of a hot five per cent. mixture of sulphuric acid and water, and then permitted to

slowly cool, beautiful tufts of needle-like crystals result. If such a solution be digested for some hours at a temperature of 80° C, its color changes to brownish red, and upon cooling, only a small portion of the salt crystallizes. These crystals have a brown color.

Cold alcohol dissolves but a small amount of mono-berberine sulphate. After agitating one part of the salt for four days with seven parts of alcohol, the solution contained but 22 hundredths of one per cent. of the salt. Boiling alcohol, however, dissolves the salt rapidly, and in large amount, the solution being of a dark yellowish red in bulk, and orange-colored in thin layer.

Mono-berberine sulphate is insoluble in carbon disulphide, benzol, chloroform, concentrated ether, and is but slightly soluble in officinal ether.

Incompatibles.—Mono-berberine sulphate is incompatible with the mineral acids, tannic acid, gallic acid, salicylic acid, picric acid, and the soluble salts of these acids, forming precipitates when mixed with solutions of them. It is also incompatible with alkalies and the alkaline carbonates, being decomposed by these substances. Vegetable astringents usually produce precipitates with it.

Di-Berberine Sulphate (Normal Sulphate of Berberine) $(C_{20}H_{17}NO_4)_2 H_2SO_4$.—This is the most beautiful salt of berberine. It has been used in medicine for some years, but never for a sulphate. A reference to the history of the alkaloid (p. 102) will show that its discoverer was probably Prof. Procter, although previous investigators were acquainted with the soluble compound that resulted when mono-berberine sulphate was added to diluted alkaline solutions. In our paper on phosphate of berberine, we introduce testimony which demonstrates that the substance sold in commerce under the name phosphate of berberine was in reality this compound. The so-called berberine (see p. 104) made according to the ammonia process was also the di-berberine sulphate. And we can not do better than to reproduce a portion of a paper contributed by us to the American Druggist * on the subject:

"In 1878, a paper on the salts of berberine, as produced from Hydrastis canadensis, was presented to the American Pharmaceutical Asssociation.† The writer announced that, when mono-berberine sulphate is added to ammonia water, by double decomposition a dark solution of berberine results, which, by mixing with alcohol, is mostly purified from the sulphate of ammonium which precipitates. . . . It is unnecessary to go over the properties of this substance in the present paper, as my object is to call attention to the fact that the substance obtained is not berberine, *but a soluble sulphate of berberine.* The writer has been aware of this fact for some years, but out of deference to an investigator who intended to consider the subject, waited for his report. However, this gentleman having withdrawn from the field, I feel at

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* American Druggist, Wm. Wood & Co., Sept., 1884, p. 166.

† This was by the writer (J. U. Lloyd).

liberty to make the foregoing statement, and in addition announce the following: . . . There are two sulphates of berberine. . . . The existence of these two sulphates was announced in New Remedies, 1877, p. 226, by Mr. H. B. Parsons and Mr. T. J. Wrampelmeier."

Thus it is shown that the so-called berberine of our process of 1878 was in reality a di-berberine sulphate, and the equation expressing its formation is as follows: $2C_{20}H_{17}NO_4.H_2SO_4+2NH_4OH=(NH_4)_2SO_4+(C_{20}H_{17}NO_4)_2H_2SO_4+2H_2O$. Therefore, we introduce the process we presented at that time as follows:

*Preparation of Di-berberine Sulphate.**—Rub eight parts of mono-berberine sulphate in a wedgewood mortar, cautiously adding ammonia water until in slight excess. Pour the dark liquid into thirty-two parts of boiling alcohol, and allow the mixture to stand thirty minutes, then filter. Stir into the filtrate thirty-two parts of cold concentrated sulphuric ether, and cover tightly. Surround the vessel with ice, and allow it to stand from twelve to twenty-four hours, then separate the magma of minute crystals of di-berberine sulphate with a muslin strainer or filtering paper, and dry by exposure to the atmosphere. Purify by crystallization from boiling alcohol.

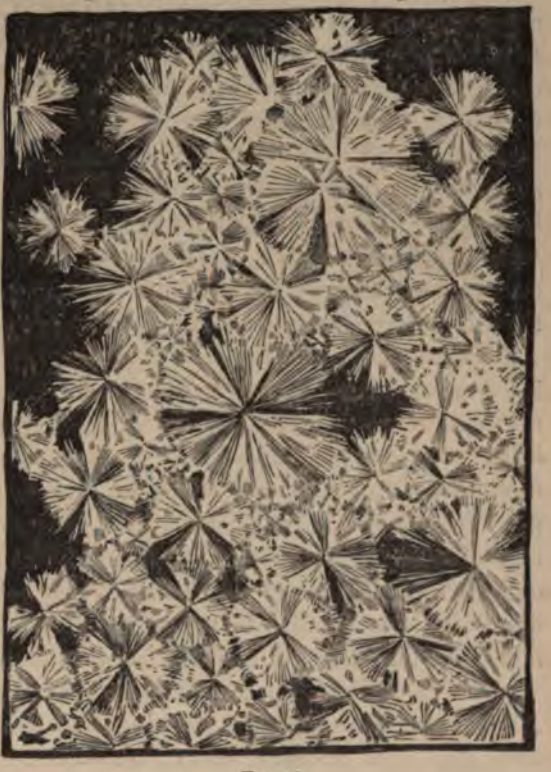


FIG. 36.
Crystals of di-berberine sulphate (natural size).

Properties.— Di-berberine sulphate is an odorless, purely bitter, lemon-yellow, crystalline powder, or orange-colored crystals (it should not be red under these conditions). It crystallizes from boiling alcohol in beautiful clumps of yellow spangles, and is the finest salt of berberine known to us. (See figure 36.) When slowly crystallized in large crystals from a concentrated aqueous solution, it is garnet red. Figure 37 (next page) represents the micro-drawing made for this publication by Mr. W. J. Huck, under the direction of Prof. F. B. Power, who describes them as follows: "These crystals are somewhat larger than those of the mono-berberine sulphate, and of an entirely different shape, several of the crystals

* In the original paper this is regarded as a process for making berberine.

frequently coalescing. As represented in the drawing (fig. 37), the crystals are magnified 60 diameters, and were mounted in Canada balsam."

Di-berberine sulphate is soluble in ten parts of water from an excess of one-eighth part of the salt, and under the same conditions in 293 parts of alcohol. When slowly added to anhydrous alcohol it dissolves, and finally a yellow magma separates, which, after being dried, is very much less soluble in water than the di-berberine sulphate, and almost insoluble in anhydrous alcohol. The chemistry of this change has not been studied, but it is not a decomposition of the di-berberine sulphate, with the formation of a molecule each of berberine and mono-berberine sulphate, as might be possible, for, $(C_{20}H_{17}NO_4)_2.H_2SO_4 = C_{20}H_{17}NO_4 + C_{20}H_{17}NO_4.H_2SO_4$. In one instance a specimen of several ounces of crystallized di-berberine sulphate, that had been kept in a securely sealed vial for three years, became altered in properties, and almost insoluble in water.



FIG. 37.
Crystals of di-berberine sulphate (magnified 60 diameters).

PHOSPHATE OF BERBERINE ($C_{20}H_{17}NO_4.7H_4PO_4 + 4H_2O$).—A substance was introduced into commerce by Dr. T. L. A. Greve, about the year 1877, under this name, and supposed to be a phosphate of berberine. It was in order to meet the demand for a more soluble salt than either the muriate or mono-berberine sulphate, which at that time were the only salts of berberine used in American medicine. This substance was made by Dr. Greve* by digesting in boiling water a mixture of mono-sulphate of berberine, and precipitated phosphate of calcium, filtering, evaporating the filtrate to dryness, dissolving the residue in boiling alcohol to free it from sulphate of calcium, and evaporating the filtered alcoholic solution to dryness.†

In 1877, Prof. H. B. Parsons presented to the Michigan Pharmaceutical Association a process for making phosphate of berberine, and in connection with Mr. T. J. Wrampelmeier, followed it in New Remedies, 1878, p. 226, by an interesting paper on the subject.

They prepared a salt in accordance with the process of Dr. Greve, but found from an analysis that it was free from phosphoric acid, the "*faint trace*" present existing as an impurity in the form of bone ash. Subsequent

* Eclectic Medical Journal, Cincinnati, 1877, p. 311.

† Dr. Greve states that, "The above process may also be varied by substituting phosphate of lead, or phosphate of barium, for the lime salt."

analyses demonstrated that the salt was a sulphate of the composition $(C_{21}H_{17}NO_4)_2.H_2SO_4$.*

Messrs. Parsons and Wrampelmeier then made the soluble calcium ortho-phosphate. An excess of this acid calcium phosphate, $CaH_4(PO_4)_2$, was then treated with mono-sulphate of berberine, when a precipitate of calcium sulphate resulted. The mixture was then evaporated nearly to dryness, and treated with hot diluted alcohol, whereby the remainder of the calcium salts were precipitated. The hot alcoholic solution of a berberine salt was then separated, by filtration, from the insoluble calcium salts, evaporated nearly to dryness, and then mixed with cold alcohol. A canary-yellow precipitate resulted, which, upon examination, proved to be a phosphate of berberine.

Phosphate of berberine was then made by Mr. Wrampelmeier, the acid phosphate of barium, $BaH_4(PO_4)_2$, being used instead of the ortho-calcium salt. This product agreed in every respect with that obtained by the other experiment.

Analysis and Properties.—Phosphate of berberine exhibited a strong affinity for water, a long exposure, at from 67° to 70° C, being required to free it from moisture. The mean of two experiments, after the salt ceased to lose weight by an exposure of 100° C, resulted as follows:

.2803 gram lost .0181 gram=6.45 per cent.
.3034 gram lost .0200 gram=6.59 per cent.
Average loss at 100° C, 6.52 per cent.

After destroying the organic matter by means of sulphuric and nitric acids, the phosphoric acid was estimated according to Fresenius' method, as magnesium pyrophosphate.

.3034 gram gave .2145 gram $Mg_2P_2O_7$=1894 of H_3PO_4.
.2803 gram gave .2000 gram $Mg_2P_2O_7$=1766 of H_3PO_4.

The average being 62.67 % of the phosphate of berberine employed.

The berberine was estimated by means of platinic chloride. According to Perrins, the precipitate has the formula $2C_{20}H_{17}NO_4.2HCl.PtCl_4$. Of which 18.22 % is platinum, and 61.899 % is berberine.

Phosphate of Berberine.	*Precipitate.*	*Berberine.*	*Berberine estimated from platinum in ash.*	*Berberine.*
.2517 gram gave	.1312 gram	=.0812.	.0815.	32.37 per cent.
.1727 gram gave	.0900 gram	=.0557.	.0526.	30.45 per cent.
.1224 gram gave	.0640 gram	=.0396.	.0390.	31.86 per cent.

The platinum in the precipitates was then estimated from the ash, and the berberine calculated, which was considered more reliable than the preceding process, as it excluded a source of error in the tared filter paper. The result is shown in the last two columns of the above table. The average of berberine from the platinum of the ash being 31.56 %.

* Dr. Greve, therefore, struck upon the soluble di-berberine sulphate, which the writer also obtained, about the same time, by another process. Neither of us assigned it to its proper position.

SUMMARY OF THE ANALYSIS.

	Percentage Found.	*Percentage Calculated.*
Water (H_2O)	6.52	6.58 per cent.
Phosphoric Acid (H_3PO_4)	62.67	62.76 per cent.
Berberine ($C_{20}H_{17}NO_4$)	31.56	30.65 per cent.
	100.75	99.99 per cent.

These results give $C_{20}H_{17}NO_4.7H_3PO_4+4H_2O$, as the formula for phosphate of berberine.* The following equation expresses the reactions: $C_{20}H_{17}NO_4.H_2SO_4+6[BaH_4(PO_4)_2]=C_{20}H_{17}NO_4.7H_3PO_4+BaSO_4+5BaHPO_4$.

This being the only analysis of a compound of phosphoric acid and berberine known to us, we deemed it desirable to add further information to this subject. Accordingly, we brought the matter to the attention of Prof. Virgil Coblentz, who agreed to make an ultimate analysis of the compound, and in this connection we call attention to the fact that the salt was made by him by the direct combination of phosphoric acid and crystallized berberine, instead of by double decomposition. We therefore introduce the following report: †

Preparation.—(Contributed to this publication by Prof. Virgil Coblentz). An accurately weighed quantity of the pure alkaloid, prepared by Prof. J. U. Lloyd, was dissolved in a sufficient amount of absolute alcohol, and into this solution exactly two grams of phosphoric acid (H_3PO_4) was weighed, the strength of which had been previously ascertained, two grams containing 1.2421 grams of absolute H_3PO_4. Then an equal bulk of absolute ether was added, and after allowing sufficient time for complete separation the mixture was thrown on a filter paper and the precipitate thoroughly washed with a mixture of alcohol and ether. The filter and contents were then removed and boiled in an excess of alcohol to remove all traces of adhering free acid, cooled, and mixed with its bulk of ether. The precipitate that formed was again thrown on a new filter and washed with a mixture of alcohol and ether until it was found to be free from uncombined phosphoric acid.

Gravimetric Estimation.—An amount of the alkaloid berberine weighing 0.460 grams was dissolved in absolute alcohol and treated as we have described. The liquids and washings were mixed and distilled water added; the ether and alcohol then evaporated by a gentle heat. To this aqueous solution of the free acid, ammonia water in slight excess was added and subsequently test magnesium mixture, until after having been well stirred and permitted to stand, no further precipitate followed the addition of the reagent. Ammonia water equal to one-fourth the volume of the liquid was then added, the vessel covered and allowed to stand for twelve hours. The precipitate of ammonio-

* "This formula seems, at first sight, an improbable one; but any person who will take the pains to look up the formulæ for the phosphates of the other alkaloids, will be surprised at their lack of uniformity, and at the fact that alkaloids exhibit no particular quantivalence."—PARSONS and WRAMPELMEIER.

† Prof. F. B. Power is also estimating the composition of phosphate of berberine, using a salt made by us, and crystallized from alcohol. Unfortunately, his report is not ready, and we will, therefore, present it to our readers at a future day in the Addenda.

magnesium phosphate was then collected on a filter and washed with a solution consisting of one part of officinal ammonia water and three parts of water, until the washings no longer produced a turbidity in a solution of nitrate of silver acidulated with nitric acid. The precipitate was then dried at 100° C., and ignited in a weighed crucible to low redness. From the weight of the resulting magnesium pyrophosphate ($Mg_2P_2O_7$), the amount of phosphoric acid contained in the solution was calculated, 100 parts of $Mg_2P_2O_7$ corresponding to 88.39 parts of H_3PO_4. 0.3297 grams of magnesium pyrophosphate were obtained from the solution, which corresponds to 0.2915 grams of phosphoric acid. Therefore, if from the 1.2421 grams of anhydrous H_3PO_4 contained in two grams of the phosphoric acid used we deduct the 0.2915 grams that remained uncombined, we have 0.9506 grams in combination with the berberine.

If one molecule of berberine $C_{20}H_{17}NO_4$ (335), combined with one molecule of H_3PO_4 (99), 0.460 grams of berberine would require 0.13595 grams of phosphoric acid. In reality nearly 0.9513 grams of acid are required theoretically to represent seven molecules of phosphoric acid, as (.9513 ÷ .13595); this number corresponds closely to that actually found, 0.9506.

Four estimations were made in accordance with the foregoing scheme, resulting as follows:

No. 1 gave 0.9506 grams of phosphoric acid (H_3PO_4), from 0.460 grams of phosphate of berberine.

No. 2 gave 0.9509 grams of phosphoric acid (H_3PO_4), from 0.460 grams of phosphate of berberine.

No. 3 gave 0.9508 grams of phosphoric acid (H_3PO_4), from 0.460 grams of phosphate of berberine.

No. 4. gave 0.9509 grams of phosphoric acid (H_3PO_4), from 0.460 grams of phosphate of berberine.

The average, 0.9508, is practically close enough to the theoretical amount, 0.9513, to show that one molecule of berberine phosphate must contain seven molecules of phosphoric acid, therefore making the formula $C_{20}H_{17}NO_4.7H_3PO_4$.

Volumetric Estimation.—This method depends on the indirect process of neutralization. 0.280 grams of the berberine were dissolved in absolute alcohol and phosphate of berberine was made as detailed on p. 124. The filtered mixture of alcohol and ether, containing the uncombined phosphoric acid, was then mixed with distilled water, and the ether and alcohol evaporated by a gentle heat. Into the aqueous solution that remained a normal solution of hydroxide of sodium was allowed to flow until sufficient of the latter was employed to insure the formation of the neutral sodium salt Na_3PO_4. Solution of chloride of barium was then added to this strongly alkaline liquid until no further precipitate was produced. After some hours, the resulting $Ba_3(PO_4)_2$ was collected on a filter and well washed with water, the filtrate and washings being collected in a beaker. This was colored with solution of

litmus and a normal solution of sulphuric acid was allowed to flow into it from a burette until a permanent pink hue resulted. The number of C. c. of normal acid solution required, deducted from the number of C. c. of the alkaline solution, was accepted as giving the amount of the latter required for the exact neutralization of the phosphoric acid; one C. c. of the normal alkali corresponding to 0.327 grams of anhydrous phosphoric acid.

SUMMARY OF THIS EXPERIMENT.

1.2421 grams of H_3PO_4 were contained in the 2 grams of acid used.
0.6638 " " " remained uncombined.

0.5783 " " " combined with the 0.280 grams berberine.

42.3 C. c. of normal solution NaOH used to neutralize the free acid.
22.0 " " " H_2SO_4 " " excess of NaOH.

20.3 C. c. amount required for exact neutralization of uncombined H_3PO_4.
Hence, 20.3 C. c. $\times$.0327=0.6638 grams of H_3PO_4 uncombined.

Four more experiments were made with the following result:

Experiment.

No. 1.	0.280	grams	berberine	$C_{20}H_{17}NO_4$	yielded of	H_3PO_4	0.5790	grams.
No. 2.	0.280	"	"	"	"	"	0.5788	"
No. 3.	0.280	"	"	"	"	"	0.5787	"
No. 4.	0.280	"	"	"	"	"	0.5788	"

If one molecule $C_{20}H_{17}NO_4$ (335) combines with one molecule of H_3PO_4 (99), then 0.280 gram alkaloid would require 0.827, but we find practically that 0.280 gram of the alkaloid combines with on an average 0.5788 gram of the acid. Then, as 0.5788÷.0827 equals about seven, hence if theoretically 0.5792 gram of the acid combine with .280 gram of the alkaloid, and practically the amount found is about 0.5788 of acid, the formula must then be $C_{20}H_{17}NO_4.7H_3PO_4$.

Properties.—Phosphate of berberine is a canary yellow powder, odorless and bitter. It changes to olive green when heated above 70° C., and gives up its water of crystallization at 100° C. It absorbs water upon exposure, and changes to a darker yellow, but does not deliquesce. Crystallized from hot alcohol, it forms irregular prismatic crystals. (P. and W.)

The crystalline structure of phosphate of berberine is represented by the micro-drawings (Fig. 38) made for our publication by Mr. W. J. Huck, under the direction of Prof. F. B. Power, who writes of them as follows: "The crystals are much broader than those of the preceding salts in consequence of the coalescence of several crystals, and the ends are very irregular in outline."

Solubilities.—One part of the crystallized salt dissolved in 10.43 parts of cold water.

One part of the salt dried at a temperature of 100° C. dissolved in 21.52

parts of cold water. It is almost insoluble in cold alcohol, and insoluble in pure alcohol, ether, and chloroform.

There is really no preference to be made for the pure phosphate over the di-berberine sulphate, which was really introduced for a phosphate. This fact has necessitated a longer paper than would be demanded by the phosphate in such a work as ours.



FIG. 38.

Crystals of phosphate of berberine (magnified 300 diameters).

NITRATE OF BERBERINE. $C_{20}H_{17}NO_4$. HNO_3+H_2O (Perrins).—Nitrate of berberine is sometimes used in medicine, but not as extensively as the muriate.

Preparation.—Nitrate of berberine is to be made according to the process employed in making the hydrochlorate, except that nitric acid is used instead of hydrochloric. This process can be followed even to the washing of the salt, for it is but slightly soluble in cold water. It should be dried, however, by exposure to a cool atmosphere, because decomposition follows when it is heated, especially if slightly moist.

Properties.—Nitrate of berberine obtained in this manner is in the form of a lemon yellow crystalline powder, odorless when fresh. It slowly dissolves in the mouth, imparting a bitterness to the taste. When kept for any length of time, especially during warm weather, or when heated in a test tube, it decomposes, evolving NO, and changes to a reddish color. The ultimate effect of this decomposition upon the constitution and properties of the residue has never been determined. According to Perrins it is perfectly stable at 100° C., but we have known it to decompose and evolve NO when kept in bulk at the ordinary temperature and become unfit for use. We do not consider it a desirable compound.

When nitrate of berberine is added to cold nitric acid, a dark brownish-red solution results, which, upon warming, changes to orange-red, with the evolution of an abundance of nitric oxide (NO). If one part of nitrate of berberine is gradually added to eight parts of hot nitric acid, nitric oxide is rapidly evolved, and finally the liquid changes from brown to a ruby red color. This solution has the characteristics which we have described (p. 113), under "Nitric Acid, Action on Hydrochlorate of Berberine," dissolving in the same solvents and contra, forming a yellow precipitate with water, and otherwise reacting so as to indicate that the products of decomposition in both cases are perhaps identical. Less heat, however, is required to produce the re-

action between nitrate of berberine and nitric acid than between hydrochlorate of berberine and nitric acid.

Nitrate of berberine dissolves in cold sulphuric acid, forming a dark brown or black liquid, which does not change upon heating. Dilute sulphuric acid (1 to 7) forms a red liquid if boiled with nitrate of berberine. This color is not affected by an excess of hydrochloric acid, but is changed to brown by an excess of ammonia water. Nitrate of berberine dissolves slightly in cold hydrochloric acid. If a mixture of nitrate of berberine and hydrochloric acid be boiled, the salt is decomposed, a dark brown liquid resulting.

Hot glacial acetic acid freely dissolves nitrate of berberine with the production of a dark orange-colored liquid, which, upon cooling, deposits an abundance of yellow crystals. These dissolve freely in ammonia water, and from this solution hydrochloric acid precipitates masses of hydrochlorate of berberine. Under the same circumstances either sulphuric or nitric acid, with the aforenamed ammoniacal solution, forms a deep red liquid.

Nitrate of berberine will dissolve to an extent in cold ammonia water and more freely upon boiling, and crystallizes from the latter solution upon cooling. It corresponds with hydrochlorate of berberine in its deportment towards dilute or concentrated solutions of the hydroxides of potassium or sodium.

Nitrate of berberine is insoluble in benzol, carbon disulphide and concentrated sulphuric ether. It is slightly soluble in alcohol, and more so in water.

The saturated solution of nitrate of berberine in cold water has a greenish yellow color. From this solution most of the berberine in the form of crystalline salts is deposited by nitric, sulphuric or hydrochloric acid, but not by the addition of acetic or phosphoric ($H_3 PO_4$), acid. No precipitate follows when magnesium sulphate, ammonium oxalate, lead acetate or copper sulphate are added to the aqueous solution, but a precipitate follows with potassium ferrocyanide (greenish), potassium chromate and potassium bichromate (yellow), and potassium iodide (yellow and gelatinous). Picric acid, picrate of ammonium, and solutions of the soluble picrates precipitate berberine completely from the solution of nitrate of berberine, the result being picrate of berberine.

CITRATE OF BERBERINE—*Preparation.*—This may be made by direct combination between solution of citric acid and berberine. When a solution of one part of di-berberine sulphate is dissolved in sixteen parts of water and two parts of citric acid are added, and the solution permitted to stand for some days in a cool location, beautiful tufts of crystals are formed. These are of a fibrous, silky texture, very bitter, permanent, and are free from sulphuric acid. (Figure 39), next page. They have never been analyzed. Citrate of berberine is not very soluble in cold alcohol or water, but more freely in boiling.

A cold aqueous solution of citrate of berberine has a greenish yellow color. Either sulphuric, hydrochloric, or nitric acid produces precipi-

tates when added to this liquid. Citrate of berberine is not precipitated from aqueous solution by solution of magnesium sulphate, ammonium oxalate or copper sulphate. Precipitates result, however, from the addition of potassium iodide (gelatinous), potassium ferrocyanide, potassium chromate, potassium bi-chromate and by acetate of lead. This last (acetate of lead), differs from the reaction with nitrate of berberine. Picric acid or picrate of ammonium precipitates the berberine completely.



FIG. 39.
Crystals of citrate of berberine, (natural size).

Citrate of berberine corresponds with nitrate of berberine and sulphate of berberine in its deportment towards concentrated sulphuric acid. If boiled with an excess of dilute sulphuric acid (1 to 7), the solution acquires a slight brownish tint and does not change by the addition of either hydrochloric acid or ammonia water. Hydrochloric acid dissolves citrate of berberine to a slight extent, forming a yellow liquid, which is not changed by boiling.

Citrate of berberine corresponds with nitrate of berberine in its deportment towards glacial acetic acid and nitric acid.

Solubilities.—Citrate of berberine is insoluble in benzol, carbon disulphide, concentrated ether, and chloroform. It is slightly soluble in officinal ether.

Ammonia water is a good solvent for citrate of berberine, a reddish-brown liquid resulting.

PICRATE OF BERBERINE.—This substance is formed when picric acid, or a soluble picrate, is added to the solution of any other salt of berberine. This compound is not used in medicine outside of the Homœopathic school, but it is of considerable interest to us as a test for berberine. We shall refer more fully to the characteristics of picrate of berberine hereafter.

Boiling distilled water dissolves very small portions of picrate of berberine, and upon cooling the solution, the salt separates entirely in crystalline form.

Picrate of berberine is insoluble in cold water, alcohol, ether, chloroform, benzol or carbon disulphide.

Nitric acid reacts with picrate of berberine in a manner similar to the action of that acid and hydrochlorate of berberine. The liquid which results from the action of hot nitric acid on picrate of berberine differs from that produced by hydrochlorate of berberine, as follows: With sulphuric acid it forms a red solution, which becomes lighter colored and cloudy on standing. It mixes with water in all proportions, forming clear solutions.

Sulphuric acid, hydrochloric acid and glacial acetic acid react with picrate of berberine similar to the manner in which they do with hydrochlorate of berberine.

Hydroxides of ammonium, sodium or potassium react as follows: Cold

dilute solutions scarcely affect it, and boiling dilute solutions dissolve it very sparingly. Concentrated solutions of these alkalies dissolve it more freely, and if these solutions are rendered acid with sulphuric acid, a cloudiness results, which is dissipated by the addition of ammonia water.

Picric acid and the soluble picrates completely separate berberine and berberine salts from aqueous solution.

DETECTION AND ESTIMATION OF BERBERINE.—In the first natural order of plants, we have yet to consider two that contain berberine. These are Coptis trifolia and Xanthorrhiza apiifolia, and we shall introduce the processes for estimating the alkaloid when we reach the latter plant.

HYDRASTINE (THE WHITE ALKALOID OF HYDRASTIS CANADENSIS). $C_{22}H_{23}NO_6$—*History of Hydrastine.*—In April, 1851, Mr. Alfred B. Durand published an essay in the American Journal of Pharmacy on Hydrastis canadensis. He had obtained, among other substances, a crystallizable body, and was inclined to view it as an alkaloid. With the light now before us, we know that his supposition was true, but in view of the fact that he could not make a crystallizable salt, he left the matter open, as follows: "For the present I shall therefore call the substance *Hydrastine*, with the hope that I will be more successful, after repeating my experiments on a large scale, in fully establishing its rank among the alkaloids." Since the alkaloid has not, as yet, yielded crystallizable salts with the acids Mr. Durand combined with it, viz.: nitric, hydrochloric, acetic and oxalic, it is not strange that he failed to obtain crystals. It seems that he neglected to continue his work; at least, he published nothing further on the subject. Hence, while the honor of the discovery belongs to Mr. Durand, the investigation of the character of the alkaloid and its salts must be placed to the credit of subsequent investigators; and in view of the opinions held by some persons, who believe that other parties discovered the alkaloid, we introduce a condensation of Mr. Durand's original process:

The crushed root of Hydrastis canadensis was macerated with cold water and then percolated with that menstruum, the percolate afterward being evaporated to dryness. 500 grains of the residue was dissolved in eight ounces of water, 125 grains of oxide of magnesium added, and the mixture digested on a sand bath for two hours, and then filtered. The residue within the filter paper was dried, digested in boiling alcohol, filtered, and the filtrate allowed to evaporate spontaneously. The result was, to use Mr. Durand's words, "beautiful, brilliant, yellow, four-sided, prismatic crystals, terminated by pyramidal summits."

In reviewing the process of Mr. Durand, it will be seen that, when the aqueous liquid obtained from the root was digested with magnesia, the acid then in natural combination with the white alkaloid united with the magnesia. This reaction was followed by precipitation of that alkaloid, which is insoluble in water, thus producing the "residue." This residue, upon being dried, was exhausted with boiling alcohol, in which menstruum, the alkaloid, is very soluble, and from it hydrastine was obtained in colored crystals by spontaneous

evaporation of the alcohol. In describing these crystals, Mr. Durand identified the white alkaloid of hydrastis so clearly as to leave no doubt in the mind of any person familiar with the alkaloids of hydrastis. He states "it is insoluble in water, sparingly so in cold ether and alcohol, more so in ether when hot, entirely dissolved by chloroform and boiling alcohol.'

The white alkaloid, hydrastine, is the only product of hydrastis that will conform to the foregoing description.

The color of Mr. Durand's alkaloid, a "brilliant yellow," was due to the presence of berberine, for that substance is most tenaciously held by hydrastine, and many re-crystallizations are necessary before it can be obtained colorless. (See preparation of hydrastine, p. 132, and Hale's "third alkaloid," p. 140).

Nothing was then written on the subject of hydrastine for a period of eleven years, although Prof. E. S. Wayne, of Cincinnati, made and presented to Prof. Procter (1856) a sample that, to use the words of Prof. Procter in the American Journal of Pharmacy, July, 1862, was "Identical in appearance and character with Durand's, except that it was lighter in color."

The next paper appeared in the American Journal of Pharmacy, July, 1862. The author, Mr. Wm. S. Merrell, speaks of having recently discovered two alkaloids in the rhizome of Hydrastis canadensis, and he proposed for them the names hydrastia and hydrastina. Both of these alkaloids had been discovered previously, one (hydrastia) being the well-known berberine. His description of that for which he proposed the name hydrastina, identified it as the alkaloid discovered in 1850,* by Durand, and prepared in 1856 by Wayne. Mr. Merrell's proposed name could not, therefore, be accepted, and as the sample Mr. Merrell submitted to the editor of the Journal of Pharmacy was darker in color than either that made by Mr. Durand or Prof. Wayne, nothing was added to the literature on this subject.

The alkaloid had not yet been purified, all the parties reporting that it was either yellow (Durand and Wayne) or greenish (Merrell). The production of the pure alkaloid was reserved for Mr. J. Dyson Perrins, who announced it in the London Pharmaceutical Journal, May, 1862. He purified it by repeated crystallizations from hot alcohol, and described it as crystallizing in "four-sided prisms, and of great brilliancy," and he said of it, "the crystals are white."

Mr. F. Mahla, of Chicago, next contributed to the American Journal of of Science and Arts, July, 1863, a paper on this alkaloid, and in 1878, the writer (J. U. Lloyd), read a paper before the American Pharmaceutical Association, on its preparation.

This brings us to the present year, and to the most important paper that has been written on the subject. It was by Prof. Frederick B. Power, of the University of Wisconsin, and was contributed to the American Pharmaceutical

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* Mr. Durand's paper was written in the summer of 1850, and published in 1851.

Association, 1884, and we shall make many references to this admirable treatise.

Preparation.—Hydrastine has always been made by decomposing the natural salt by means of an alkali. We introduce the process contributed by us to Prof. Power, by which we prepared the alkaloid examined by that gentleman, it is as follows:

"One thousand pounds of powdered Hydrastis canadensis were properly moistened with alcohol, packed in a suitable percolator, and percolation then conducted with the use of officinal alcohol as a menstruum. Sulphuric acid, in strong excess, was added to the percolate, and, after four hours, the supernatant liquid was filtered from the mass of crystals of sulphate of berberine ($C_{20}H_{17}NO_4.H_2SO_4$). To this filtrate ammonia water was added until it showed but a slightly acid reaction, then strained to separate the precipitated sulphate of ammonium, distilled to a syrupy consistence, and the residue poured into ten times its bulk of cold water. After twenty-four hours the precipitated resinous substances, oils, etc., were separated from the liquid by filtration, the filtrate being an impure solution of sulphate of hydrastine. Ammonia water, in decided excess, was then added to this resultant liquid, and the precipitate of impure hydrastine collected and dried. It was then digested with one hundred times its weight of cold water, to which sulphuric acid was carefully added to *slight* acid reaction, and, after twenty-four hours, filtered. The filtrate was again precipitated with excess of ammonia water, the precipitate collected on a strainer and dried. This precipitate was powdered and extracted with boiling alcohol, from which impure, dark yellow crystals of hydrastine separated when the alcoholic solution was cooled. The crystals were purified by repeated crystallizations from boiling alcohol. In order to obtain the hydrastine perfectly colorless, when in the form of large crystals, many crystallizations are necessary."

Where the operator labors under the disadvantages of imperfect apparatus, thus entailing a great loss of alcohol, water can be used as a menstruum. However, under these circumstances, impurities are introduced that are not present when alcohol is used. The mother liquor from berberine sulphate (see page 117) can be used and adapted to this process.

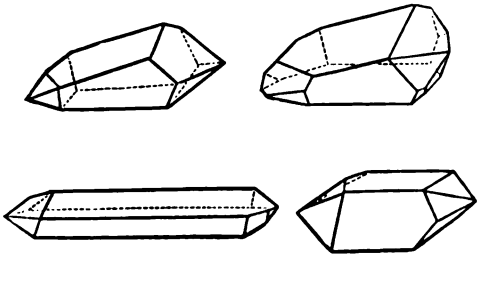


FIG. 40.
Crystals of Hydrastine (natural size).

Crystalline Form and Appearances.—Hydrastine always forms imperfect crystals. Even when slowly crystallized, in large quantity, they are irregularly developed, and as they almost invariably form in such a way as to present their lateral surfaces to the solution, it is difficult to obtain good specimens. Figure 40 illus-

trates a few crystals that were selected from a batch of eight pounds of the alkaloid, and present the most perfect of the specimens, and as they appeared in the solution. They are such as Prof. Power employed in making his measurements. The following description is that of Prof. Power, and figures 41 and 42 represent the perfected crystals as constructed by that gentleman.

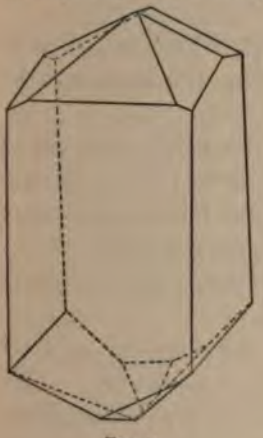


FIG. 41.

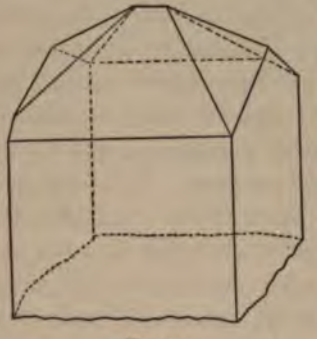


FIG. 42.

Crystals of Hydrastine (enlarged and perfected by Prof. F. B. Power).

"The crystals, which attain a maximum length of from eight to ten millimeters, have the form of four-sided prisms (Fig. 41 and 42), and apparently belong to the ortho-rhombic system, although the goniometer at my disposal did not admit of the exact measurement of the angles. The drawings here presented, which represent typical crystals, were formed by making an orthographic projection, and the angles may be said to be as geometrically accurate as is possible to obtain them without absolute measurements. In Fig. 42 the terminal faces are shown to be very perfectly developed, while Fig. 41 represents a crystal as viewed somewhat from the side and from above, the terminal faces not so symmetrically developed, and therefore having a somewhat more complicated form. It is interesting to observe that when both ends of the crystals are developed, as shown in Fig. 41, the corresponding terminal faces of opposite ends are invariably inclined to each other at an angle of exactly 90°."

Hydrastine can be crystallized in glassy crystals, perfectly colorless and very brilliant. As a rule, however, the crystals are opaque and white, owing to the presence of numerous fractures. When in this form and in small crystals, it may be quite colored and appear white.

Chemistry of Hydrastine.—The first analysis was made by Mr. F. Mahla,* who assigned to it the composition $C_{22}H_{24}NO_6$. From his figures Kraut deduced the formula $C_{22}H_{23}NO_6$†. Thus it is that the investigation of Prof. Power, in 1884, is the second published contribution to the subject, although Prof. J. F. Eykman, of Tokio, Japan, has investigated the subject, but has not, as yet, published the results of his analysis.‡ Prof. Power's analysis coincided very nearly with that of Mr. Mahla, although he followed a different method for making his determination. The following table compares the results of the analyses:

* Silliman's American Journal, Vol. 36, No. CVI., p. 57.

† See Power's paper on Hydrastine, Proceedings of the American Pharmaceutical Association, 1884.

‡ We are informed by Prof. Eykman that he is especially interested in the decomposition products of this alkaloid, and we hope some day to present his paper.

Calculated for $C_{22}H_{23}NO_6$	Prof. Power found.	Mr. Mahla found.	
C=66.48 per cent.	66.69 per cent.	66.69	66.38
H= 5.79 per cent.	5.61 per cent.	6.01	5.69
N= 3.53 per cent.	3.46 per cent.	3.83	3.76
O=24.20 per cent.			
100.			

Prof. Power states that "The results of both our analyses are seen to agree quite closely with the accepted formula, which may, therefore, now be presumed to be correct.

Properties of Hydrastine.—Hydrastine unites with the acids, and forms salts, none of which have as yet been crystallized. Prof. Power failed to produce a crystal, and we have exposed large amounts of the muriate, sulphate and citrate, to the most favorable conditions, and to a temperature of —28° C. in lots of ten pounds, without success. By spontaneous evaporation a glassy substance invariably remains, destitute of crystalline form.

When a salt of hydrastine is dissolved in water and then precipitated by an alkali, the result is a bulky amorphous magma of the alkaloid. This begins to shrink in bulk in a short time, and finally assumes a crystalline form, when the product will occupy but a small proportion of the bulk of the original magma. The addition of alcohol to such a precipitate hastens the change from the amorphous to the crystalline. Impure hydrastine precipitates white, owing to the minute division, but becomes very dark after assuming the crystalline form, carrying the coloring matters with it. For this reason it is not practical to purify the alkaloid by repeated solutions in acid water and precipitations with an alkali. Although mono-berberine sulphate is quite soluble in dilute ammonia water (forming the di-berberine sulphate), and hydrastine is perfectly insoluble in that menstruum, it is impossible to separate the berberine from sulphate of hydrastine by the method of precipitation. The tenacity with which the hydrastine holds this yellow alkaloid under these conditions led the writer to doubt for a long time the identity of this yellow substance and berberine (and others have been misled); but by repeated crystallizations of impure (yellow) hydrastine from boiling alcohol, a deep yellow liquid was obtained that, upon purification, yielded a considerable amount of berberine. One experiment, wherein a batch of six and one-half pounds of impure hydrastine was worked, yielded three and one-half ounces of mono-sulphate of berberine. (See Hale's "Third Alkaloid," p. 142.)

Hydrastine is tasteless if the saliva is of alkaline reaction. Its soluble salts are acrid.

Action of Reagents on Hydrastine.—According to Prof. Power, "The crystals of hydrastine are affected in the following manner by reagents:

"Concentrated sulphuric acid produces a yellow color, which, in contact with a crystal of potassium bichromate, becomes brown. Concentrated sulphuric acid, on warming, produces a bright red color. Concentrated nitric acid produces, in the cold, a yellow color, changing to reddish-yellow. Con-

centrated hydrochloric acid gives no coloration, either in the cold or upon warming. Concentrated sulphuric acid and monolybdate of ammonium gives an olive-green color, which appears to be its most characteristic test."

The solution of the hydrochlorate is affected as follows by reagents (Power):

"Ammonia water and the fixed alkalies give a white, curdy precipitate, sparingly soluble in excess; potassium iodide, potassio-mercurio iodide, potassium ferrocyanide, potassium sulphocyanide, mercuric chloride and tannic acid produce white precipitates; iodine and potassium iodide, a light brown precipitate; potassium bichromate, a yellow precipitate; picric acid, a bright yellow precipitate; platanic chloride, an orange yellow precipitate; auric chloride, a deep yellowish-red precipitate."

Decomposition Products of Hydrastine.—Crystals of hydrastine fuse "at 132° C. (Mahla states 135° C.), to a light amber-colored liquid. When heated on platinum-foil they decompose with the evolution of empyreumatic, inflammable vapors, reminding, as Mahla had previously observed, somewhat of carbolic acid, and leaving a large amount of ash, which burns slowly away at a red heat. In order to ascertain whether hydrastine is capable of yielding a hydro compound, five grams of the alkaloid were dissolved in dilute sulphuric acid, and subjected for about two days to the action of nascent hydrogen, as developed from metallic zinc and platinum. The liquid was then filtered, precipitated by ammonia water, in slight excess, and the precipitate, after washing, dissolved in hot alcohol, and allowed to crystallize. The crystals are insoluble in water, and closely resemble in appearance those of hydrastine, but possess a slightly yellowish tint, which could not be removed by repeated crystallization. The melting point also lies close to that of hydrastine, being observed at 131° C. I have not as yet subjected these crystals to ultimate analysis, but have formed therefrom and analyzed the hydrochlorate. The latter, like the hydrochlorate of hydrastine, is amorphous, and remains, by the evaporation of its solution, in the form of a transparent, yellowish varnish, yielding, however, a nearly white powder, freely soluble in water. After drying at 100° C., 0.7830 gram of substance gave 0.2560 gram AgCl=0.0651 gram HCl., or 8.31 %.

"This result would therefore indicate that a *hydro-hydrastine* is thereby formed, by the absorption of four atoms of hydrogen, and is analogous in composition to hydroberberine, $C_{20}H_{21}NO_4$ (Ann. Chem. Pharm. Suppl., 2, 191).

Calculated for $C_{22}H_{17}NO_6$ HCl.	Found.
HCl=8.34 per cent.	8.31 per cent."

—*Power.*

Prof. Power also formed combinations of hydrastine and both bromine or iodine, such reactions being accompanied by the evolution of considerable

heat, but he did not determine the composition of such compounds. By distilling a mixture of the alkaloid and caustic potash, unpleasant, inflammable vapors escaped, and a yellowish brown mass remained. Upon dissolving this in water and adding sulphuric acid until in slight excess, and distilling the liquid, formic acid was detected in the distillate. The residual acid liquid upon agitation with ether, and evaporation of the ethereal solution, yielded protocatechuic acid ($C_7H_6O_4$); and no other acids were identified. (This acid is also obtained as a decomposition product of berberine; see p. 109).

Upon treating hydrastine in alcoholic solution with ethyl iodide and subjecting it to heat, hydriodic acid was evolved, and the reddish yellow syrup that remained upon dilution with alcohol deposited a white crystalline powder. This dissolved freely in warm water, and crystallized colorless upon cooling. These were anhydrous, fused at about 183° C., but underwent decomposition by the application of heat. An analysis of this substance demonstrated that it had the composition $C_{22}H_{22}$ (C_2H_5), NO_6HI, and was evidently the *hydriodate of ethyl-hydrastine*. Since this compound was formed by the substitution of the ethyl radical (C_2H_5), for one atom of hydrogen of the molecule of hydrastine, Prof. Power considers hydrastine to be a secondary or imide base, and he writes as follows:

"In this respect, according to Henry* and Bernheimer,† it occupies an analogous position to berberine, since they obtained from the latter mono-ethyl and methyl derivatives, while, according to Perrins and Schmidt, in the case of berberine, the simple hydriodate of the base is thereby formed.

"That the crystalline compound obtained from hydrastine is really an ethyl derivate is evident, not only from the analysis, but I have also prepared the simple hydriodate by dissolving the alkaloid in freshly prepared hydriodic acid. As thus obtained, it is an amorphous substance, and very easily decomposed."

Solubility of Hydrastine.—Hydrastine is perfectly insoluble in water, or dilute alkaline solutions. Chloroform dissolves it freely, and is the best solvent we have found. It also dissolves in benzol, ether and cold alcohol, and freely in boiling alcohol. According to Prof. Power, it is insoluble in petroleum benzine, and its relative solubilities in the following liquids are as follows: One part of hydrastine in 1.75 parts of chloroform, in 15.70 parts of benzol, and in 120.27 parts of cold alcohol. Hydrastine unites with acids to form salts which are mostly soluble, tannic acid and picric acid forming insoluble combinations. These artificial salts are of acid reaction.

Salts of Hydrastine.—Muriate of hydrastine is used in medicine more extensively than any other salt, but the citrate is in some demand. These are both very soluble, and are colorless, although if a prolonged temperature be applied to the muriate, even if not above 82° C, it turns yellow.

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* Ann. Chem. Pharm. 115, p. 132.

† Gazz. Chim. Ital. xiii., pp. 329-342.

Alkalies decompose solutions of the salts of hydrastine, the alkaloid being precipitated.

These salts are best prepared by dissolving the acid in alcohol, and then adding an excess of hydrastine. After the solution ceases to take up the alkaloid, it is filtered and brought, if necessary, to a *very slight* acid reaction by means of the acid employed, and then evaporated at a low temperature to dryness. Salts of hdyrastine and some of the volatile acids are not permanent, but decompose upon drying them, the acid escaping. Prof. Power calls attention to this fact with acetic acid. The composition of the salts of hydrastine are as follows: Muriate of hydrastine $C_{22}H_{23}NO_6.HCl$ (Mahla & Power). Double chloride of hydrastine and platinum $(C_{22}H_{23}NO_6.HCl)_2+PtCl$ (Mahla & Power). Sulphate of hydrastine $(C_{22}H_{23}NO_6)_2.H_2SO_4$(Power). Double chloride of hydrastine and gold $(C_{22}H_{23}NO_6.HCl)_2AuCl_3$ (Power).

YIELD OF HYDRASTINE AND BERBERINE FROM HYDRASTIS CANADENSIS.—The proportion in which these substances exist in hydrastis is quite variable. The season of year in which the rhizome is gathered, the method of curing the drug, and its age, being instrumental in varying the amounts of the alkaloïds. If the drug is gathered in July or August, and quickly dried in the shade, it is in the best and most valuable condition. If it is gathered in the spring of the year, it is of inferior quality. Under any circumstance, carelessness in curing of the drug injures it, and may render it completely worthless. We have a constant experience in this variability of quality, and every year are compelled to reject considerable amounts that will not, in yield of alkaloids, repay the expense of working the material (see p. 95). That such a drug is not lost to the world may be inferred by consulting the table that we offer under powdered hydrastis, and it is to be hoped that in a day to come hydrastis (and other American drugs) may command a price in accordance with its real value.

The amount of berberine that exists in hydrastis is also influenced by the length of time the rhizome has been exposed to the atmosphere. It is constantly decomposing, even though the drug is stored in a comparatively protected position (see pp. 84 and 85). There seems to be a kind of decay that finally will result in the destruction of a considerable amount of berberine. In order to determine the progress with which this decay continues, we selected, 1870, pounds of freshly gathered, dried, hydrastis. Of this lot 500 pounds were worked at once, in a single percolatior; 700 pounds in like manner were worked in twelve months, and 670 pounds in twenty-four months. Every precaution was taken to insure the same manipulation with each batch. The result was as follows:

The first batch,	500	pounds,	yielded	9	pounds	of	mono-berberine	sulphate,	or	1.8 per cent.
" second "	700	"	"	9¾	"	"	"	"	"	1.39 "
" third "	670	"	"	9	"	"	"	"	"	1.34 "
Average of	1870	"	being	27¾	"	"	"	"	"	1.48 "

(The average yield of commercial hydrastis is from 18 to 28 ounces of sulphate of berberine to the hundred pounds. It is not profitable to carry the extraction to the utmost limit, and from 18 to 24 ounces is a fair product.)

Hence it follows that it is not economy to store hydrastis from year to year, and manufacturers of these alkaloids have learned to work the drug while recent. Regarding the white alkaloid, hydrastine, we can not present a similar line of comparison. It is our custom to reserve several batches in crude form, and work the product of about 5,000 pounds of hydrastis at once. The yield of purified hydrastine, perfectly white crystals, averages from one-fourth of one per cent. to three fourths of one per cent. of the drug employed.

In this connection we will remark, that we have often noticed that batches of the drug which gave unusually low amounts of berberine, were liable to yield an increased amount of hydrastine. Mr. J. W. Forbes informs us that he has also noted this peculiarity, in working the drug in large amounts. In one instance (recorded by us in 1879) a lot of 1,000 pounds of ground hydrastis was moistened with water, and, by an accident, only half of it could be worked at once. The remainder became heated and changed in appearance (becoming greener in color), and when it was worked, the berberine proved to have mostly perished. The result, however, was a yield of hydrastine very much in excess of that obtained from the other half of the drug.

These circumstances, taken together, would suggest that there was a natural connection between the alkaloids, the indication being that, if such is the case, hydrastine is produced in the economy of the plant, by the disintegration of berberine. Prof. F. B. Power, in reviewing the analyses of these alkaloids, is inclined to view this relationship as complex, if it exists at all, and he writes: "It is also quite evident that there is no simple relationship between hydrastine and the alkaloid berberine, $C_{20}H_{17}NO_4$, such as exists, between the associate alkaloids, morphine and codeine, or caffeine and theobromine." It must be admitted that, if such changes occur, they are perfectly obscure and beyond the light of our present knowledge of the chemistry of these substances. It must also be recognized that there are several constituents in hydrastis that, together with their decomposition products, are unknown. In this connection we are sometimes led to compare together the plants that yield berberine, and it is usual to find the alkaloid associated with more or less of another alkaloid. It is not unreasonable to infer that a connection exists between them.

HALE'S "THIRD ALKALOID OF HYDRASTIS."—*History.*—This substance is recorded under the name "Hale's Third Alkaloid." While it is true that Mr. A. K. Hale* obtained a body from hydrastis that seemingly possessed properties that would distinguish it from both berberine and hydrastine, he did not really announce that it was a new alkaloid, as some persons seem to suppose. The heading of his paper, "Is there a Third Alkaloid in Hydrastis Canadensis," indicates that the author was undecided, and took this method to bring his experiments before the public, in order that subsequent investigators might determine the matter.

* American Journal of Pharmacy, 1873, p. 247.

The material obtained by Mr. Hale was afterward identified by Mr. John C. Burt,* who gave a number of additional reactions. He also presented a micro-drawing of the sulphate, which we reproduce herewith (Fig. 43). Finally it was obtained by Mr. Herman Lerchen,† who affixed to it the name xanthopuccine.



FIG. 43.

Crystals of the Sulphate of Hale's "Third Alkaloid" (magnified).‡

It would seem that these determinations should establish the fact that such an alkaloid existed, but we can not pass the matter without presenting evidence that we feel is worthy of consideration, and which leads us to view the impure substance obtained by these gentlemen as a mixture of berberine, hydrastine, and impurities of hydrastis. We will first review Mr. Hale's process, as follows: "I treated the powdered root of Hydrastis canadensis in a percolator with distilled water until the strength seemed to be exhausted; then I proceeded to remove the berberine as a hydrochlorate by the addition of hydrochloric acid. Removing this precipitate of hydrochlorate of berberine by filtration, I then proceeded to obtain the hydrastine by adding water of ammonia (10 per cent.) until a precipitate ceased to be thrown down. This precipitate I separated by filtration, and dissolved in and crystallized from alcohol, when, instead of hydrastine, as the books described it, I found that the characteristic prisms of hydrastine were colored by and intimately mixed with a yellow powder, which I supposed to be berberine that had not been thrown down as a hydrochlorate. Being thus a little disconcerted at not obtaining the result I hoped for, I made another percolate of the drug, and to the mother liquor of berberine I carefully added water of ammonia (10 per cent.) to the neutral point. The precipitate thus obtained I dissolved in and crystallized from alcohol, which furnished beautiful and well-defined prismatic crystals of hydrastine, free from yellow coloring matter at all resembling berberine.

"To the neutral mother liquor of hydrastine, I now added water of ammonia (10 per cent.) to a strong alkaline reaction. This gave me a yellow precipitate, which I separated, and found to correspond with the yellow powder above mentioned as accompanying the first attempt to obtain hydrastine, and to be darker in color than berberine."

Mr. Hale thought that this yellow substance might be a new alkaloid, and it has since been referred to as "Hale's Third Alkaloid."

Remarks.—An important point in the foregoing paper is the oversight

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* American Journal of Pharmacy, 1875, p. 481.

† American Journal of Pharmacy, 1878, p. 470.

‡ Reproduced from American Journal of Pharmacy, Nov., 1875, as represented by Mr. John C. Burt.

made in neglecting to state whether the hydrochloric acid was added to the percolate until it was in *strong excess* (see p. 113).*

If it is only added until a decided acid reaction ensues, the natural combination in which the berberine exists is but partially overcome, and a large amount of berberine remains in solution. This is a feature that manufacturers of these alkaloids have to guard against, for if a considerable proportion of berberine is left in the mother liquid, it is largely thrown down with the hydrastine, and after being associated in this manner, its removal is difficult (see p. 134). Hence it follows that, if this precaution is not observed, the second precipitate by Mr. Hale's method is exactly as he describes it, but the yellow substance, as we have every reason to believe, is impure berberine.

The experimentor must also not overlook the fact that the alkaloids, hydrastine and berberine, are not the only substances thrown from solution by the *excess of ammonia*. A dark-colored, resinous body is also separated, and it adheres with some tenacity to the precipitate.† Thus it follows that, according to our views, also, and according to the results of our experience, a yellow precipitate may be obtained by means of Mr. Hale's process. Before introducing further testimony that we have to offer concerning the nature of this precipitate, we shall call particular attention to the following points:

1st. When ammonia water is added to the percolate until this liquid is neutral, a portion only of the hydrastine precipitates. This percolate contains salts of calcium and aluminium (doubtless from adhering soil), and especially is the hydroxide of aluminium thrown down before the hydrastine, or with the first portions of it. Therefore it may happen that, by exercising care in neutralization, the larger share of the hydrastine may really remain in solution after the liquid ceases to affect litmus paper. The filtration of such a neutral liquid, and addition of excess of ammonia water to the filtrate, produces a precipitate of hydrastine that is much purer than the first precipitate; *providing the operator had taken the precaution to add hydrochloric acid enough to the original percolate to separate the berberine*, and had waited for it to separate before filtering the liquid from the precipitated hydrochlorate of berberine.

If, however, the hydrochlorate of berberine has been but partially thrown down, in consequence of an insufficient amount of hydrochloric acid having been added to the percolate, the second precipitate is of a deep yellow color, and may be mixed with yellow nodules of impure berberine.

If the percolate is very concentrated, the chloride of ammonium may be in sufficient amount to keep the liquid of acid reaction until nearly all of the hydrastine is precipitated.

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* Mr. Lerchen, it is true, used the expression, "acidulating it strongly with hydrochloric acid," but he might have considered a decided acid reaction towards litmus as sufficient. In our experience, in order to precipitate all of the berberine possible (and it can not all be thrown down), hydrochloric acid to the extent of one-fourth the bulk of the percolate should be used.

† This substance is of considerable general interest, but it is not desirable to study it in this paper. Prof. E. Scheffer made an interesting line of experiments with it some years ago, and communicated his observations to us, but they have not been completed.

3rd. It is not safe to argue that because a distinct acid reaction (with HCl) will precipitate most of the berberine from an aqueous solution of pure berberine, and because a slight alkaline reaction is sufficient to throw down all of the hydrastine from an aqueous solution of pure hydrochlorate of hydrastine, these results will necessarily follow with an aqueous percolate of hydrastis. This liquid differs in solvent powers from pure water, and the natural combination in which these alkaloids exists is far stronger than any artificial union that we have been able to make by associating them together, after they have been purified. Indeed, we have no reason to hesitate in saying that we have failed to find satisfactory evidence to disprove the supposition that berberine and hydrastine exist in the rhizome as a double salt.

4th. If Mr. Hale's process of adding ammonia water in fractions, one to neutralization and the other to excess, produced two precipitates, why will not the immediate addition of a strong excess of ammonia throw down these two as a mixture? If such a mixture is obtained, it should contain the third alkaloid.

It has been our experience to work some thousands of pounds of hydrastis each year for the alkaloids. We obtain by this process a precipitate that contains hydrastine, berberine, and some other products, but we have not been able to purify the crystallizable yellow third alkaloid.

We have, also, time and again, followed Mr. Hale's directions, while working large amounts of the drug. We obtain a second precipitate, but by appropriate methods the yellow, bitter substance resolves itself into berberine.

Method of Separation.—There are several processes whereby this object can be accomplished, but one of the most successful is as follows:

Dry the precipitate, powder it, and then extract it with boiling alcohol and filter, which will leave the hydroxides of the alkaline earths; distil most of the alcohol and add the syrupy residue to several times its weight of water acidulated with sulphuric acid; filter and precipitate the filtrate with an excess of ammonia water; collect this precipitate, dry, and powder it. Then mix it with ten times its weight of cold alcohol and acidulate with sulphuric acid. The hydrastine dissolves, forming sulphate of hydrastine, while most of the berberine remains insoluble as sulphate of berberine. Collect and wash the precipitate, and purify it by re-crystallizations from hot alcohol. The product is sulphate of berberine. By collecting the residues, of the various steps, treating them again in the same manner, and repeating the operation, the crystallizable bitter yellow substance can be mostly separated, and will also be found to be berberine.

The hydrastine of the alcoholic solution contains still considerable berberine, which can be separated by repeated crystallizations.* By this method the two alkaloids can be separated from each other and from the associated im-

*We do not wish to be understood as saying that berberine is the only yellow substance present in the crude precipitate. It is not, for resinous and other bodies exist in it. To our experience, however, impure berberine is the only body that conforms to the third alkaloid.

purities; the berberine crystallized as sulphate of berberine, the hydrastine as the pure alkaloid. The result of one experiment of this kind, in which the precipitated crude hydrastine from several hundred pounds of hydrastis had been well washed with water, is recorded as follows:

Ninety-six ounces of crude precipitated hydrastine yielded 3½ ounces of *pure* crystallized sulphate of berberine, and 79 ounces of crystallized hydrastine. The residues did not seem to contain any substance to conform with the third alkaloid. Thus it happens that each attempt we have made to obtain this substance has failed.

Naturally, others have been interested in the matter, and, although we have questioned manufacturers of alkaloids, none have yet to our knowledge obtained it. Prof. Edward S. Wayne informs us that he has not been successful. Mr. J. W. Forbes, who for some years worked hydrastis in considerable quantities, recently denied its existence.

In order to determine if by any oversight of manipulation we were being misled, we laid the result of our work before Prof. A. B. Prescott (Mr. A. K. Hale was in his class at the time he made his determination), and sent to Prof. Prescott a sufficient quantity of the percolate to go over the matter. His investigation did not terminate successfully, and he kindly wrote us to that effect; remarking that this alkaloid doubtless should be ranked among the substances that had been recorded without sufficient examination.

Finally, we made a lot of the crude precipitate according to Mr. Hale's process; purified it, and separated the yellow crystalline sulphate (berberine), from the white alkaloid (hydrastine); and then sent a portion of each in a perfectly pure form to Prof. F. B. Power; and the yellow sulphate to Prof. Virgil Coblentz. Neither of these gentlemen were aware of the method employed in producing them, and their combustions supported each other. The yellow substance had the composition $C_{20}H_{17}NO_4.H_2SO_4$; the white crystals were $C_{22}H_{23}NO_6$.

Having thus reviewed this subject, we can only answer Mr. Hale's query by saying that the substance obtained by his process is, in our opinion, a mixture, and that the yellow crystalline body is impure hydrochlorate of berberine. We think that Mr. Hale's error has been caused by the small amount of hydrastis used in the investigation, which we understand was less than five pounds, and we believe that, had he obtained the substance in sufficiently large quantities, he would, in purifying it, have discovered its complex nature.

Other Constituents of Hydrastis.—There are additional constituents, some of which are of considerable interest in a general way, but none have come into use in medicine.

A fluorescent body exists in very small amount, and adheres to the hydrastine with considerable tenacity, but is mostly separated during the last crystallizations. It is soluble in chloroform, and is more soluble than hydrastine, in cold alcohol. Its solution in cold alcohol is colorless, but with a

strong blue fluorescence. If we mistake not, it has been recorded that hydrastine possesses fluorescent properties, but our experience is to a contrary effect. When crude hydrastine in considerable amount is dissolved in acidulated water, and the solution is rendered alkaline with ammonia water, sufficient of this principle remains in solution to impart a deep blue color. Since it presents fluorescent properties in alkaline solution instead of in acid liquids, it may be the same as æsculin, which substance is asserted to be identical with the fluorescent principle of Gelsemium sempervirens.

Among the products that precipitate in making berberine and hydrastine when the liquid from which the alcohol was distilled is mixed with water, are a greenish oil and acid bodies that may prove of considerable interest, as shown by Prof. E. Scheffer, who had them under consideration some time ago.

Hydrastine and berberine exist in natural combination with at least one acid, of a purely sour taste, which we obtained in considerable amount as a syrupy solution, but just as we completed its purification our laboratory and all its contents were destroyed by fire. We made it by throwing out the sulphuric acid from the refuse of sulphate of berberine, by means of carbonate of barium, and after purifying the barium salt of the vegetable acid, decomposing it with an exact amount of sulphuric acid. We shall repeat the experiment.

It is to be presumed that some of the other products of hydrastis will prove of great interest to the investigator.

Powdered Hydrastis.—The consideration of this substance would naturally follow that of the drug, but we have thought it best to first introduce the constituents of hydrastis, inasmuch as the quality of the powdered rhizome really depends upon the proportions of these substances. The history of our powdered drugs is, in many instances, not an inviting one, and hydrastis seems not to have escaped the stigma that is affixed to many other substances of this nature. It is true that, as a rule, the price of the rhizome is but a trifle, and yet it may perhaps be safely said that where there is a desire to cheapen a drug, it matters little how cheap it may be, something can be found to mix with it that is less expensive. However, we do not accept that an inferior powder must necessarily be deficient in quality from an intentional adulteration. The remarks we have made in the preceding pages, regarding the variation in quality of crude hydrastis will indicate that the powder may really be from the rhizome of hydrastis; unmixed with extraneous substances and still be of inferior quality. If a worthless drug is employed the powder can not be an improvement on the crude material. It is true, we think, that the inferior qualities of many American drugs may find their way into commercial powders. This, doubtless, was true to a greater extent formerly than at present. In our opinion wholesale druggists generally desire to furnish the better qualities of all drugs, crude or powdered. That they can not always do so is perhaps largely because it is understood too often that the value of a given drug is the same, regardless of its quality; and none will

deny the strong competition that the price brings to bear on dealers. Pharmacists are, in our opinion, more careful than formerly, and by the united efforts of these two bodies of men, pharmacists and jobbers, we doubt not that the progress towards a better day will continue. If we are correct, the present day is far in advance of a few years ago. We doubt if the time has ever been in the history of this country (since pharmacists commenced depending on dealers for their powdered drugs), that the qualities were equal to those of the present. The causes for an inferior powdered hydrastis, aside from intentional admixture, are the same as for the inferior drug. In considering the powdered hydrastis of commerce, should we, therefore, compare it with the average quality of the crude material such as is accepted without objection by a good pharmacist, or, with the choicest that can be obtained?

We must now leave this matter with the reader to judge as to the attention that is given this subject by pharmacists at large; but it seems to us that a dealer in a substance like powdered hydrastis can not be very severely criticised for supplying an inferior powder (shown to be inferior by analysis), if the same quality of crude hydrastis is accepted without objection by those who should act as authorities. It would be out of place for us to argue the question here, as to whether the standard of powdered hydrastis should be higher than that of the drug, but this phase of the question can with propriety be applied to other American drugs. It is a subject that will confront us before many years.

The description of hydrastis, as given in the United States Pharmacopæia, is not such as can afford a standard of comparison. There is no recognition of the powdered drug in that work, and no standard for the crude other than that derived from a description of the physical appearances.

In 1882, Mr. C. B. Allaire presented a report to the American Pharmaceutical Association, in which he records the microscopic examination of eleven specimens of commercial powdered hydrastis, all of which were adulterated. Mr. Allaire informs us, in a communication, that many of these specimens had been intentionally mixed with extraneous substances, but that in some instances the admixture was an earth that might have been present in the unwashed drug. However, it constituted such a large percentage that it could only be viewed in the light of an adulterant.

In 1883, Mr. E. C. Bassett, then in the chemical laboratory of the University of Michigan, examined, by the microscope, eighteen specimens of commercial powdered hydrastis. Of these, twelve were unadulterated; three contained a little curcuma as a coloring; one was about one fifth curcuma; one a mixture of curcuma and bean starch; and one curcuma and a foreign root that could not be identified. Thus it appears that two-thirds of these specimens were free from admixtures.

However, while the microscope will detect such foreign substances as may be mechanically added to the powdered drug, or powdered with it, it is obvious that it can not indicate the comparative value of the specimens that

are unmixed; and it is essential that a chemical method of detection be employed under such circumstances. That it can be made readily and simply is demonstrated by the nature of the constituents, and as at present the berberine is considered the important one, a comparison of the proportions of berberine is probably our best method of standardizing the drug. *

Appearance of Powdered Hydrastis.—This powder is not a bright yellow. Upon the contrary, it is usually of a dull yellowish hue, and often with a slight tinge of green. The brown surface of the rhizome and rootlets, and the decayed fragments that are always more or less intermixed with the crude drug, destroying the rich yellow that would otherwise be a characteristic; and thus, if commercial powdered hydrastis is a bright yellow, it is perhaps open to suspicion. Powdered hydrastis has the characteristic odor of the rhizome, as described on page 85 of this publication.

Estimation of Berberine in Powdered Hydrastis.—The remarks that we have made in the preceding pages on the berberine subject will indicate that a method of estimating this alkaloid under one condition may perhaps be unreliable under certain other circumstances.

We shall not consume time in this place with the difficulties that accompany the processes that we have tried; for in the future we must consider this alkaloid in a broader field than it occupies in this one plant, and our remarks will then be more pertinent. The fact that it is associated with one, and perhaps, other alkaloids, necessitates a scheme that will disentangle it from such associations or combinations, and it is desirable also that the scheme should be as simple as possible and as easily applied as is practicable. We prefer the following process: †

Reduce the hydrastis to an impalpable powder, if it is not already in that condition, and then macerate one part of the powder with eleven parts of officinal alcohol, shaking often. After four days permit the powder to subside completely, and decant the overlying liquid. Add to the magma sufficient alcohol to produce the original bulk, and repeat the operation. Repeat the maceration with a third portion of alcohol and decant as before. Mix these decanted liquids, and after twelve hours filter them, washing the filter paper with a little alcohol. Add to the filtrate one-third its bulk of officinal sulphuric ether, and then hydrochloric acid to the extent of three-tenths, and sulphuric acid to the extent of one-tenth the weight of the hydrastis employed. Place the liquid, after mixing well, in a cool place, and after forty-eight hours collect the crystalline precipitate on a filter paper and wash it with a mixture of equal parts of sulphuric ether and alcohol until the crystals are free from uncombined acid; then dry it at a temperature of 125° Fah. and weigh it.

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* Since this sentence was in type, the investigations of eminent medical authorities have drawn attention particularly to *Hydrastine*, and the indications are that this alkaloid may become the most important constituent.

† The berberine is not as completely extracted by this as by a process that we shall introduce at a future day; but for simplicity this process is desirable.

This process practically abstracts from the hydrastis its berberine, and precipitates it almost completely and as a nearly pure salt. It is true that some may prefer to employ percolation, but to our experience, in unskillful hands the process of maceration is less likely to be followed by variation in product. We do not deny that some berberine remains in the drug, for by another process the extraction is more perfect; but this process will answer as a method of comparison.

The addition of the sulphuric ether to the alcoholic solution produces a menstruum in which, if acidulated as we direct, the hydrochlorate of berberine is so nearly insoluble as to leave no trace of bitterness after separation of the salt.* It must be also observed that, while this process is capable of precipitating a larger amount of berberine than can be obtained by the process we use in making hydrochlorate of berberine (see p. 113), it is less economical on a manufacturing scale, for the increased yield is more than counterbalanced by the expense of the ethereal menstruum; and at the usual price of hydrastis it is false economy to carry the extraction of the drug beyond a limit that is sufficient to repay in yield of berberine, the loss of material and the time consumed. Hence, in connection with our remarks on page 137, in which we present the average economical yield of berberine from ordinary commercial hydrastis, we record the following table, which gives us the comparative qualities of powdered hydrastis, as found in the American market: †

TABLE SHOWING THE EXAMINATION OF FORTY-NINE SPECIMENS OF COMMERCIAL POWDERED HYDRASTIS.

Specimen	1	yielded from	60	parts	Powdered Hydrastis	1.34	parts	Berberine Hydrochlorate, equalling	2.23	per cent.
do	2	do	do	do		1.335	do	do	2.22	do
do	3	do	do	do		1.26	do	do	2.10	do
do	4	do	do	do		1.25	do	do	2.08	do
do	5	do	do	do		1.25	do	do	2.08	do
do	6	do	do	do		1.23	do	do	2.05	do
do	7	do	do	do		1.21	do	do	2.04	do
do	8	do	do	do		1.19	do	do	1.98	do
do	9	do	do	do		1.19	do	do	1.98	do
do	10	do	do	do		1.18	do	do	1.96	do
do	11	do	do	do		1.16	do	do	1.93	do
do	12	do	do	do		1.15	do	do	1.91	do
do	13	do	do	do		1.12	do	do	1.86	do
do	14	do	do	do		1.12	do	do	1.86	do
do	15	do	do	do		1.10	do	do	1.83	do
do	16	do	do	do		1.10	do	do	1.83	do
do	17	do	do	do		1.10	do	do	1.83	do
do	18	do	do	do		1.08	do	do	1.80	do
do	19	do	do	do		1.08	do	do	1.80	do
do	20	do	do	do		1.08	do	do	1.80	do
do	21	do	do	do		1.08	do	do	1.80	do
do	22	do	do	do		1.08	do	do	1.80	do
do	23	do	do	do		1.05	do	do	1.75	do
do	24	do	do	do		1.04	do	do	1.73	do
do	25	do	do	do		1.04	do	do	1.73	do
do	26	do	do	do		1.01	do	do	1.68	do

* Hydrastis contains coloring matters besides berberine, hence the liquid is not decolorized.

† This line of experiment was instituted by Mr. Leslie Soule in our laboratory, the method of investigation being in accordance with the scheme announced on preceding page. The specimens came from Indianapolis, Philadelphia, Little Rock, Louisville, Zanesville, South Bend, Ind., Pottsville, Pa., Chillicothe, O., and Lynn, Mass. Equal amounts of each were operated upon, and all carried simultaneously until the work was completed.

Specimen	27	yielded	from	60	parts	Powdered Hydrastis	0.98	parts	Berberine Hydrochlorate, equalling	1.63 per cent.
do	28	do	do	do		0.97	do	do	do	1.61 do
do	29	do	do	do		0.97	do	do	do	1.61 do
do	30	do	do	do		0.97	do	do	do	1.61 do
do	31	do	do	do		0.94	do	do	do	1.56 do
do	32	do	do	do		0.94	do	do	do	1.56 do
do	33	do	do	do		0.91	do	do	do	1.51 do
do	34	do	do	do		0.90	do	do	do	1.50 do
do	35	do	do	do		0.85	do	do	do	1.41 do
do	36	do	do	do		0.83	do	do	do	1.37 do
do	37	do	do	do		0.83	do	do	do	1.37 do
do	38	do	do	do		0.79	do	do	do	1.31 do
do	39	do	do	do		0.70	do	do	do	1.16 do
do	40	do	do	do		0.70	do	do	do	1.16 do
do	41	do	do	do		0.62	do	do	do	1.03 do
do	42	do	do	do		0.61	do	do	do	1.01 do
do	43	do	do	do		0.57	do	do	do	0.95 do
do	44	do	do	do		0.54	do	do	do	0.90 do
do	45	do	do	do		0.35	do	do	do	0.58 do
do	46	do	do	do		0.31	do	do	do	0.51 do
do	47	do	do	do		0.24	do	do	do	0.40 do
do	48	do	do	do		0.21	do	do	do	0.35 do
do	49	do	do	do		0.205	do	do	do	0.34 do

REMARKS.—It will be observed that the yield of hydrochlorate of berberine varies from 2.23 per cent. to 0.34 per cent. Twenty-seven of the specimens were below the average working yield (1.8 per cent.) of fresh commercial hydrastis, as recorded on page 137, and seventeen specimens were above it. Five of the specimens gave the exact amount. It may safely be said that the specimens below this were inferior, for a quality of hydrastis that yields 1.8 per cent. by our working process will assay considerably better; and our experience is that the average assay of berberine hydrochlorate is not less than 2 per cent. That it may be above this is shown by the first seven specimens of our table. Averaging, however, those recorded above 1.8 per cent., we have a result of 1.98½. The powdered hydrastis of commerce should, in our opinion, not only reach this figure by this process, but assay 2 per cent. Allowing, however, for age and imperfect rhizomes, which some may contend should have a consideration, we may possibly lower the figure to 1.95 per cent. It will be observed that of the 49 specimens assayed but 10 reached this standard and 7 were actually less than one per cent. Of these very low specimens we can only say that, even though gathered in early spring-time and imperfectly cured, we have never met with so small a yield of berberine from hydrastis, and there is but one inference in regard to the matter. The pharmacist who purchases such a powder pays an exorbitant price when quality is considered. The physician who prescribes such a drug can not hope for a positive action.

To sum up, accepting the berberine as a standard, commercial powdered hydrastis as found in the drug market of this country is nearly four-fifths below grade, and a very considerable porportion of it is certainly adulterated with foreign bodies, or it may be with the dried and powdered hydrastis muck from which the alkaloids have been extracted.

*The Detection of Curcuma in Powdered Hydrastis.**—Solution of caustic potassa with curcuma gives an immediate deep orange brown coloration which, in the course of a few hours, assumes a decided purple hue. With pure powdered hydrastis no change occurs. In mixtures of the two the deepness of both the primal and ultimate colors is in direct proportion to the curcuma. Hydrochloric acid furnishes a somewhat lighter orange red which slowly fades to a pink with curcuma, but no coloration whatever with the pure

* Mr. E. S. Ely made in our laboratory a series of examinations of hydrastis, curcuma, and admixtures of hydrastis with curcuma and such indigenous drugs as we have found associated with hydrastis. This interesting paper is to be found in the Druggists' Circular, May, 1885, and in acknowledgment of his work, and that of Mr. Soule, we herewith extend our thanks for their value to this publication. The necessity for the introduction of the test for curcuma is evident from Mr. E. C. Bassett's investigations (see page 144).

hydrastis. In mixtures of the two the same colors are produced as with curcuma alone, but varying in density according to the percentage of the latter. The caustic potassa solution is much the more delicate test of the two, giving immediate and distinct colorations where the acid entirely failed. The best method to conduct the foregoing tests is to place about a drachm of the suspected powder upon white filtering paper, and then carefully drop sulphuric ether upon it until the coloring matter is well extracted and diffused over the surface beyond the powder. The ether is allowed to evaporate, when a drop of caustic potassa or hydrochloric acid is added to the colored portion of the paper. A coloration will follow if curcuma is present, as described under tincture of hydrastis.

This test is so delicate as to actually show an admixture of one part of curcuma with 10,000 parts of hydrastis, a perceptible delicate red color appearing at the margin of the spreading alkaline liquid as it passes through the ether stain.

The Detection of Curcuma in Tincture of Hydrastis.—Saturate white filtering paper with the tincture, and allow it to dry. Upon the addition of solution of caustic potassa an immediate orange brown color is produced which gradually assumes a purple hue if curcuma is present, the colors being more or less deep according to the percentage of the latter. Tincture of pure hydrastis is not affected when treated likewise. If a small amount of the suspected tincture be placed in a test tube and caustic potassa added, the orange brown coloration quickly appears if the curcuma is present, even where the paper test fails. Pure tincture of hydrastis, under the same conditions, is not discolored, but rendered turbid, owing to an alkaloidal disturbance. Concentrated hydrochloric acid colors curcuma paper prepared from the tincture a deep reddish brown, which gradually fades to a pink. The hydrastis paper furnishes no coloration. In the test tube, hydrochloric acid furnishes an intense cherry red liquid with the curcuma tincture, but only renders the tincture of hydrastis slightly turbid, and finally a crystalline mass of hydrochlorate of berberine separates, with no coloration. In each of these tests upon mixtures of the tinctures of hydrastis and curcuma, the colorations and their intensity are directly proportioned to the percentages of curcuma.

These reactions are conclusive, and may be summed up as follows: Neither hydrastis nor tincture of hydrastis affords the color reactions of curcuma or tincture of curcuma. If celastrus root be mixed with the hydrastis, the potash reactions of curcuma may be masked, as the former affords a black or deep brown coloration, according to its percentage, that might predominate the orange brown and purple of curcuma. In this case the hydrochloric acid test serves to detect the latter, since with it the celastrus gives but a very slight reddish coloration, with no pink after-color.

We scarcely consider it necessary to consume more time with this subject. Our work supports the report of Mr. Allaire and Mr. Bassett, and we doubt not that if our pharmacopœia revisers find it advisable to standardize hydras-

tis, the act will be followed by an improvement in the quality of the commercial drug.

PHARMACEUTICAL PREPARATIONS.—*Fluid Extract of Hydrastis.*—The present officinal process for making this fluid extract is as follows:

"Hydrastis, in No. 60 powder, one hundred grammes, alcohol, water, each a sufficient quantity to make one hundred cubic centimeters.

"Mix three parts of alcohol with one part of water, and, having moistened the powder with thirty grammes of the mixture, pack it firmly in a cylindrical percolator; then add enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding menstruum, until the hydrastis is exhausted. Reserve the first eighty-five cubic centimeters of the percolate. By means of a water-bath, distil off the alcohol from the remainder, and evaporate the residue to a soft extract; dissolve this in the reserved portion, and add enough menstruum to make the fluid extract measure 100 cubic centimeters."—U. S. P., 1880.

This produces a very bitter, dark-colored liquid of a reddish yellow color in thin layer, and upon shaking the bottle that contains it, a deep yellow stain remains where the liquid adheres to the glass. When freshly prepared it is transparent, but it sometimes becomes of a muddy appearance by age. If it be prepared of prime hydrastis, and perfectly percolated, a deposit follows, often within a few days of the time of its preparation. In cool weather, especially if the fluid extract was prepared (as it should have been) in a warm location, this precipitate is abundant, forming a deposit that will perhaps occupy one-fourth the bulk of the liquid. This sediment is largely made up of yellow crystals, and in very cold weather beautiful spangles of crystals form upon the inside of the container. This crystalline sediment is a berberine compound, and in accordance with its production the berberine value of the solution decreases. For this reason, a fluid extract of hydrastis that has precipitated in this manner should be shaken before using it. If it be heated, the sediment mostly dissolves, to re-precipitate when cooled. Taken altogether, we do not feel that the officinal fluid extract of hydrastis is a very acceptable pharmaceutical, but by the crude and simple method of percolation it may be difficult to obtain a more satisfactory liquid by using any menstruum that is a mixture of alcohol and water. Within three weeks' time a specimen that had been made under our direction, very carefully, from prime hydrastis, lost 18.85 per cent. of its berberine by precipitation.* Hence we should not expect the commercial fluid extracts of hydrastis to be of uniform strength even when made of standard hydrastis.

Test.—Transparent fluid extract of hydrastis, when added to a mixture

* Mr. W. M. Schmitt made, in our laboratory, a number of determinations of the berberine in commercial fluid extracts. This paper will be found in the Pharmaceutical Record during 1885, and is of considerable interest. The variation in percentage of berberine announced by us as taking place inside of three weeks from the time of preparation was in a standard fluid extract made by Mr. Schmitt.

of alcohol three parts and water one part, should form a transparent mixture. It should produce a yellow crystalline precipitate (hydrochlorate of berberine) when mixed with one-fourth its bulk of hydrochloric acid; and a dirty yellowish brown sediment (impure hydrastine) when mixed with an excess of ammonia water. It should yield at least two per cent. of berberine salts by the following assay process:

Mix one fluid ounce of fluid extract of hydrastis with two fluid ounces of a mixture of equal bulks of sulphuric ether and alcohol, and after twenty-four hours decant the overlying liquid. Dissolve the precipitate in two fluid drachms of dilute alcohol, and add one fluid ounce of a mixture of alcohol two parts and sulphuric ether one part, by measure. Allow to stand twenty-four hours, and again decant the overlying liquid and mix with the reserved portion. Then treat the precipitate with one fluid drachm of the above mixture for three successive times, mix with the reserve and filter the mixture. To the filtrate add two fluid drachms of muriatic acid and one-half fluid drachm of sulphuric acid. After an exposure of twenty-four hours in a cool location, separate the crystalline precipitate by means of a filter paper, wash it with a mixture of equal bulks of alcohol and sulphuric ether, until the free acid is removed; then dry it by exposure in a drying closet to a temperature of 125° Fah. and weigh immediately. The yield should not be less than two per cent. of the hydrastis employed; it may reach three and one-half per cent.* Curcuma is detected by the methods given under powdered hydrastis, using the fluid extract instead of the tincture.

Fluid Extract of Hydrastis without Alcohol.—We object to the foregoing name. If applied to the substances originally introduced, and which the liquids sold under the above name are designed to imitate, it is a misnomer. They certainly were not fluid extracts. The earliest record that we have of such a preparation was about 1874, when the writer prepared for topical purposes a liquid that was to be free from alcohol, and transparent. It gave excellent satisfaction, and came into quite general use, finally being thrown upon the market under various names to distinguish it from the officinal fluid extract. We believe it to be fully as efficacious, and a preferable pharmaceutical, as it is more permanent, and miscible without precipitation with either syrup, glycerine, water, wine or alcohol.

Preparation.—Percolate powdered hydrastis with officinal alcohol until the hydrastis is exhausted. Add to the percolate one-third as much by weight of water as there was of the hydrastis, and evaporate the alcohol. After all the alcohol is driven off, mix with the residue enough cold water to bring the entire weight to two-thirds that of the hydrastis. After twenty-four hours, filter the liquid, and add to the filtrate enough glycerine to bring to the weight of the hydrastis employed.

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* If the hydrastis is prime, and the percolation complete, a larger amount of this berberine salt is obtained than by our process (p. 145) for assaying powdered hydrastis. The berberine salt is not as pure, however, and we usually prefer the other method for a direct estimation of hydrastis.

It will be observed that by this simple process the desirable constituents of the hydrastis are extracted by means of the alcohol, without the gums and inert extractive matters; although the oil and resins are associated in the percolate. The subsequent evaporation of the alcohol and admixture of the residue with water precipitates the oils and resins which are then separated by filtration. Thus a very pure solution of the natural alkaloidal constituents of hydrastis is obtained, and the addition of the glycerine produces a menstruum from which they do not separate by standing, and which will not ferment. This pharmaceutical, in our opinion, and we have made some thousands of pounds of it, is preferable to the officinal fluid extract. It can be administered whenever that substance is indicated and as an injection, or wash, is admissible in many cases when the fluid extract can not be employed. We hope that a similar preparation may become officinal. It will be observed that the process is such as to forbid the name fluid extract, unless the product is made officinal under that term, and we believe that the proper location is among the liquors. We therefore prefer the name *Liquid Hydrastis*, having used it for many years. We reproduce our description of this pharmaceutical as follows:

"Liquid hydrastis has a beautiful, deep yellow color, and when shaken, stains the bottle clear yellow. The taste is bitter, but not unpleasant and nauseating, like some bitter drugs. There is no odor of alcohol, none being present, but it possesses the exact odor of fresh powdered hydrastis. It will mix with water, glycerine, wine, or syrups, in any and all proportions, and the mixtures will not become turbid. It will not ferment, and the freezing point is much less than that of water. It contains all of the alkaloids and acids of hydrastis, in their natural combinations."

Tincture of Hydrastis.—This is officinal, as follows: "Hydrastis, in No. 60 powder, twenty parts. Diluted alcohol, a sufficient quantity. To make one hundred parts.

"Moisten the powder with fifteen parts of diluted alcohol, and macerate for twenty-four hours; then pack it in a cylindrical percolator, and gradually pour diluted alcohol upon it, until one hundred parts of tincture are obtained." —U. S. P., 1880.

The chief feature in connection with this pharmaceutical is the difference in menstruum used in it and that of fluid extract of hydrastis. If this tincture were designed for a different purpose than the fluid extract, this change would perhaps be obvious; or, if the menstruum of either were incapable of extracting the increased, or decreased amount of hydrastis of the other. In our opinion, tincture of hydrastis should be made of the menstruum employed in producing the fluid extract, for the increased amount of alcohol will not affect its administration.*

* When admissible, we favor a uniformity in the menstruum that is used in making both the tincture and fluid extract of a given drug. Conditions may possibly exist in which a break is necessary, but we think that as a rule it will be found that a menstruum best adapted to making one of these preparations is the one to use with the other.

*Essence of Hydrastis.**—The Pharmacopœa Homœopathica Polyglotta recognizes this preparation as follows: The rhizome (fresh root) is pounded to a fine pulp and weighed. "Then two parts by weight of strong alcohol are taken, and after thoroughly mixing the pulp with one-sixth part of it, the rest of the alcohol is added. After having stirred the whole well, and having filled it into a well-stoppered bottle, let it stand for eight days in a dark, cool place. The essence is then separated by decanting, straining and filtering."

MEDICAL HISTORY.—The root of this plant was highly prized as a dye by the North American Indians on account of its yellow coloring matter, and also for its medicinal value; but Kalm, in 1772, Cutler, in his Indigenous Vegetables, 1783, and Schoepf, in his Materia Medica Americana, 1785, overlooked it. This seems remarkable when we consider the important position that hydrastis occupied with the various tribes of Indians and with our settlers. Although the Indians introduced hydrastis to the whites (see medical properties), and it has always been a domestic remedy, it was reserved for Barton to bring the plant before the medical profession. The first medical reference that we have been able to find occurs in Barton's Collections for a Vegetable Materia Medica, 1798 (part first), wherein credit for its introduction is given the Cherokee Indians. In the third part of this work, page 13 (1804), he devotes considerable attention to the drug, and mentions the fact that it "supplies us with one of the most brilliant yellow colors with which we are acquainted." From this date until the appearance of Rafinesque's Medical Flora of the United States, 1828, nothing of importance was published in medical literature, and nothing added to Barton's remarks. His statements were either copied verbatim or condensed by writers upon materia medica, although few gave him any credit for his work. † Rafinesque next (1828) devoted considerable space to this plant, and produced a rude figure of it. ‡

In 1833 a paper from the editor of the Thomsonian Recorder appeared in that work (Vol. I., p. 397) which was the most important communication we have been enabled to find to that date. This paper gave a synopsis of the previously ascribed values of hydrastis, and added the uses Dr. Thomson made of it and the position it occupied in Thomsonian practice. §

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* This essence, or mother tincture as it is called, of hydrastis is the only pharmaceutical preparation of hydrastis used in homœopathic medicine, and peculiar to homœopathists. From it, in the usual manner, their dilutions are made. Homœopathic physicians use the alkaloidal salts defined by us in preceding pages.

† Captain Lewis (of the Lewis and Clarke expedition) attached a paper to his herbarium specimens of Hydrastis canadensis, May 24th, 1804, in which attention is called to the fact that "it is said to be a sovereign remedy" in eye diseases, and prized by the inhabitants of the country where it grows. This paper was not published until 1834, when it appeared in the American Journal of Pharmacy, p. 201.

‡ This figure has been reproduced, time and again, by subsequent authors, and in no instance have we found a credit given to Rafinesque's work. His engravings seem to have been considered as common property, and few, if any copyists, had the courtesy to acknowledge the source.

§ Hydrastis seems not to have been a conspicuous remedy of the early Thomsonians. It was mentioned in a paper which appeared in the Thomsonian Recorder, 1834, p. 313, entitled, "The Materia Medica of Dr. Samuel Thomson's Guide and Narrative, being a correct catalogue of all the plants recommended by him," but it occupied little space in his works. Many of Thomson's early followers scarcely recognized it. Comfort's "Practice of Medicine on Thomsonian Principles" gives but a brief notice of hydrastis.

Beach introduced hydrastis into the first edition of his American Practice of Medicine (1833), and it has always been an important member of the materia medica of his followers.*

The United States Dispensatory, first edition, 1833, omitted hydrastis, but the second edition, 1834, gave it a brief consideration in the appendix. †

Between this date and 1852 the standard works upon materia medica usually noticed the plant, but very briefly, and really added nothing to the preceding literature. Short extracts were usually made from the works of Barton, Rafinesque, Beach, or Thomson, the selection of authorities being usually in accordance with the affiliations of each writer. Hydrastis had, however, at this time become a recognized remedy. In 1852 King's Eclectic Dispensatory appeared, and hydrastis was highly recommended as an Eclectic remedy, in the following language: "This remedy is peculiar to Eclectics, and ranks among their best articles." In that work the medical uses and properties of hydrastis were prominently drawn by Prof. King, thus bringing the plant conspicuously before the Eclectic section of the medical profession. About this date interest was excited in certain products of the plant which were at that time commencing to be liberally advertised. These facts, together with frequent contributions from physicians who wrote for the Eclectic Medical Journal of Cincinnati, produced an extensive demand for the plant and its products, although this demand was almost exclusively among Eclectics. Hydrastis rapidly became more popular, however, and soon overstepped the bounds of sectionalism. In 1860 it was made officinal in the United States Pharmacopœia.

In the Regular section of medicine, Prof. Roberts Bartholow has given considerable attention to hydrastis, as is indicated by his paper on the subject in the various editions of his Materia Medica, and our readers are indebted to this author for a communication that follows regarding the uses of hydrastis. In 1862 hydrastis excited interest sufficient to merit a paper from Prof. Bentley, of England, under the heading, "New American Drugs," which appeared in the Pharmaceutical Journal and Transactions, 1862, p. 540, but which was mainly devoted to a consideration of the proximate principles of the plant. This is the only important foreign contribution we have in the early medical literature pertaining to this plant, although in 1873 Dr. Van der Espt presented a lengthy paper to the Royal Society of Medicine and National Sciences, Brussels, Belgium, without, however, adding any new facts; and recently the plant has excited some little attention in Germany.‡ It has

* Hydrastis was in reality brought out by the Eclectics, and is often known as an Eclectic Remedy. Prof. John King has valued it since 1833. The late Wm. S. Merrell introduced its products perhaps more extensively than any other person. In connection with this subject, it should be recognized that Dr. Walter Beach and the early Eclectics worked together.

† This unimportant notice passed unchanged through nine editions of that recognized authority, and was only slightly enlarged in the tenth edition, 1854, occupying still a position in the appendix. In the twelfth edition, however, it was placed in the primary department, the plant having been honored by an officinal position in the Pharmacopœia of 1860.

‡ The recent literature upon the therapeutics of hydrastis will be considered in the medical contributions of our contributors.

steadily grown in favor, all schools of medicine use it, and many members of each school value it very highly. The converse is also true, and many physicians neglect it, while others do not use it at all.

MEDICAL PROPERTIES (HISTORY).—In 1798 Prof. B. S. Barton issued the first part of his "Collections for an essay towards a Materia Medica of the United States." In it he writes, p. 9: "I am informed that the Cherake† cure it [cancer] with a plant which is thought to be Hydrastis canadensis." In the third part of his "Collections," 1804, he again refers to hydrastis: "The root of this plant is a very powerful bitter" (p. 13), and says (p. 14): "The hydrastis is a popular remedy in some parts of the United States. A spirituous infusion of the root is employed as a tonic bitter in the western parts of Pennsylvania, etc., and there can be no doubt that both in this and in other shapes, our medicine may be used with much advantage. An infusion of the root in cold water is also employed as a wash in inflammations of the eyes."†

Hand (House Surgeon, 1820,) adds: "It may be given in form of powder or of strong tea made by boiling, in indigestion, the secondary stages of low fevers, and all cases of weakness in general."

Rafinesque's Medical Flora, 1828, Vol. I., pp. 253 and 254, supports the foregoing, and in addition states that "they [natives] also employ it for sore legs and many external complaints as a topical tonic. Internally, in infusion or tincture, in disorders of the stomach, the liver, etc. It appears to be slightly narcotic and available in many other disorders. Some Indians employ it as a diuretic, stimulant and escharotic, using the powder for blistering§ and the infusion for dropsy." In Elisha Smith's Botanic Physician, 1830, we find several compounds containing hydrastis, to-wit: "Stimulating Cathartic Powders," "Bone's Bitters," and "Tonic Powders." Howard's Improved System of Botanic Medicine, 1832, p. 327, recommends it, also, in dyspepsia. Beach (1833), American Practice of Medicine, states that in connection with tonic properties it is "at the same time laxative, which makes it very appropriate in dyspeptic disorders." Next, the edition of the Thomsonian Recorder of 1833, p. 398, reviewed the medical properties as previously announced by others, and added to them as follows: "The importance of this article, taken in teaspoonful doses, for the relief and removal of bowel complaints in children should be extensively known. It is not only a corrector of the stomach, a regulator of the bowels, and a vermifuge for children, but it is an admirable remedy for the peculiar sickness attendant on females during their periods of utero-gestation, called morning sickness. It admirably relieves stomachic oppression, nausea, and heart-burn." Of the use of hydrastis in

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* Cherokee Indians.—ED.

† Rafinesque's Medical Flora, Vol. I., 1828, p. 253, adds: "It is considered a specific by the Indians for that disorder." Captain Lewis, 1804, supports the above, saying: "It is said to be a sovereign remedy in a disorder common to the inhabitants of the country where found, usually termed *sore eyes*."

§ This must be a mistake; phytolacca, or sanguinaria, will blister, but hydrastis can not be used for this purpose.

sore eyes he writes: "It is not a decoction of the dried root in boiling water that relieves ophthalmia, but is the freshly dug root, well cleansed and bruised, and infused in cold, soft water, that is to be particularly relied upon."* Sanborn's Medical Botany, 1835, p. 63, states that the Indians use hydrastis as a diuretic. If the root be chewed it will cure white aphtha or ulcers in the mouth. † Kost (Elements of Materia Medica and Therapeutics) states that it is good as an application in infusion to inflammations of the mucous tissues, leucorrhœa, blenhorrhœa, etc., and is of value in erysipelas. Dunglison (Medical Dictionary, 1852, p. 450) is the authority for a statement to the effect that in Kentucky hydrastis is used as an outward application in wounds. ‡

In 1852 Prof. John King issued the first edition of his dispensatory, under the title, "The Eclectic Dispensatory of the United States of America," and therein gave the medicinal uses of hydrastis a more careful review than had previously been awarded, although many of the values that early writers had ascribed to the plant were omitted as being overdrawn. § The indications for the administration and use of the drug and its preparations were carefully discussed in that work, and the remedy was thereby brought legitimately before the Eclectic branch of the medical profession (see Medical History), and in consequence of its general adoption by Eclectics it was from that time generally known as an Eclectic medicine. King was first, that we can find recorded, to recommend the plant in gleet and chronic gonorrhœa, and he wrote: "I have used this preparation likewise with much success in incipient stricture, spermatorrhea, and inflammation and ulceration of the internal coat of the bladder." From that time hydrastis was a popular remedy. It became officinal in 1860, and it now occupies a higher position than at any previous day, and the Homœopathic branch of the medical profession also use it extensively, as is shown by Prof. Hale's paper on the subject.

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* In contradiction to the fresh root part of this statement we quote from Captain Lewis, 1804. In speaking of the eye troubles of the settlers, he remarks as follows: "This disease is a violent inflammation of the eyes, frequently attended with a high fever, and sometimes terminates in the loss of sight, always gives great pain, and continues for a length of time in most cases. The preparation and application of this remedy is as follows: Having procured a sufficient quantity of the roots, wash them clean and suffer them to dry in the shade, break them with the fingers as fine as you can conveniently, put them in a glass vessel, taking care to fill it about two-thirds with the broken root, add rain or river water until the vessel is filled, shake it frequently and it will be ready for use in the course of six hours. The water must not be decanted, but remaining with the root is to be frequently applied by wetting a piece of fine linen and touching the eyes gently with it."—Am. Journ. Pharm., 1834, p. 201.

† We have testimony to the fact that in portions of Kentucky hydrastis is the domestic remedy for ordinary forms of sore mouth. The patient simply chews small fragments of the root from time to time. After chewing the root, if the saliva be applied to indolent sores, beneficial results are said to follow.—L.

‡ We have an extensive acquaintance in several sections of Kentucky, and have known of infusions of hydrastis being applied to indolent ulcers as a stimulant, but have never known it used on fresh wounds.

§ It is too true that many of these assertions regarding the uses of a drug are unsupported by a single fact that will bear the light. Empiricism in medicine seems to have been a necessity, for our most valued remedies have been handed down to us by men who scarcely recorded a systematic line of investigation. Indeed, we must go back to the aborigines time and again. It is to be hoped that the day will come when medical men as scientists will unite to demonstrate facts, to glean the grain from the chaff. Then as this or that statement is verified or disproved, we trust that a spirit of charity will prevail for those who were misguided, for these same men will be found to have announced many valuable truths.

We have endeavored in the foregoing pages to give a plain, systematically connected record of the introduction of hydrastis into medicine, and its past uses. Modern investigations have disproved many of the statements of other times, but writers still differ considerably from each other, and there is yet room for investigation. This plant is of such importance as to merit more attention than our brief medical record, and we are pleased to present the following independent papers from leading representatives of the various bodies of practitioners.

THE PHYSIOLOGICAL EFFECTS AND THERAPEUTICAL USES OF HYDRASTIS.—(Written for this publication by Prof. Roberts Bartholow, M. D., LL. D., of the Jefferson Medical College of Philadelphia.)*—But little attention has, heretofore, been given to the physiological actions of hydrastis. It is true Schatz,† Felluer, Sclavatinsky, and some others,‡ have made some studies, but their results differ so widely from those herein detailed that it may be questioned whether they operated with sufficiently good specimens of the drug. The alkaloid hydrastine with which the following experiments were made was sent to me by Prof. J. U. Lloyd, the editor of this journal, who is, I hope I may be permitted to say, unimpeachable authority. As hydrastine is quite insoluble, a solution of the hydrochlorate was prepared for me by Messrs. John Wyeth & Bro., which contained 33 per cent. of the salt. The effects of the alkaloid were compared with those of the fluid extract. As the actions of hydrastis consist of the sum of the effects of its active constituents, it is necessary to know how far each contributes to the results. It was soon ascertained that the alkaloid hydrastine is the true active principle—for the very characteristic effects of this were simply repeated by sufficient doses of the fluid extract. The latter is, as might be expected, slower in action, but in respect to the manner of action there was between them no appreciable difference. Three grains of the hydrochlorate caused the death of a frog in four minutes, whilst forty minims of the fluid extract proved fatal in twelve minutes, the mode and character of the action being the same. The results in rabbits were corresponding. In general terms, the effects of hydrastis are those of hydrastine in both classes of animals, but minute differences may hereafter be detected on closer examination.

General Effects of Hydrastine Hydrochlorate in Cold-Blooded Animals.—When ten minims of the 33 per cent. solution are injected into the abdominal cavity of a frog, the following phenomena ensue: In two minutes, muscular rigidity is manifest, with extension of the limbs and inability to move; in three minutes the cutaneous reflex is so heightened that the gentlest tap on the skin causes a tonic convulsion from above downwards; successive tonic convulsions then ensue, with fibrillary trembling between, until at the end of

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* Dr. Bartholow desires to acknowledge his indebtedness to Dr. A. B. Brubaker, Demonstrator of Physiology in the Jefferson Medical College, for valuable assistance in conducting the experiments.

† Centralblatt für gesanuute Therapie, Band 2, p. 82.

‡ Meditz. Horz. No. 16, 1884. Quoted from the London Med. Record for November 15, 1884.

four minutes death occurs in a strong tetanus. On opening the chest, the heart is still found in action, but in a few minutes more ceases in diastole, all the cavities being full of blood, and its muscular tissue is found to be irresponsive to electrical irritation.

In a rabbit weighing about fifty ounces, forty minims of the same solution, or thirteen grains, caused death in five minutes with the same phenomena—that is, with successive tetanic convulsions, the head drawn forcibly back, the limbs extended, and the respiration fixed, with increasing cyanosis of the ears and mouth. The heart continues in action after respiration has entirely ceased, and on opening the chest then it is still found in slow movement, the auricles most active and all the cavities distended with blood. The muscular tissue of the heart, does not respond to electrical or mechanical irritation.

It follows from the foregoing that hydrastis belongs to the group of excito-motor agents. It heightens preception, the cutaneous excitability and the reflex functions, and it causes death by tetanic fixation of the respiratory muscles.

Determination of the seat of the actions, whether spinal or peripheral.—A frog weighing about twelve ounces was pithed. After division of the medulla, the whole length of the spinal cord was carefully destroyed. No other injury was done, and very little blood lost. Ten minims of the hydrastine solution were then thrown into the peritoneal cavity. The frog remained perfectly limp and flaccid, and no spasm or convulsion of any kind occurred. The heart, on opening the chest some time after the death of the frog, was no longer in movement, the action having ceased in the diastole, and the cavities, as in other instances, were distended with blood.

The spasms and convulsions caused by hydrastine are, therefore, central or spinal, and not peripheral.

Has hydrastine any effect on the peripheral nerves and muscles?—To ascertain this, the left sciatic nerve was dissected out, isolated and a strong ligature applied around the limb the nerve excluded, thus cutting off the circulation from the parts below. Ten minims of the hydrastine solution were now thrown into the abdominal cavity. The usual effects followed—stiffness, rigidity and spasm of the muscles, general tonic convulsions, and intermediate fibrillary contractions. On stimulating the sciatic of the ligatured limb, contractions, not active, of the gastrocnemius followed; but on direct excitation of the unpoisoned muscles of the calf, they responded readily. In the other, the poisoned limb, feeble contractions of the calf muscles ensued on stimulation of the nerve, and similar contractions took place when these muscles themselves were directly acted on. After a time when the influence of the hydrastine had attained the maximum, and immediately after suspension of respiration, both nerves failed on stimulation to excite muscular contractions, and the poisoned muscles became entirely inexcitable.

The foregoing experiments prove that hydrastine exhausts the irritability of motor nerves and muscles.

Action of Hydrastine Hydrochlorate on the Heart.—A freshly removed frog's heart suspended in the solution, rapidly loses its electric excitability, and in a minute no longer responds to a strong current. Applied to the exposed heart *in situ*, the same effect is produced more slowly, and in five minutes an arrest of the movements takes place in diastole, the cavities being fully distended with blood. The auricles resist the action somewhat longer.

[redacted] divided, ten minims of the solution are in-

The Action of Hydrastine on the Blood Pressure.—A chloralized rabbit weighing about fifty ounces was used for the purpose. The right carotid artery was connected with the manometer and the revolving cylinder in the usual way. The attached tracing exhibits the effects of hydrastine. Up to the point *a* the pressure was at the normal for a rabbit under the influence of chloral, and then began the effects of the drug. It causes, as the tracing shows, some lowering of the blood pressure. The sudden rise at *b* was due to a convulsion, the quantity of chloral not being sufficient to prevent them entirely.

Antagonism between Hydrastine and Chloral.—The number of experiments has been too small to formulate positive conclusions, but enough has been learned to indicate that chloral antagonizes to a large extent the increased reflex excitability and the tonic convulsions caused by hydrastine. It is probable, indeed, that the antagonism will be found as extensive in range as between chloral and strychnine. Thus far I have not had the opportunity to ascertain the lethal dose of hydrastine. Until that is determined, the power

of its physiological antagonists can not be measured with accuracy. Further experiments are making on this point, and will be announced hereafter.

Strychnine and Hydrastine.—A remarkable correspondence can be traced between the actions of strychnine and hydrastine, but the power of the former seems to be the greater, whilst in extent of action the latter seems far more. Both exalt the reflex function of the cord; both induce tetanic convulsions, and both cause death by arrest of the respiratory movements in a tonic spasm. Hydrastine more affects the peripheral nerves and muscles, and to a much greater extent impairs the contractility of the cardiac muscle.

The Therapeutical Applications of Hydrastis.—As the results obtained from the administration of hydrastis constitute the sum of the actions of its several constituents, it may be best to consider the powers of the active principles separately, before treating of the effects of the drug as a whole.

The plants containing berberine are, as a rule, members of the tonic and reconstituant group. Hydrastine being peculiar to hydrastis, much of the effect produced by this agent must be due to the presence of this principle. Prescribed alone, hydrastine has been supposed to have the effects of a tonic, antiperiodic, and to some extent alterant—a term used to signify the power to promote the waste and excretion of morbific materials. The physiological study of hydrastine, as made by Schatz, Fellner, Slavatinsky, and others,* has not contributed to the subject of its therapeutical power, although it forms a groundwork for the therapy of the future. If, however, the physiological actions as detailed in this paper be confirmed by subsequent researches, quite a new phase will be given to its therapeutical applications.

As the fluid extract contains all the constituents of hydrastis, it is the most concentrated form available for administration and, therefore, will be the best preparation for procuring the effects of the remedy as a whole, whether given by the stomach or applied externally.

Hydrastis in Gastro-Intestinal Disorders.—As a stomachic tonic, when the condition of the stomach is that of debility, as we find it in atonic dyspepsia, so-called, and in convalescence from acute diseases, hydrastis serves a useful purpose. In common with the bitters, it stimulates appetite and increases the secretion of the gastric glands. Disposing thus of an increased supply of aliment, the constructive metamorphosis is promoted. For this purpose, it is best to administer ten to twenty drops of the fluid extract a few minutes before meals.

Both the alkaloids of hydrastis, exerting an inhibitory influence on fermentation, the fluid extract can be given with excellent effects in cases of catarrh of the stomach accompanied with fermentative changes in certain foods, whether or no, the *Sarcina Ventriculi* be present. The result of the action will be more permanent than the above remark implies, seeing that this remedy can modify, if not remove, that alteration of the mucous membrane

* Centralblatt für die gesammte Therapie, Band 2, p. 82, and Meditz. Obozr. No. 16, 1884. The latter, quoted by London Med. Record, Nov. 15, 1884.

which is accompanied by an outpouring of pathological mucus. To effect this purpose it were better to administer the fluid extract, two or three hours after meals, and the dose should range from fifteen to thirty minims.

As a tonic and reconstituent in the classes of cases above mentioned, quinine is now largely used: it is quite certain that hydrastis can be substituted for the most part with advantage.

The experiments of Rutherford* have confirmed the belief, founded on empirical observations, that hydrastis is an hepatic stimulant, although not one of the most active. As he operated with "hydrastin" so-called, which consists for the most part of berberine, it is probable that the results which he obtained are not equalled by those produced by the exhibition of the fluid extract. Hydrastis has been found useful in gastro-duodenal catarrh, associated with catarrh of the bile ducts—a morbid condition in which the output of bile is lessened by the mechanical obstruction, and the intestinal digestion is impaired in consequence of the insufficient supply of bile, the fermentative changes set up by the mucus which plays the part of a ferment, and the consequent absorption of imperfectly prepared materials. In this state of things we find the true explanation of some cases of jaundice, of most cases of "biliousness," and the initial changes of lithaemia.

The gastro-duodenal catarrh of chronic alcoholism is a condition in which the use of hydrastis has a decidedly beneficial effect, and the improvement in the digestion has seemed to lessen the appetite for alcoholic stimulants. This statement, made by several observers,† has been rather sarcastically commented on by the authors of the National Dispensatory,‡ who are, however, pessimistic if not nihilistic in their therapeutical conceptions. The new facts, demonstrating the effects of hydrastine as a spinal stimulant, are additional reasons for supposing it to be possessed of the powers claimed.

For the relief of the intestinal troubles above mentioned, the fluid extract of hydrastis should be given in the interval between the meals, and the dose should be larger (℥ss—℥i) than in the case of the corresponding stomachal troubles.

As an antipyretic and antiperiodic, the alkaloid—hydrastine—has had no adequate clinical study. Twelve years ago, I made some experimental trials at the Hospital of the Good Samaritan, in Cincinnati, in seven cases of tertian intermittent. White hydrastine in crystals was furnished me by Prof. E. S. Wayne, M. D., of Cincinnati, the well-known chemist and pharmacologist. Two of the cases were recent, uncomplicated, and but a few paroxysms had occurred. Twenty grains of hydrastine, administered in three doses, in anticipation of the seizure, merely modified its violence, but did not prevent it in either case. The second attempt proved successful. Three of the cases more chronic in character required sixty, sixty-five and eighty grains respect-

* The British Medical Journal, 1879, Vols. I. and II. Report of the Committee of the British Med. Association, etc.

† The Practitioner, London, Vol. XVI., p. 121, *et seq.*

‡ Third edition, p. 798.

ively. The two remaining proved still more rebellious, and the patients becoming uneasy, I was forced to resort to quinine. The supply of pure hydrastine was not sufficient to carry on further experiments, and a suitable opportunity to resume the investigation not occurring, I have no further clinical experience in this direction to report.* Nevertheless, these trials, whilst not numerous, are at least significant. They indicate the possession of real antiperiodic power, inferior to quinine, it is true, but apparently inferior only to the great antiperiodic. Since that time, the chemist's skill has produced by synthesis various products approaching in composition closely to quinine, and possessed of powers very similar but still inferior. It may be that under these circumstances, hydrastine will never rival quinine or its analogues, but the powers which it is now shown to possess may require a different statement hereafter.

Topical Applications.—For local use, the best mode of applying hydrastis is in the form of the fluid extract, which may be employed undiluted or diluted with glycerine. Its staining power is an objection, since the color which it imparts to cotton cloth, if not permanent, is at least not readily washed out.

The fluid extract of hydrastis is an excellent topical application in cases of catarrhal inflammation of the mucous membranes. In nasal, faucial, uretheal and vaginal catarrh, and in otorrhœa and conjunctivitis, there can be no doubt of its good effects. It may be applied freely in the undiluted state without fear of injury, if no good be accomplished by it. It has proved to be a very efficient injection in gonorrhœa, more especially after the acuter symptoms have subsided. For this purpose it may be diluted with glycerine or mucilage, or both, to the required extent. Formerly when I used to see these cases in considerable numbers, I found it a capital application in cervicitis. I had, also, excellent results in such cases, and in gonorrhœa, from "hydrastine" suspended in mucilage.

To express a final judgment as to its therapeutical value, my conviction is that hydrastis is a useful remedy, and well deserves a trial in the various conditions in which it is recommended above.

THE HOMŒOPATHIC USES OF HYDRASTIS CANADENSIS.—(Written for this publication by Edwin M. Hale, M. D., Emeritus Professor of Materia Medica and Therapeutics in the Chicago Homœopathic College.)—This indigenous drug, first introduced into our school by myself in 1856, has since obtained a great popularity. Many provings and physiological experiments have been made with it, which, combined with an extensive clinical experience, have pretty clearly defined its sphere of action and its place in homœopathic therapeutics.

* The remarkable activity of the pure hydrastine furnished me by Prof. Lloyd, necessitates caution in its administration, until its lethal power in man can be determined. It is now evident that the hydrastine used by me formerly in the treatment of diseases was not pure. I must therefore caution my readers in respect to the administration of the pure alkaloid, and especially its salts, and warn them not to employ this active agent, as they have heretofore been giving berberine, or a mixture of hydrastine and berberine.

Its sphere of action, although not wide, is yet very important. It appears to me to have a decided and specific affinity for

(1) The mucous surfaces—especially those with which it may come in contact.

(2) The mucous glandular system.

(3) The nutritive system.

(4) The circulatory system.

Action on the Mucous Surfaces.—The natural secretion is at first increased; then it becomes abnormal in quantity and quality. At first clear, white, tenacious and transparent, it becomes yellow, thick, green and even bloody, but always tenacious, capable of being drawn out in long strings. In this respect it resembles the mucus discharge caused by kali bichromicum, ammonii bromidum and cubebs. It differs from the mucus flux of stannum, copaiva and ammonii chloridum, which is thick, lumpy and falls in masses. This primary mucous flux of hydrastis may pass on to erosion, muco-purulent discharge and ulceration. It probably causes this condition by inducing a primary capillary hyperæmia; next a passie stasis, together with a stimulation of the mucous glands. Finally, from exhaustion or atrophy, the sources of the secretion are cut off, and the mucous membrane becomes dry, glazed, ulcerated and its functions destroyed. Pathologically, this disease of the mucous membranes may be called catarrh, or blenorrhœa. Other medicines cause similar conditions when taken internally, not only in the mucous surfaces with which they come in contact, but through which they may be eliminated (copaiva, kali iodidum, cubebs, grindelia, etc.); but we have as yet no proof that hydrastis is eliminated through any mucous surface, such as the bronchii, urinary or generative tract. If it acts on these surfaces at all when taken internally, it must act on them by disturbing the circulation in the capillaries. I have never been able to cure blenorrhœas of the above named surfaces by its internal administration, unless it was used at the same time topically; but I do not mean to dispute its ability to do so. Certain it is that we get the best curative effects when it is locally applied to diseased mucous membranes. We have used it successfully in mucous conjunctivitis; otorrhœa; diseases of the eustachian tubes; catarrh of the nasal passages, pharynx, fauces, stomach, intestines, part of the gall duct, urethra, vagina, uterus (leucorrhœa, gonorrhœa, etc.). These catarrhal affections may be simple, or severe, and may extend to erosions or ulceration. If they begin in simple blenorrhœa, they are all amenable to the curative action of hydrastis.

Method of Application.—When topically applied we use the tincture, or the muriate of hydrastine. The so-called "liquid hydrastis" is probably the best preparation. The infusion of the powdered root, when strained or filtered, is very efficacious. The strength of the lotion should vary according to the nature of the disorder, and the amount of the irritability of the surface. When the mucous membrane is red and irritable, a few drops of the tincture, or "liquid hydrastis," or gr.i of the muriate, to the ounce of water is sufficient.

In chronic or torpid conditions the strength may be increased to ℥i of the fluid preparations, or gr.v of the muriate, to ℥i of water. It may be applied with a syringe, atomizer, or as a simple wash, or on bougies (in urethra or uterus), or with a brush (in pharyngitis or conjunctivitis).

Action on the Skin.—The skin being analogous to mucous membrane, it has been supposed that a drug which acts on the one would act simularly on the other. One of our provers records that it caused an erysipelatous rash on the face, neck, hands and fingers, with great heat and irritation, which continued for six days, when the skin exfoliated; others that it caused pustular eruptions. Now the cutaneous analogues of a mucous catarrh, are erythema, moist eruptions, eczema, and even ulcers. In domestic as well as homœopathic practice it has been used successfully in similar skin affections. We have recorded cures of lupus, psoriasis, excoriations, rhagades, ulcers, boils, and even variola.

It was once highly praised as a remedy for cancer, but I can not find any authentic reports of its successful use when used alone. It was generally mixed with chloride of zinc, or some other escharotic.

Action on the Nutritive System.—The Eclectics have always believed hydrastis to be a general tonic. Our experiments seem to show that it acts similarly to cinchona, columbo, gentian, berberis, and others of that class. When given in medicinal doses of the crude drug, it seems to increase the general tone of the organs of nutrition and assimilation. The appetite is increased, digestion is more vigorous, and the bodily weight and strength increases. But if the drug is continued too long, the improvement ceases, and retrograde processes set in. A gastro-intestinal catarrh obtains, digestion fails, assimilation is deficient, constipation and hepatic torpor are present. All tonics, even iron, act similarly when the doses are too large or are continued too long. In these facts we see that hydrastis and its analogues are homœopathic to debility, atony, retrograde metamorphosis, and that the drug should be used in small (not infinitesimal) doses, and not continued too long even in small doses.

It is curative in all disorders depending on the above conditions: namely, generally impoverished blood, emaciation, stomatitis, dyspepsia, indigestion either in the stomach or intestines, biliousness, constipation, etc. The action of hydrastine on the liver was established by the experiments of Rutherford, who calls it "a hepatic stimulant of considerable power, and but a feeble intestinal stimulant." He refers to its purgative power. Hydrastis is not a purgative in any sense. It may cause during its first effects some looseness of the bowels, owing to the increase of mucus, but as the catarrh increases the intestines become sluggish, obstructed and very constipated. English Homœopaths value it more highly than do those of America as a remedy in hepatic torpor and constipation. They find it very useful for hæmorrhoids, congestion of the liver and portal system, sallow, dirty skin, and jaundice. I have found it useful for "mucous piles," as well as "bleeding piles." In

large doses it first causes acute hyperæmia of the liver, but this is followed by passive venous stasis of that organ and of the whole portal system.

On the lymphatic glandular system its action is not yet proven. I doubt if it has any.

Action on the Muscular System.—Hydrastis acts as a tonic. I do not think this acts through the nervous system, as does nux vomica, but through the blood. The increased assimilation of well-digested food allows the muscles to be better fed and better nourished. If the theory of Prof. Schatz, hereafter referred to, be true—that hydrastis acts directly on the muscular coats of the blood-vessels, contracting them—why should it not act on each and every muscular fibre in the body? Not, perhaps, to contract them, but by imparting a peculiar form of tonicity.

But in whatever way it may act, it has been the observation of all practitioners who have used hydrastis, and particularly the muriate of hydrastine (salt of white alkaloid), that the first signs of improvement mentioned by patients is the increase of muscular strength and powers of endurance, and this, too, in chronic, incurable diseases.

While I believe hydrastis to be a powerful tonic and restorative, I am obliged to deny it any specific anti-periodic (anti-malarial) properties. I tested it thoroughly during a practice of fifteen years in a malarious district. It is not and can never be a rival or substitute for cinchona. The practical physician knows that all bitter tonics have some reputation in ague, *e. g.*, chelone, ostrya, euonymus, and others; but they are not anti-malarial medicines. They may be, and doubtless are, capable of removing the malarial cachexia, in which the recuperative forces of the system are too feeble to resist the habit of recurring paroxysms, which are not true ague paroxysms. All these bitter tonics, particularly hydrastis and its active principles, berberine and hydrastine, have the power of restoring the vital forces sufficient to overcome this habit. In this respect hydrastis is more than a rival of cinchona (which is worse than useless in the cachexia)—it is a most valuable substitute. In all cachexias hydrastis is an indispensable remedy. Even in anæmia and chlorosis, it greatly aids iron in restoring the integrity of the blood.

In the debility after wasting diseases, fevers—typhoid or gastric; after losses of blood, or due to depressing emotions, also in neurasthenia, the hydrastia berberine phosphate or hypophosphite have done me excellent service. We have found it very useful in gall-stones, not so much for the colic caused by their passage as to remove the tendency to their formation. It may dissolve the biliary concretions by causing a flow of thinner bile, or aid in their expulsion by removing (as in jaundice) the catarrh of the gall duct. Several German Homœopathists have reported cases of tumors of the stomach and pylorus which disappeared under the careful and protracted use of hydrastis.

It is a curious fact in the history of our indigenous remedies that just about the time we think we understand all their qualities, and know all their uses, some foreign physician discovers new qualities and new uses for them.

This is partly true of hydrastis. I have recently read a lecture delivered before the Gynæcological Section of the Congress of German Philosophers and Physicians, held at Freiburg, in 1883, by Prof. Schatz, of Rostock, Germany. He gives as a result of his investigations that "hydrastis acts on the mucous membranes by contracting the vascular system."

But such a condition must be due to its action in large doses, and must be followed by its secondary effects, which would be of an opposite character, namely: passive congestion of these tissues. This action can not, however, account fully for its blenorrhagic effects. It must have some other action, especially when locally applied, and this action I am sure is that of an irritant to the glands of the mucous membranes. It probably has, in crude quantities, a double and simultaneous primary action, namely: contraction of the vascular supply, and irritation of the glandular supply. This vascular tension will after a time be followed by vascular relaxation; and the acute primary blenorrhagia by a chronic blenorrhœa with tissue paresis.

Further, Prof. Schatz says that "in many particulars, hydrastis and ergot are not unlike, but not infrequently hydrastis is efficient in cases of hæmorrhage where ergot is powerless, or even of positive injury, as also in some cases of myoma. It appears to me that we can attribute the action of hydrastis to the contraction, pure and simple, of the blood-vessel-wall, thereby lessening the congestion of the genital organs, while ergot spends its action on the muscular fibres of the uterus." "In the non-gravid uterus," he says, "the continuous administration of hydrastis causes a retardation of the menstrual period, with a diminution of the amount; it causes the pain to be less; even in menorrhagia and dysmenorrhœa of virgins, without any local causes, when pain is absent. Its action in myoma is often quite remarkable. Hæmorrhages caused in this manner diminish very much, or disappear entirely, after the use of hydrastis— even where Bombelin's ergotine has been employed most energetically; I have observed a number of times that where hydrastis had been administered to virgins for menorrhagia, normal menstruation set in, and occasionally the catamenia did not make their appearance for one, two or three months." This result was caused by massive doses. Prof. Schatz gives twenty drops of the fluid extract four times a day, causing, we may presume, the extreme primary effects of the drug. He does not give a differential comparison of the effects of hydrastis and ergot, which would be of great value and interest, but he admits, or implies, that he is not yet able to make such a comparison.

The best authorities describe the action of ergot to be as follows: "The action of the heart becomes slower, and an enormous rise takes place in the blood-pressure. This influence on the circulatory system modern research has shown to be due to the action of ergot on the vaso-motor system; it increases the action of this system, and causes a contraction of the aterioles."

Again, it is said to diminish the blood-supply to the cerebro-spinal axis, to the vegetative organs, the skin and muscular system. It is therefore diffi-

cult to explain the difference in the action of the two drugs, unless we suppose that hydrastis acts directly on the blood-vessel walls and not through the vaso-motor centers. But we doubt if this can be the case. There are many symptoms of hydrastis, in our meager provings of it, which indicate that it also diminishes the blood-supply of the brain—as witness the "tinnitus aurium, vertigo, dimness of vision, roaring in the head, with dull headache; a 'narcotized' feeling in the brain, feeling as if intoxicated; terrible headache and vertigo, horrible dreams."—Hale's New Remedies, third edition.

It is possible that a more heroic series of provings would evolve more vaso-motor symptoms, but when we consider the large quantities, continued for a long time, used in Eclectic and domestic practice, such a supposition does not seem probable.

But, while its full and true action is yet unexplained, we may take advantage of clinical experience to teach us the action of the drug and its value in certain diseases.

Prof. Schatz, in his memorable lecture, fortifies his statements by the narration of six cases of fibroid tumors of the uterus (myoma), in which he used hydrastis successfully in controlling and curing the hæmorrhages, but he does not say what became of the tumors. We know that not all cases of uterine fibroids are attended by hæmorrhage. If hydrastis acts by diminishing the vascular supply, it ought to arrest the growth of the myoma, or other non-malignant tumors. Now this brings us back to the alleged curative power of hydrastis in cancer. I have carefully examined all the records of our school relating to the use of hydrastis in tumors and cancer, and I can not find a single case where it entirely removed a cancer, or scirrous growth, before or after the stage of ulceration. But there are cases reported where hard, movable tumors appearing in the breast, stomach and uterus, have decreased in size, or disappeared altogether, after the internal and topical use of hydrastis.

It is my belief, based on a large personal experience and observation, that all the tumors benefited by this drug were fibroid in character, and the result was brought about, not by any "absorbent" action, but by diminishing the supply of blood, and thus cutting off the nutrition of the growth.

Ergot has certainly arrested and diminished the growth of myoma in the uterus, but we do not know that it has acted as well in fibroid tumors elsewhere.

Strychnine has the same action as ergot on the muscular structure of the uterus; so has caulophyllum, cimicifuga, and other drugs, but we do not hear of them as being of value in fibroid and other growths in the uterus.

Hamamelis, trillium, turpentine, phoradendron, millefoil, and others, act as well as ergot in controlling hæmorrhages, but we do not know them to be useful in any kind of tumor.

These are mysteries of drug action which yet remain unsolved.

It would appear from the foregoing that if the *modus operandi* of hydrastis

is as stated, its analogues are viburnum, ammonium bromide, ammonium chloride, and a few others.

Viburnum arrests and prevents the pain of dysmenorrhœa and hæmorrhages. It is supposed to act on the motor nerves of the uterus, relaxing contractions of muscular tissue. If so, it must act opposite to ergot. How, then, does it arrest hæmorrhage? It would seem that it could not affect the coats of the blood-vessels in a manner opposite to its action on the muscles.

Here is an anomaly which can only be explained by accepting the theory advanced by some Scotch obstetrician, that hæmorrhage from the uterus often arises from undue contraction of the muscles of that organ.

The bromide of ammonium has been found curative in ovarian and uterine tumors. It is capable of arresting hæmorrhage, and acts on the muscular structure of the uterus and its vessels similarly to hydrastis.

Muriate of ammonium has the same specific action on morbid growths, but is not known to arrest uterine hæmorrhage.

The action of hydrastis on the uterus may be said to be unique; it has no close analogue. It is not alone in hæmorrhage from uterine fibroids or myoma that hydrastis is useful. Prof. Schatz reports one case of congestive dysmenorrhœa; six cases of hæmorrhage in virgins, where the bleeding continued after the use of the curette; three cases due to parametritis, cicatrices and contractions; two from incomplete involution of the puerperal uterus; three cases from endometritis and metritis; and five cases of climacteric hæmorrhage. In all these cases various other means, drugs and operations had been used, and failed, but hydrastis performed a cure.

Dr. Schatz warns us to use the proper dose. Too small doses have no action; too large too much effect. The quantity he found generally useful was 20 gtts of the tincture three times a day.

I mention this because the illogical custom of many of our school is to select the dose in accordance with some arbitrary notion or preconceived theory. It is absurd to prescribe ergot in a middle or high attenuation for non-contractility of the uterus; and it would be just as absurd to give 20 gtts of the crude in uterine spasms. The dosage in these cases must be reversed, or it is not curative.

By Dr. Schatz's observations we learn that the sphere of curative action of hydrastis, already wider than we supposed, bids fair to become more and more enlarged, especially in the direction of its action on the circulatory system. If hydrastis increases the tonicity of the muscular fibres of the terminal blood-vessels, it must also increase that of the large arterial and venous trunks, and even of the heart itself. And if it does this without acting on the vaso-motor centers, it must prove far more valuable than ergot, for its effects must be more lasting. It follows that it may prove to be one of the chief remedies, if not *the* remedy, for chronic congestion, or more properly, stasis of the various organs of the body. It may prove to be to the arteries what hamamelis is to the veins, or it may rival the latter in its own

sphere of usefulness. Further experiments and clinical observations are needed to substantiate this theory, but I can safely say that it is my conviction, based on many years' experience in its use, that it is of veritable value in chronic blood stasis in the liver, spleen, uterus, abdomen and portal system. I believe too that I have seen proofs of its value in passive stasis of the brain and lungs, for within the last year or two I have observed excellent results from the use of the hypophosphite of hydrastine in affections of the latter organs. I am sure I have seen its good effects in weakness of the muscular structure of the heart, with tendency to dilatation. It seems to build up the muscular tissue, while digitalis or convalaria regulates the rythm.

I will close this paper by giving an excellent pen picture of the gastro-intestinal troubles, for which hydrastis is specific. It is copied from an article written by Dr. Clifton, of Northampton, England:

"*The Facial Expression* is dull, heavy, of a yellowish white color, sodden looking, not unlike that in which mercurious is indicated, but whiter, and having less animation. Though there is in its provings no reference to the expression or complexion, as affording reasons for selecting hydrastis, I have frequently found that when the gastric symptoms calling for this medicine have been present, the character of the face has been as I have described.

"*The Tongue* is large, flabby and slimy-looking. Underneath the fur the tongue is of a bluish white color, having in its edges the imprints of the teeth. So far it is like the mercurius tongue, but lacks the tremulous character of this organ, so often seen in cases benefited by mercurius. The coating is of a yellow, slimy, sticky fur.

"There are morbid states occurring in other organs, to which hydrastis is Homœopathic, but where the appearances of the face and tongue I have described are not present. In the dyspepsia it relieves. Both are met with.

"*The Eructations* are generally sour or putrid, more commonly the former than the latter.

"*The Appetite* is generally bad; the power of digesting bread and vegetables being especially weak. Both are followed by eructations.

"*The Stomach* has a sensation of weight (not as after nux and bryonia, 'weight like a stone'), and with the weight and fullness, an empty, aching, 'gone' feeling, more or less constant, but aggravated by taking a meal. The aching, 'gone' feeling is something like that produced by gelsemium, but is attended by more general fullness of the stomach, and more sour eructations. Further, although the gelsemium tongue is sometimes coated white or yellow, it is not so large and flabby as is the hydrastis tongue. This symptom is, I am aware, produced by many other medicines besides gelsemium, especially by ignatia and cimicifuga, but ignatia and cimicifuga do not give rise to the other symptoms peculiar to hydrastis. In tea-drinkers this symptom occurs frequently, but with them the tongue is generally white (except when colored by the tea), and in their dyspepsia cinchona is often found

to answer better than other medicines, especially in removing the flatulence with which they are commonly troubled.

"*The Action of the Bowels* may be either infrequent and constipated, or frequent, with the stools loose, soft, light colored, and with flatus. But as a rule the bowels are constipated, and stools lumpy and covered with slimy mucus, in cases indicating hydrastis."

THE USES OF HYDRASTIS IN THE ECLECTIC SCHOOL.—(Written for this publication by Prof. John M. Scudder, M. D., Professor of the Practice of Medicine in the Eclectic Medical Institute, Cincinnati.)—In some respects the hydrastis has been much over-estimated. It has been recommended as an antiperiodic, but it has but a feeble influence either as a prophylactic or a remedy opposed to malarial disease. It has been recommended as one of the best if not the best of bitter "tonics"—meaning a remedy to increase the appetite, digestion, blood-making and nutrition. But in this it is much overrated, and will not give satisfaction unless a special pathological condition exists.

This brings us to the consideration of the indications for its use, and its contra-indications. It is a remedy in atony of mucous tissues, with increased secretion; it is a remedy in irritation or inflammation of mucous tissues if secretion is free, whether it be mucus or pus. In this case it is a tonic, and improves nutrition, giving a better circulation and innervation. It has been claimed that it relieves irritation and gives tone to the parts, and with the conditions named this is a fact.

In catarrhal gastritis it is tonic and peptic, as it is in intestinal catarrh or catarrhal dyspepsia. It is a good remedy in stomatitis with increased secretion, in acute or chronic pharyngitis, and in some cases of nasal catarrh.

A solution of the soluble salts has proven very useful as an injection in the second stage of gonorrhœa, and in gleet. It is an excellent remedy in disease of the cervix uteri, and in cervical metritis, with profuse secretion from the cervical canal. In these cases the application should be thorough. In ulceration of the rectum it will sometimes prove a most efficient remedy.

In the second stage of purulent conjunctivitis a solution of these salts will give good results, and in some cases of chronic conjunctivitis the effect will be beneficial.

The salts of berberine (sulphate or phosphate), as well as the alkaloid itself are very convenient for dispensing, especially when the physician carries his own medicine. One to four grains to a half glass (℥iv) of water makes an excellent bitter, and with three or four drops of tincture of nux vomica, a good peptic. A collyrium or an injection for the purposes named is as readily prepared.

One use of hydrastis is yet to be named. In some cases of cancer with sloughing of tissues, and in malignant ulceration, no application will do more to retard the progress of the disease than an infusion of the crude article or a solution of the alkaloid. It has been claimed that the internal administration of the remedy will prove curative. I am satisfied that in some cases this use

of hydrastis will do much to relieve pain and to lengthen life even if it does not prove curative.

THE USES OF HYDRASTIS CANADENSIS IN THE ECLECTIC SCHOOL.—(Written for this publication by Prof. John King, M. D., Professor of Obstetrics and Diseases of Women, in the Eclectic Medical Institute, Cincinnati). While as a general vegetable tonic, hydrastis is inferior to certain other bitter tonics, as, gentian, colombo, etc., it will be found superior to them in the treatment of subacute and chronic inflammation of mucous membranes, upon which it exerts a peculiar tonic and slightly astringent effect, whether taken internally, or applied locally. In the majority of cases, its local application is followed by more prompt and positive action than its internal administration. Whether its power of contracting vessels be owing to a tannic acid, or to a principle similar to that in ergot which causes a like effect, has yet to be determined.* Administered internally, it has proved efficacious as a tonic, in enfeebled conditions of the alimentary canal with infants and children; in restoring tone to the intestinal mucous coat after severe attacks of diarrhea, dysentery, and other debilitating maladies; and in removing the indigestion, and restoring the appetite in those cases of indigestion and anorexia of adults due to an abnormal condition of the mucous coat of the stomach. As a local application it has proved valuable in conjunctivitis, in ulcerations of the mouth and fauces, in vaginal and uterine leucorrhea, and in all cases of enfeebled mucous tissues. In the chronic forms of cervical and corporeal endometritis, it has acted with success, being applied in the form of powder, made by evaporation of a decoction of the root, rubbed up with simple cerate or vaseline, and introduced into the uterine cavity by means of a tube made for such a purpose. In combination with other agents, it exerts beneficial influences that can not be had by the employment of either of the articles separately. Thus, a strong decoction of the root, to which has been added one-third or one-fourth its volume of tincture of capsicum forms a successful application to corneal ulcerations, and to all atonic ulcerations ofmucous tissues. In ulceration of the bladder, the decoction mixed with an equal volume of decoction of geranium, and injected into the bladder, has effected cures even in cases where all previous treatment had failed. This same decoction has never failed me yet, as a local application in ophthalmianeonatorum. The decoction, employed in combination with decoction of caulophyllum, has been found efficacious in thrush, and aphthæ of infants and children. Berberine, or muriate of berberin, does not appear to posses the positive action upon abnormal mucous tissues that is manifested by the root in decoction, fluid extracts, or a powder made by evaporating the decoction to dryness."

The preceding statement was written some four or five months ago, and placed in the hands of Prof J. U. Lloyd. To my great pleasure and surprise I have just noticed that in the section of Gynæcology in the Congress of naturalists and German physicians, held at Fribourg, in Brigau, Dr. Schatz, of

* Do not confound this with the yellow alkaloid berberine.

Rostock, invited the attention of his colleagues to the American Hydrastis Canadensis, the therapeutical effects of which rather astonished him. He found this agent efficacious in hemorrhages from myoma, from congestive dysmenorrhea, from subinvolution, also in those attending metritis and endometritis, as well as those occurring at the period of the menopause. He supposes the medicine acts upon the uterine mucous membrane, exciting vascular contractions, through which mechanism it diminishes congestion of the genital organs, thus acting very differently from ergot, the influence of which is exerted upon the uterine muscular tissue.*

REMARKS.—The foregoing independent papers on the therapy of hydrastis and its products, will be of general interest to the medical profession of America. To us, one feature is unexpected, namely, the announcement of Prof. Bartholow that "the alkaloid hydrastine† is the true active principle."

The physiological action of hydrochlorate of hydrastine as demonstrated by Prof. Bartholow is such as to warrant a close clinical study of this salt, which has been heretofore generally neglected. The negative results that followed the investigations of early experimentors, were doubtless owing to the use of the insoluble alkaloid, or impure hydrastine, for the active nature of the salt, as shown by the investigations of Prof. Bartholow, would lead us to infer that the popularity of hydrastis and its pharmacentical preparations is largely owing to a natural salt of hydrastine, modified, perhaps, by the berberine with which it is intimately associated, rather than the reverse. In the plant, this alkaloid, and berberine exist in the form of very soluble salts, and the long accepted uses of hydrastis in diseases of mucous surfaces, instead of as a mere tonic, like other berberine yielding plants, would alone indicate that berberine is not the prime factor. Indeed, it has long been known that solutions of berberine were not, in eye diseases of the value of infusion of hydrastis. This has always been accepted by Prof. King. This new light would lead to the opinion that the estimation of the value of hydrastis by our berberine process was fallacious, and that we should rather estimate the hydrastine of the drug.

Acting, therefore, on the information conveyed by Prof. Bartholow, we placed the hydrochlorate of hydrastine in the hands of several acknowleged authorities of the medical profession, and as a result we are enabled to present the following clinical contributions. It will be noticed that Prof. Sattler, having examined both berberine and hydrastine, also reports that hydrastine is the active agent.

THE PHYSIOLOGICAL EFFECTS AND THERAPEUTIC USES OF BERBERINE AND HYDRASTINE IN OPHTHALMIC AND AURAL PRACTICE.—(Written for this publication by Prof. Robert Sattler, M. D., Ophthalmic Surgeon to the Cincinnati Hospital, etc).—The want of a satisfactory preparation of Hydrastis Canadensis, perfectly soluble and free from the well-known objectionable features of

* The balance of this statement as to the form employed, doses, etc., of this medicine, are so nearly similar to those related by Dr. Hale, that we have with Dr. King's consent, omitted them, and refer our readers to the article by Dr. Hale, for further information concerning Dr. Schatz s investigations.—ED.

† Do not confound this with the yellow alkaloid berberine.

the drug, has until recently prevented its more general and extensive use and application in the management of the various catarrhal affections of the eye and ear.

At the request of Prof. J. U. Lloyd, I commenced a series of observations to test the physiological properties and therapeutic uses of two soluble salts of hydrastis, *i. e.*, diberberine sulphate and hydrochlorate of hydrastine, which he kindly furnished me, in powder form and in one, two and four per cent. solutions.

The investigations were conducted at my clinic and the records of the progress and results of the cases in which either remedy was resorted to, were carefully compiled by the clinical assistants, Drs. C. H. Castle and C. R. Holmes.

BERBERINE DISULPHATE.—*Physiological Action.*—Observations were begun with the berberine solutions. Two or three drops of a two per cent. solution dropped into the conjunctival sac caused slight irritation and injection of the palpebral and ocular conjunctiva. The objective and subjective disturbance, however, subsided quickly.

A four per cent. solution excited greater local irritation, more profuse flow of tears and mucous and also more pronounced subjective discomfort. The duration, however, of these symptoms was brief.

Therapeutic Application of Berberine.—To test its efficacy to relieve or modify catarrhal alterations of the conjunctiva (conjunctivitis simplex, acute catarrhal conjunctivitis, etc.), two and four per cent. solutions were resorted to, but in every case the results were negative, or at least, unattended by appreciable good effects, even after prolonged and systematic use.

The principal objection to the disulphate of berberine solution was, not so much the discomfort and irritation it induced, but principally on account of the deep staining (yellow) of the adjacent parts.

The hyperaemia of the conjunctiva, produced by the instillation was too transitory and was not effectual in modifying, after repeated trials, the local symptoms; or in bringing about relief from the scratching and burning sensations produced by the disease. Owing to almost uniformly negative results, additional observations were not made.

If the use of the berberine solutions proved of little or no value in the treatment of catarrhal affections of the eye, the use of both strong solutions and the powder in substance proved absolutely ineffectual when resorted to for the purpose of modifying or arresting catarrhal or purulent discharges from the middle ear.

In the following cases it was applied,—a four per cent. solution dropped into the ear twice a day, after syringing and the insufflation of the powder was resorted to once a day.

Case I. R. H. æt 4. Acute catarrhal otitis media, perforation of membrana tympani, slight discharge. Applied powder and solutions Nov. 2, 3, 4, and 5. The discharge became very profuse during this time, the powder incrustated and caused pain and suffering. Nov. 6, discontinued berberine, and used powdered boric acid, and discharge stopped in two days.

Case II. K. F. æt 16. Chronic otitis media purulenta. First application Oct. 15, continued until Oct, 28. No change of symptoms. Oct. 29, complained of pain in the ear, discharge more profuse. In spite of great care in the introduction of the powder, and the daily cleansing, it underwent incrustation.

Case III. G. B. æt 13, Chronic purulent otitis media. Oct. 26, First application, continued until Nov. 7. No favorable change, incrustation also troublesome.

Case IV. Subacute purulent otitis media. First application Oct. 24. Continued to Nov. 7. In this case there occurred considerable improvement. Incrustation also troublesome.

Case V. Chronic otitis media purulent, was tried for ten days: symptoms became worse.

In a number of other cases the remedy was used, but after several days was abandoned, for the reason that no improvement or change occurred to warrant its continuance.

When resorted to in solution, coagulation or precipitation occurred at once but no pain attended its use. The principal objection to its use in this locality, and this applies particularly to the powder, is, that rapid incrustation, due to chemical transformation from contact with the discharge occurs. The staining of the parts also constituted an objectionable feature. The removal of the incrustated masses from the external canal became necessary, on account of discomfort and pain produced. In some of the cases the removal was tedious, difficult and painful.

HYDRASTINE.—*The Physiological Action and Effects of Instillations of Hydrochlorate of Hydrastine.*—Two or three drops of a two per cent. solution dropped into the conjunctival sac of a healthy eye, causes at once active stimulation of the palpebral and ocular divisions, attended by the usual reflex symptoms—lachrymation, blepharo-spasm, and a pungent and burning pain, which, however, is of short duration, rarely lasting longer than two or three minutes. With the subsidence of the pain, more or less moisture of the eye remains, and a watery mucus secretion often accumulates at the outer and inner canthus. After the expiration of one hour, all evidences of the instillation have disappeared.

A four per cent. solution causes more marked subjective discomfort, more active and persistent hyperæmia of the conjunctival area, more pronounced reflex symptoms, together with increased stimulation of the secretory apparatus. Stronger solutions cause an intensification of all these symptoms, and in addition, probably in consequence of the irritation to the sensory nerves of the cornea, contraction of the pupil. The myosis is most probably the immediate result of the irritation of the superficial sensory nerves of the globe, and is not due to a direct action upon the sensory and muscular structures of the iris.

Cold applications to the lids modify greatly the local symptoms, and also the discomfort attending instillations of weaker solutions; and the application of stronger solutions is greatly mitigated by immediate washing off the conjunctival surfaces with camels hair brush and tepid water. The inferences from a number of trials establishes that in mild solutions, hydrochlorate of hydrastine is a tonic and stimulant to the conjunctiva, increasing for the time

being, its functional activity. It can also be inferred that the remedy exerts its beneficial effects, by its action in arousing and stimulating the functional activity of the complex glandular structures, by the active hyperæmia produced by its instillation. This was corroborated by numerous trials in those cases, in which the remedy was resorted to in variable strength of solution, to accomplish such effects, in diseased states of the conjunctiva, which the instillation into the normal eye rendered probable. It appeared therefore of probable value in those pathological processes of the mucous membrane attended by more or less pronounced passive congestion, relaxation of structure, and altered or suspended functional activity of its glandular apparatus.

In all catarrhal forms of conjunctivitis and in the first or catarrhal stage of more serious lesions, one and two per cent. solutions exerted a beneficial influence on the local symptoms. The secretions appeared less acrid and were reduced in quantity and perhaps altered also in composition; particularly was this observed, if in addition to frequent instillations of weaker solution, an application of a stronger solution five per cent. was made once a day to the conjunctival surfaces of the everted lids, by the aid of a camel's hair brush and the surfaces immediately washed off with water.

In follicular conjunctivitis, an affection quite common among anemic and scrofulous children, and also among adults living amidst unfavorable hygienic surroundings, it was found to possess decided advantages over the customary astringents and local stimulants ordinarily resorted to. The disease is eminently chronic and contagious. In many cases it exists in a latent form and gives rise to little annoyance, or the discomfort is ignored by the patients, until vision is interfered with by the accumulation of mucus and irritation of the lid borders, due to the acrid or irritating character of the discharges. Often it appears in an endemic form in certain localities, and in other instances it affects all the members of one or more families. Lack of cleanliness on the part of the person or persons affected, and the careless use of towels and handkerchiefs by the other members of the family constitute the principal channels of contagion. On account of its chronic course and the general or frequent vitiated state of the constitution of persons affected, it is a most troublesome affection to manage. The use of hydrochlorate of hydrastine solutions in this annoying affection has been particularly satisfactory, and local and subjective symptoms have been effectually modified and the course of this always tedious affection, has been altered and shortened. Compared with other remedies the subjective discomfort attending its use was less annoying and subsided more rapidly, and the improvement was more lasting.

Therapeutic Indications of Hydrochlorate of Hydrastine.—Bearing in mind its local action when instilled into the healthy eye it was resorted to in a large number of cases in which this action would appear desirable in order to promote, modify, or arrest those local symptoms which are the common and frequent attendants of acute, subacute and chronic catarrhal, follicular, granular, blennorrhœal, etc., inflammations of the conjunctiva.

In the treatment of chronic catarrhal conjunctivitis, and particularly that variety known as conjunctivitis siccus, it was found of great service. This affection is eminently tedious and annoying, to both physician and patient. Among the most distressing symptoms, is a sensation of dryness and scratching, attended by a feeling of weight and heaviness of the upper lids. A perceptible reduction in the quantity, and also an alteration of the quality of the secretions of the conjunctiva can be observed. In the majority of instances anæmia, physical exhaustion, or other disturbances which depress the general health, are present, and to the local and general symptoms are added, failure of the accommodative power of the eyes and most annoying asthenopic symptoms. In those cases in which an optical error of the eyes co-exists, these symptoms appear in a most pronounced form and defy or effectually prevent all application of the eyes for close work. In the management of this variety of conjunctivitis, ordinarily so troublesome and tedious, hydrochlorate of hydrastine, in 1 and 2 per cent. and even stronger solutions, was found of particular advantage. The favorable influence exerted upon the progress of the disease, and also in modifying the annoying subjective symptoms, was probably assignable to the quick and decided stimulation of the vascular and secretory apparatus of the conjunctiva.

In chronic granular conjunctivitis, it was also found of benefit. In a large number of cases it was resorted to systematically during the second or stage of granular infiltration. In these cases daily applications of a stronger solution (5 per cent.) were made to the everted surfaces of the conjunctiva and immediately washed off with water. Both the use of weak collyria and the topical application of a stronger solution exerted a beneficial local and subjective influence, and effectually modified the protracted course of this most troublesome and chronic affection. In the transition or third stage of the disease, weaker solutions were used, and occasionally an application of a stronger solution. In the treatment of this extremely chronic and intractable affection it was not found to possess advantages over the customary remedies resorted to, and in several cases its use had to be discontinued, on account of the severe reaction and suffering which followed the application. In blepharitis marginalis it was applied in solution (2 per cent.) to the eroded and ulcerated margin of the lid. These cases progressed favorably and the improvement was assignable without doubt to the local stimulating effect of the remedy.

Reviewing briefly the advantages of this remedy in the management of the various diseases of the conjunctiva and its value as a therapeutic agent, it can be stated, that it is of principal advantage in catarrhal conjunctivitis, and especially in the chronic forms. It is of particular benefit in follicular conjunctivitis, and also an efficient remedy in granular conjunctivitis, blepharitis marginalis, etc. It appears to exert its specific local effect by exciting a temporary more or less pronounced hyperæmia of the conjunctiva, and, in consequence, active stimulation of its vascular and secretory structures. The action of hydrochlorate of hydrastine is prompt and decided.

In weak solutions it is a tonic to the mucous membrane; in stronger solutions a more or less pronounced irritant effect is added, and in still stronger solutions it is a powerful irritant. As a choice of remedy it deserves attention and preference in all the various affections of the conjunctiva attended by a disturbance of its functional activity, due to an acute, sub-acute or chronic process of inflammation. On account of its active stimulant properties, it modifies and aids in arresting the secretions and relieves in this way the annoying symptoms and almost invariable concomitants of catarrhal inflammations. It is, therefore, a valuable tonic, stimulant or irritant to the mucous membrane. In those cases where the remedy has not been the first choice it may prove a valuable substitute for other astringents or stimulants, which may have been unsuccessfully resorted to. In other cases it will prove a serviceable agent, occasionally resorted to in conjunction with other remedies.

Hydrochlorate of hydrastine is contra-indicated in all affections of the cornea or its other primary or occurring as complications in connection with or the result of conjunctivitis. It is also of no value, and therefore contra-indicated in all deep-seated affections of the eye. It is primarily and principally a tonic, stimulant or irritant to the mucous lining of the lids or conjunctiva, and its scope and efficiency of action is limited to functional or structural alterations of this important membrane.

In the ear the use of solutions of hydrochlorate of hydrastine was also resorted to, but the number of observations was more limited. It was used to modify or arrest irritating catarrhal and purulent discharges from the external auditory meatus, and its use was attended and followed by the same good, and in some instances even better results, than after installations of the customary mineral astringents, as iodoform, boric acid, etc. In two cases of acute and five of chronic purulent otitis media the results were carefully noted. After thoroughly syringing the external auditory canal and middle ear, inflation by Politzer's method was practiced. This accomplished, the bottom of the meatus and those parts of the middle ear which were accessible through the perforation of the membrana tympani were carefully cleansed and dried by means of absorbent cotton attached to a holder, and the powder applied to the eroded and exuberant mucous membrane. In three out of the five cases this was an easy task, as the membrana tympani had been almost completely destroyed. The results of systematic applications in these chronic cases were certainly favorable; in two of the five cases a marked reduction in the quantity and quality of the discharge occurred. All the cases had been under treatment and hydrochlorate of hydrastine solutions were substituted. All were apparently benefited; the discharge was reduced in quantity and lost its irritant and offensive characteristics. It can safely be said that in many cases, carefully selected, the remedy is of advantage and deserves a trial either as a substitute or as a first choice. In several cases of granulations and polypoid formations, the result of otitis media purulenta, it was applied in substance, and, although it caused severe pain, it effected by systematic application a disappearance of the exuberant growths.

HYDRASTIS AND HYDRASTINE HYDROCHLORATE IN DISEASES OF THE SKIN. —(Written for this publication by Dr. John V. Shoemaker, of the Jefferson Medical College of Philadelphia).—Hydrastis is a valuable drug in diseases of the skin, both internally and as a topical application. It is especially useful as a stomachic tonic, and as a hepatic stimulant in cutaneous affections depending upon gastro-intestinal disorders.

It is best administered in the form of the fluid extract of hydrastis which Prof. Roberts Bartholow has shown to contain all the constituents of the drug and is the preferable preparation to use. In seborrhœa-sicca or oleosa, which frequently develops from some alimentary trouble, the scaly, reddened or greasy state of the skin may lessen or disappear by the use of ten or twenty drops of the fluid extract of hydrastis three times daily. The red or white of papules black points or pustules of acne or the enlargement of the blood vessels and tissue of acne-rosacea due to the same cause may alone be relieved or cured by the internal administration of hydrastis. It is an excellent remedy to use in scrofulous diseases of the skin, in patients having feeble digestion, loss of flesh and enlarged glands, with or without unhealthy ulcers. In cases of this nature it will stimulate the appetite, lessen the involvement of the skin and assist the action of local medication in removing the disease. It has also acted in a happy manner upon some cases of lupus, sycosis, boils, carbuncles and ulcers, on which the local condition was largely due to a lack of nutrition of the system. Eczema which is so often depending upon debility or some gastro-intestional disorder, may at times be greatly relieved or cured by free doses of the fluid extract of hydrastis.

Children suffering with the pustular form of this disease, known as eczema impetiginodes or milk crust, small doses of the fluid extract from one to five drops in mucilage or glycerine three times daily increases the digestive power, lessens the formation of pus, and has a powerful tonic action upon the previously enfeebled system. In broken down syphilitic subjects, especially in those in whom the alimentary canal is weak and irritable, often from alcoholic excess, or from the use of too much mercury or one of the iodides, the use of hydrastis is attended with most marked and beneficial results.

Hydrastis may be employed alone internally or in some cases its conjoined internal and external use will at times be found most efficacious. The range of usefulness, however, as a topical application, is even greater than from its internal administration. The fluid extract, which is the preparation generally employed for local use, has both a stimulant and an astringent action on the integument which is well marked when the skin is denuded or inflamed. It may be used undiluted, or what is even better, diluted one-half or one-third with water, oil, mucilage, or glycerine. Inflammatory affections of the mucous membrane, especially stomatitis, syphilitic lesions, and eczema are greatly benefited or even at times removed by the application of the fluid extract of hydrastis. The fissured form of the latter diseases which occurs around the

mucous outlets, as on the lips and about the anus, or on the flexor surfaces and between the fingers and toes are sometimes rapidly improved by its use. It also exerts a most efficacious action or lessens the inflammation and thickening in chronic eczema, whether involving the parts just referred to or other regions. Abrasions, sinuses, ulcers and granulations are greatly improved by the application of this remedy.

While the use of the fluid extract of hydrastis has been attended with much benefit in many of the diseases just cited yet its employment has been open to a very great objection from the staining which follows everything with which it comes in contact. This staining power which is usually imparted to the clothes of patients, is not easily removed even by washing and the unpleasant effect that follows the employment of this drug would almost entirely preclude its adoption in private practice, when so many other, elegant, cleanly and efficacious preparations are now constantly on hand for use. Fortunately, however, the objection referred to has been entirely overcome by the recent investigations of Prof. Bartholow, who has demonstrated the active principle of the drug hydrastine, which can be combined to form hydrastine hydrochlorate, which has all the physiological effect of the former drug. Further, the salt so formed not only possesses all the good qualities for cutaneous application, claimed for hydrastis, but it is also perfectly free from the staining qualities of the latter drug.

Hydrastine Hydrochlorate.—This salt occurs as a fine white powder slightly tinged with yellow, inodorous but very bitter and soluble in water, alcohol, oils and fats. Its color, its odorless character, and its great solubility furnishes a remedy of unusual advantage for topical application in diseases of the skin.

During a short experience with this preparation I have found it most useful mixed with water, alcohol or fat in hyperiodrosis, seborrhœa, acne, eczema and in ulcers. Thus from five to twenty grains of hydrastine hydrochlorate to the ounce of alcohol, has a most beneficial effect on excessive secretion which may occur in the axillary or inguinal regions, or on the palmar and plantar surfaces. This same combination acts well in seborrhœa-sicca, especially of the scalp, attended with loss of hair, the stimulant and astringent action of the solution lessening or relieving the irritability of the follicles and glands of the part. The papules and black spots of acne yield sometimes very rapid to the application of the alcoholic solution of hydrastine hydrochlorate. Acne rosacea and seborrhœa oleosa or the greasy state of the skin so often seen in the face of young women have in several instances improved much on an application of an aqueous solution of this drug, or a mixture of the salts with a fatty substance in the proportion of from five to twenty grains to the ounce.

The ointment of hydrastine hydrochlorate, the salt being incorporated in the fat in from ten to sixty grains to the ounce, has proved a most excellent application in some cases of subacute and chronic eczema; the thickened and irritable state of the skin in the latter condition subsiding at times very rapidly

on its application. It has also been serviceable in some scrofulous and varicose ulcers used in the form of an ointment. The good results so far realized from the topical application of hydrastine hydrochlorate may be illustrated by the following cases in which it has been employed in the clinical service of the Philadelphia Hospital for Skin Diseases.

Acne.—Robert T. æt 17. Forehead, cheeks and chin covered with small red papules associated with black points—acne punctata—and papulo-pustules, digestion feeble, bowels torpid. Ten drop doses of the fluid extract of hydrastis were given three times daily before meals and the face was sponged night and morning with an aqueous solution of hydrastine hydrochlorate containing ten grains of the salt to the ounce. In ten days the patient showed signs of improvement, and in six weeks after being placed under treatment he was discharged cured.

Eczema of the Face.—Anna B. æt 3. Scalp and face covered with thick crusts, which upon removal exposed red raw and infiltrated patches, digestion poor, constipation at times followed with diarrhœa. Half a drop increased to a drop of the fluid extract of hydrastis was administered in milk three times daily with the effect, in course of twelve days, of improving the child's general condition and lessening somewhat the local inflammation. The red and infiltrated patches still remained stubborn, notwithstanding the use of the ordinary ointments. At the end of the second week of the constitutional treatment, one ounce of lard with twenty grains of hydrastine hydrochlorate was used freely over the parts. The red and thickened patches gradually disappeared and in two weeks time from the beginning of the topical application only a slightly desquamating surface remained.

Eczema of the Anus.—James T. æt 32. Had been under treatment at various times with only temporary relief. The margins around the anus was thickened and fissured, many of which extended well into the mucous membrane of the parts. No apparent exciting cause could be detected. The application of the ointment of hydrastine hydrochlorate twenty grains of the salt to the ounce being employed was followed by relief within a few days. Several weeks have now passed and the patient having failed to report has doubtless obtained permanent relief.

Eczema of the Ears.—Mary W. æt 27. The right and left ears were red, somewhat thickened and covered with scales. The skin back of each pinna was in a similar condition with several fissures at their connection with the side of the head. The inflammation of the ears had originally been excited by a dye, and had resisted the usual local remedies. The ointment of hydrastine hydrochlorate, of the same strength as mentioned in the previous case, was used with good effect within six days. The ears in about three weeks had acquired their natural size. The fissures healed quickly, and when last seen, about ten days ago, only a little roughness of the integument was apparent.

Eczema of the Feet.—Mrs. G. æt 36. The dorsal surface of both feet were red, slightly infiltrated, especially about the toes, between which were some well marked fissures. The disease had been in existence for some time and had been caused by using some remedy to remove corns from the feet. At first, a five, and afterward, a ten per cent. ointment of hydrastine hydrochlorate was used which completely removed the disease in from five to six weeks time.

Seborrhœa Sicca of the Scalp.—Wm. S. æt 22. The scalp was caked over with a thick sebaceous secretion, the hair being dry and lustreless. The disease had followed after typhoid fever, the patient at the time of examination was weak and poorly nourished. Cod liver oil in large doses soon improved the systemic condition, but the local trouble continued the same. The parts were sponged once daily with an alcoholic solution of hydrastine hydrochlorate, thirty grains of the salt being employed to the ounce with the effect of removing within eight or ten days all the crusts and scales, and after some three weeks topical application but a slight evidence of the disease existed.

Inflammation of the hair follicles of the Beard.—Thomas R. æt 24. The upper lip was the seat of many pustules and papules, especially around the margin of the anterior nares. Two grain doses of the iron iodide was administered and a ten per cent. hydrastine hydrochlorate ointment applied to the parts, brought relief within six or eight days, the patient then disappeared and has not since reported.

Seborrhœa Oleosa.—Maggie C. æt 19. Forehead, cheeks and nose slightly red and very greasy.

Many of the follicles of the parts were plugged with comedones, and the skin in patches presented even a dirty hue. A uterine cause which excited the disease had been removed by one of the physicians at a general hospital, but the local condition, although lessened by the previous treatment, continued annoying. An aqueous solution of first five and afterward twenty grains of hydrastine hydrochlorate to the ounce lessened the poured out oily fluid and improved decidedly the deformity of the skin in about two weeks time. Patient has since ceased her visits to the hospital and perhaps has concluded she is now cured.

Hyperidrosis.—Mrs. L. æt 39. Applied for the relief of excessive sweating from the arm pits, which had been very annoying for some time. Health good and local trouble could not be traced to any constitutional cause. The frequent use of an aqueous solution containing thirty grains of hydrastine hydrochlorate to the ounce proved an effective application within a few weeks time.

Ulcers.—Carrie H. æt 13. Had two small ulcers, one on the right and the other on the left side beneath the inferior maxillary from broken drown lymphatic glands. The floor and margins of the ulcers were covered with indolent granulations and with an unhealthy and scanty pus. Constitutional treatment improved without removing the ulcers. A ten increased to a twenty per cent. hydrastine hydrochlorate ointment healed them completely in a little over one month's time.

Hydrastine hydrochlorate from the cases just cited and others now improving under its use will no doubt prove a valuable topical application, especially in diseases of the skin. Its stimulant and astringent properties may make it available, not only in the affections alluded to, but also in many others. From present experience it is better adapted for use in diseases in which the inflammation is not too active, more particularly in the subacute and chronic stages. Precautions should be exercised in using it, on an acute eruption and if employed the solution or ointment should be very weak otherwise the active stimulant and astringent effect of the salt may increase instead of diminish the disease. It is better and much more effective even in those diseases in which it is indicated not to use too strong a solution or ointment in beginning the application to the skin.

ACTION OF HYDRASTINE HYDROCHLORATE ON THE GENITO-URINARY MUCOUS MEMBRANES—(Written for this publication by Prof. F. W. LANGDON, M. D., of the Miami Medical College of Cincinnati).—Prominent amongst the features which have characterized the progress of modern medicine are those improvements in pharmaceutical chemistry whereby we are enabled to obtain, in concentrated form, the active principles of various vegetable remedies, such as morphine, atropine, quinine, strychnine, piperine, theine, cocaine, etc. We have another instance of this dominion of mind over matter in the preparation which forms the subject of the present observations, viz: The Hydrochlorate of Hydrastine, prepared from the white alkaloid of the well-known plant, Hydrastis canadensis.

At the request of the Messrs. Lloyd, I have instituted a series of clinical experiments with this preparation, somewhat limited as regards time and number, but sufficient to demonstrate the fact that the drug in this form possesses the power of influencing favorably certain morbid conditions of the secreting structures of the male urethra. I have used the drug, as an injection only, in the strength of one-half grain to three grains to the ounce of distilled water.

To sum up, briefly, the results of this series of observations, we may classify the cases under three heads, namely:

1.—Acute Gonorrhœa. Here the use of an injection containing one to two grains to the ounce, *after* the subsidence of the first acute symptoms, swelling, pain, etc., arrested the discharge in a few days in several cases. This, however, as is well known, is so common a result of the use of many other remedies (and even, at times, occurs spontaneously, if patients are to be believed) that its significance may readily be overestimated. The fact, however, that it has been uniformly successful in even a small number of cases (six) is worthy of note.

2.—Gleet dependent on stricture or localized ulceration. Here, as might be expected, its use was attended by unsatisfactory results, as would be any measures short of treating the actual lesion. While a slight improvement seemed to follow its use in some of these cases, in others it exerted a decidedly irritant action, even in the strength of one grain to the ounce.

3.—Gleet dependent on a relaxed condition of the urethral mucous membrane purely functional; the discharge a mere weeping, almost watery in character—*a true catarrh*, in fact. It is in these cases that the drug seems to exert a most favorable influence, producing immediate improvement and final cure in troublesome cases which had resisted the variety of men and measures to which they are usually subjected. Its use, however, requires caution as regards the strength of solution. While an injection of two to three grains to the ounce of distilled water produces the best results in some, others manifest an immediate increase of irritation and discharge upon using even a one-grain solution; so that, to begin with, a half-grain solution is sufficient for most cases, to be gradually increased according to indications.

The drug certainly deserves further attention at the hands of the profession.

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1878.—Pharmaceutical Journal and Transactions, London, p. 567. Phosphate of Berberine.
1878.—Proceedings American Pharmaceutical Association, p. 599, Hypophosphite of Berberine; p. 800, Salts of Berberine, Oil and Resin of Hydrastis, Berberine and Hydrastine.
1878.—American Journal of Pharmacy, p. 470. Berberine, Hydrastine, Third Alkaloid.
1878.—The United States Homœopathic Pharmacopœia. Hydrastis.
1878.—New Remedies, Wm. Wood & Co., New York, p. 226, Phosphate of Berberine; p. 361, Berberine and Hydrastine.
1878.—Dispensatory and Pharmacopœia of North America and Great Britain, p. 175; Berberine, p. 176.
1879.—National Dispensatory, p. 729 (and subsequent editions). Hydrastis, Berberine, Hydrastine, Third Alkaloid.
1879.—Pharmaceutical Jonrnal and Transactions, London, p. 897. Phosphate of Berberine.
1879.—Proceedings American Pharmaceutical Association, p. 196.
1879.—Eclectic Medical Journal, Cincinnati, p. 174. Hydrastine.
1879.—New Remedies, Wm. Wood & Co., p. 19.
1879.—Students' Pocket Medical Lexicon, Longley, p. 38, Berberine; p. 137, Hydrastine and Hydrastis.
1879.—Pharmaceutical Journal and Transactions, London, p. 125, Berberine and Hydrastine; p. 163, Berberine.
1880.—New Remedies, Wm. Wood & Co., p. 375.
1880.—Preliminary Report on Revision of U. S. Pharmacopœia, p. 51.
1880 and 1881.—British Medical Journal.
1881.—New Remedies, Wm. Wood & Co., p. 183, Hydrastis and Berberine.
1881.—Medical Formulary, Laurence Johnson, pp. 220, 221, Hydrastis; pp. 221, 222, Berberine Muriate and Sulphate; p. 221, Hydrastine.
1881.—Lancet and Clinic.
1881.—American Journal of Pharmacy, p. 138. Berberine and Hydrastine.
1881.—Proceedings American Pharmaceutical Association, p. 345. Hydrastine and Berberine.
1882.—United States Pharmacopœia, sixth revision, pp. 181, 125.
1882.—American Pharmacist, p. 290.
1882.—Pharmacopœia of the United States, p. 181.
1882.—Pharmaceutical Journal and Transactions, p. 318. Berberine and Thymol.
1882.—American Practice of Medicine, Goss, pp. 69, 148, 153, 158, 182, 203, 216, 243, 249, 495, 572, 579, 596. Hydrastis and Berberine Salts.
1882.—Dictionary of Economic Plants, Smith, London, p. 446. Hydrastis.
1882.—Druggists' Circular, p. 51.
1884.—Companion to the Pharmacopœia, Oldberg and Wall, p. 579. Hydrastis, Berberine, and Third Alkaloid.
1884.—Plant Analysis, Dragendorff, pp. 49, 62, 258. Berberine.
1884.—Materia Medica and Therapeutics, Roberts Bartholow, p. 165 (and other editions). Hydrastis and Alkaloids.

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1789.—Hydrastis canadensis ——.—Aiton, Hortus Kewensis, 1st edition, Vol. II., p. 273; 2d edition, 1811, Vol. III, p. 362.
1789.—Hydrastis canadensis, *Linn.*—Lamarck, Encyclopédie méthodique Botanique, Vol. III., p. 151.
1799.—Hydrastis canadensis ——.—Willdenow, Species Plantarum of Linnæus, 4th edition, Vol. II., Part II., p. 1339.
1803.—Hydrastis Canadensis ——.—Michaux, Flora Boreali-Americana, Vol. I., p. 317.
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* In making these references, care has been taken to capitalize the specific name only when capitalized in the original work. A dash after the name indicates that no authority is given for it.

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1814.—Hydrastis canadensis ——.—Pursh, Flora Americæ Septentrionalis, Vol. II., p. 389.
1815.—Hydrastis Canadensis *Linn.*—Barton, Floræ Philadelphicæ prodromus, p. 61.
1817.—Hydrastis canadensis ——.—Eaton, Manual of Botany of Northern and Middle States, 1st edition, p. —; 2d edition, 1818, p. 276; 3d edition, 1822, p. 210; 4th edition, 1824, p. 325; 5th edition, 1829, p. 248; 6th edition, 1833, Part II., p. 179; 7th edition, 1836, p. ——.
1818.—Hydrastis canadensis ——.—De Candolle, Systema Naturale Regni Vegetabilis, Vol. I., p. 218.
1818.—Hydrastis Canadensis ——.—Nuttall, Genera of North American Plants, Vol. II., p. 21.
1818.—Hydrastis Canadensis *Linn.*—Barton, Vegetable Materia Medica of the United States, Vol. II., p. 17. Illustrated with a good colored engraving of the Plant (inaccurately showing, however, an expanded flower *with sepals*); also with the outline of a mature leaf and parts of the flower.
1818.—Hydrastis Canadensis ——.—Muehlenberg, Catalogue Plants Americæ Septentrionalis, 2d edition, p. 57.
1818.—Hydrastis Canadensis ——.—Barton, Compendium Floræ Philadelphicæ, Vol. II., p. 22.
1824.—Hydrastis canadensis *Linn.*—De Candolle, Prodromus Systematis Naturalis, Vol. I., p. 23.
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1826.—Hydrastis canadensis ——.—Torrey, Compendium of the Flora of Northern and Middle States, p. 224.
1828.—Hydrastis Canadensis ——.—Rafinesque, Medical Flora of North America, Vol. I., p. 251. Illustrated with a plate (No. 51) of the flowering plant (flowers inaccurate).
1830.—Hydrastis canadensis *Linn.*—Hooker, Botanical Magazine, Vol. LVII. (Vol. IV., new series), No. 3019. Illustrated with a good colored plate showing a flowering plant and dissections of the flower.
1831.—Hydrastis Canadensis *Linn.*—Don, Dichlamydeous Plants, Vol. I., p. 22. Illustrated with a small, inaccurate cut (fig. 7) of plant and fruit.
1833.—Hydrastis canadensis *Linn.*—Hooker, Botanical Magazine, Vol. LX. (Vol. VII., new series), No. 3232. Illustrated with a good colored plate of fruiting plant, with root and dissections of the fruit.
1833.—Hydrastis canadensis *Linn.*—Beck, Plants of the Northern and Middle States, p. 7.
1837.—Hydrastis Canadensis *Linn.*—Darlington, Flora Cestrica, 2d edition, p. 336; 3d edition, 1853, Part II., p. 7.
1838.—Hydrastis canadensis *Linn.*—Torrey and Gray, Flora of North America, Vol. I., p. 40.
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1843.—Hydrastis canadensis *Linn.*—Dietrich, Synopsis Plantarum, Vol. III., p. 338.
1845.—Hydrastis Canadensis ——.—Wood, Class-Book of Botany, 1st edition, Part II., p. 21; 2d edition, 1847, p. 148; 3d edition, 18—, p. 212.
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1849.—Hydrastis canadensis *Linn.*—Gray, Genera of Plants of the United States, Vol. I., p. 48. Illustrated with a lithographic plate (No. 18) showing a flowering plant and dissections of the flower and fruit.
1849.—Hydrastis canadensis ——.—Strong, American Flora, Vol. III., p. 174. Illustrated with a colored plate of the fruiting plant, good except the root, which is inaccurate.
1860.—Hydrastis Canadensis *Linn.*—Chapman, Flora of the Southern United States, p. 11.
1866.—Hydrastis Canadensis *Linn.*—Baillon, Histoire des plantes, Vol. I., p. 87. Illustrated with a longitudinal section of the carpel (fig. 88)—(English translation by Hartog, 1871, Vol. I., p. 49).
1866.—Hydrastis canadensis *Linn.*—Darby, Botany of the Southern States, p. 210.
1869.—Hydrastis Canadensis *Linn.*—Lawson, Ranunculaceæ of the Dominion of Canada, p. 51.
1870.—Hydrastis Canadensis *Linn.*—Wood, The American Botanist and Florist, p. 23.
1880.—Hydrastis canadensis *Linn.*—Bentley and Trimen, Medicinal Plants, Vol. I., No. 1. Illustrated with a good colored plate (No. 1) of a flowering plant and parts of flower and fruit, also outline of mature leaf.
1884.—Hydrastis Canadensis *Linn.*—Millspaugh, American Medicinal Plants, No. 9. Illustrated with a colored lithographic plate of the plant.

Original Document

PLATE XII.



TROLLIUS LAXUS.

TROLLIUS LAXUS.

Natural Order Ranunculaceæ, Tribe Helleboreæ.

DESCRIPTION.—This is a rare plant, even to botanists. It grows in deep swamps in a few localities from Michigan to New Hampshire, and south to New Jersey and Delaware. It is perennial, and in general appearance resembles a large-flowered species of Ranunculus (see Plate XII.). The leaves are generally one to two inches in diameter, but they are sometimes found even five or six inches broad. They are palmately divided, with many cleft segments; they are mostly radical, and borne on smooth leaf-stalks from four to eight inches long. The stems are one to two feet high, smooth, round, hollow, erect, nearly naked, bearing one or two leaves, the upper being near the flower, and sessile. Two or more stems often grow from the same bundle of coarse, fibrous roots, and the plants are disposed to form clusters, and, by developing a succession of stems, they continue in flower for some time. The flowers are terminal, large, and showy, usually of a light greenish-yellow color, but when exposed to the sun they are sometimes of a brighter or golden yellow. They are from one and a half to two inches in diameter. The sepals are generally five, spreading, petaloid, and tinged with green on the external or lower surface. The petals are more numerous, ten to fifteen; they are much smaller than the sepals, and shorter even than the stamens, and they might readily be mistaken for abortive stamens. They are of a deep yellow or orange color, gland-like, thickish, and have a tubular, nectariferous excavation on the inner side near the base. The stamens are numerous, with oblong or linear anthers. The pistils are ten to twenty, sessile, and arranged in a compact whorl. The fruit is a capitate whorl of dry, veiny follicles, tipped by the persistent style, and opening at the apex. Each follicle contains from five to ten angular seeds. The plant is not plentiful enough in this country to have received any common name from the people, but in the text-books it is known as Globeflower, which name properly belongs to the European species, *Trollius europæus*, the sepals of which are convergent into a globular shape. In the American plant the calyx is spreading, and the name Globeflower as applied to our native species is entirely inappropriate, though in order to distinguish our plant from the European species it is sometimes designated as the American Globeflower or the Spreading Globeflower.



FIG. 44.
a, stamens (magnified); *b*, section of carpel (magnified) of Trollius laxus.



FIG. 45.
Pistils of Trollius laxus.

MEDICAL PROPERTIES.—The medical properties of this plant have never been properly investigated, and it is not really entitled to a place in this

work.* On the authority of Lee,† which induced us to consider it, the medical properties of this plant resemble those of Ranunculus. If this is the case, and we are by no means assured that anemonin exists in it, we here have a plant belonging to the Helleboreæ, where it is placed by its botanical structure, but related in its medical properties to plants of the tribe Anemoneæ.

COPTIS TRIFOLIA.

GOLD-THREAD.

PART USED.—The rhizome of Coptis trifolia *Salisb.*
Natural Order Ranunculaceæ, Tribe Helleboreæ.

BOTANICAL ANALYSIS.—Rhizome, slender, creeping, bright yellow, branched, sending up at intervals of four to six inches clusters of leaves and flowers. Leaves all radical in tufts, surrounded at the base by yellowish scales; petiole slender, erect or reclining, two to four inches long; leaves, evergreen, veiny, firm, smooth, shining, palmately ternate; leaflets, obovate, about an inch in diameter, tapering to a sessile base, obtuse and somewhat three-lobed at the apex; margins sharply, mucronately and crenately toothed. Flowers, solitary, radical, white, about half an inch in diameter, borne on a slender, erect scape, slightly longer than the leaves, and bearing, above the middle, a single small bract. Sepals, five, spreading, petaloid, white, equal, deciduous. Petals, five, very small, gland-like, thickened and hood-shaped at the apex, and terete and tapering at the base. Stamens numerous, with slender filaments and globular, innate anthers, opening longitudinally. Pistils, three to ten, whorled, short stipitate; ovary one-celled, with numerous ovules, arranged horizontally in two rows; style recurved, stigmatose on the inner face. Fruit, three to ten, dry membranous follicles, slenderly stipitate at the base, and tipped with the persistent curved style at the apex. Seed five to ten, small, horizontal, black.

COMMON NAMES.—Coptis trifolia is almost universally known as Goldthread. This name is very appropriate from the slender, wiry, bright-yellow rhizomes. Having been used for sore mouth, it is sometimes called Mouth-root and Canker-root, names which express the domestic use of the plant as a remedy. In French towns in Canada, we are informed by Dr. Mignault, it is known among the people under the name of *Savoyanne*, from some old plant of France. It is sold in all the French markets, and is extensively used in domestic medicine as a tonic and appetizer. Don Miller states that it is known as *Tisavoyanne* by the Canadian French.‡

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* We prepared our engraving on the promise of a physician in a neighborhood favored by an abundant growth of the plant, and who promised to investigate it, and prepare a paper on its medical properties. He was prevented from making the investigation, however, and we are unable to present any definite information on this head.

† 1848.—Catalogue of the Medical Plants of the State of New York, p. 4.

‡ In answer to our inquiry regarding the meaning and derivation of these French names, Dr. Chas. Rice, the eminent linguist, has kindly replied with such an interesting letter that we reproduce it in full:

"I regret that I can not give a reliable derivation of these words, but may be permitted to make a guess. According to Nemnich (Lexicon Polyglott., p. 1355), the French name *tisavoyanne* had two applications: *tisavoyanne rouge* (red) denoted madder (Rubia tinctorum); *tisavoyanne jaune* (yellow) denoted Helleborus trifolius L. (Coptis trifolia Salisb.). From whence Nemnich took the term I do not at present know. But there is no doubt in my mind that the syllable 'savoyanne' is a dialectic adjective of the name of Savoy (once a French province), where madder has been grown for a long time. The syllable *ti* may be a patois for the name of the plant, or some other corruption. As I am not much posted on ancient French and its dialects, I can throw no light upon this. It would be quite natural for persons who call madder the *red Savoy 'ti'* (whatever this may mean) to call Goldthread or Coptis the *yellow Savoy 'ti.'* The names were, of course, carried by settlers to Canada."

PLATE XIII.



COPTIS TRIFOLIA.

Classified

BOTANICAL DESCRIPTION.—Coptis trifolia is a modest little evergreen, and among the smaller of our native plants. It is an herbaceous perennial, and generally grows in abundance in situations where it is found at all, and sometimes covers the surface of the ground. It sends out, just below the surface, fine, blackish, fibrous, and long roots and creeping and often branching rhizomes, which produce, at their nodes, minute scales and fibrous roots, and occasionally send up clusters of a few root-leaves. This rhizome is very slender, almost thread-like, of a bitter taste, and of a very bright yellow color, and will attract the attention even of a casual observer if by any accident it is exposed to view. It is this that suggests the common name, Goldthread, which is given to the plant. The leaves are evergreen, and of a firm texture. They are three-foliate, and somewhat the shape of a strawberry leaf; indeed, the whole plant in appearance and habits can be well likened to a small strawberry plant, though, unlike that plant, its creeping stems are subterranean and root-like. The leaflets are toothed on the margin, the teeth ending in a sharp point or bristle, and the central one especially is often slightly three-lobed.

The small, delicate flowers appear in May, generally one from the center of each cluster of root-leaves. They are solitary, white,* and borne on a strictly erect and very slender radical flower-stalk, which usually surpasses the leaves in height, and which gives the flowers a very graceful appearance. The flowers are about half an inch across when fully expanded, and have a somewhat stellate appearance. The true petals are much smaller than the white petaloid sepals, and are liable to be overlooked (see *a*, Fig. 46). They are shorter even than the stamens, and are enlarged and hollow at the apex, of a yellowish color, and somewhat club-shaped.



FIG. 46.
Flower of Coptis trifolia; *a*, petal (magnified).



FIG. 47.
Fruit of Coptis trifolia; *a*, longitudinal section of carpel (magnified).

The fruit is a terminal whorl or umbel of four to eight small, thin pods, each terminating in a slender point, which is hooked or sometimes even coiled at the summit. Each pod is supported on a slender stalk about as long as the pod itself, and contains several (four to ten) small, oblong, smooth, shining, black seeds.

BOTANICAL HISTORY. — This plant was first described by Linnæus in the second volume of his Amœnitates Academicæ (1750), from a specimen brought by Halenius from Kamtchatka. It was included in the genus Helleborus, and named Helleborus trifolius. Under this name it was described by botanical writers for fifty years, though Michaux and

* Sometimes the plant is found without the petaloid sepals and sometimes with them as yellow as those of Viola rotundifolia.

Bigelow were the only writers to apply it to the American plant. In 1771, Müller, in the fourth volume of the "Floræ Danica," figured and described it as Anemone grœnlandica.*

The plant is closely allied to the genus Helleborus, and the only characters of distinction afforded by the flowers are the deciduous sepals and the distinct stipitate carpels. In habits and properties, however, it widely differs. At the present day botanists who are liberal in drawing the generic boundary lines, notably some eminent French writers, still include the plant in the genus Helleborus.

In 1805, Salisbury read a paper before the Linnæan Society on the genera that now constitute most of the tribe Helleboreæ.† In this paper he divided what had before been the genus Helleborus into four genera, one of them being Coptis,‡ and the plant under consideration he named Coptis trifolia. By this name the plant is known to most subsequent writers, which include all, but two, writers on American botany.§ Rafinesque, in 1808, no doubt unaware of the publication of Salisbury, also proposed to separate the plant from Helleborus, and he called it Chrysa borealis.‖

GEOGRAPHICAL DISTRIBUTION.—Coptis is of wide distribution in the Northern Hemisphere, and is found in the cold countries of Europe, Asia, and America extending around the North Pole.

In America it is abundant from Central New York north throughout British America and to the limit of common vegetation. In the United States it is most common in Maine, New England, Northern New York, and the northern peninsula of Michigan. Over this territory it grows everywhere in damp places such as swamps, wet meadows, and damp woods. In Central and Southern New York, Pennsylvania except the southeast portion, and Southern Michigan, it can generally be found in locations adapted to its growth, such as damp swamps, and in situations where it occurs at all it is usually abundant. The plant follows the Allegheny Mountains south, growing in the cold, wet soil of the table-lands, and extends into Northeastern Alabama. In Ohio and Indiana it is of rare occurrence, but reported from a few localities. Westward, the plant extends through Minnesota, Dakota, and Montana, mostly in the northern sections, to the Rocky Mountains, where it disappears, being replaced by other species.

Under the evergreens is a favorite haunt, and it thrives luxuriantly in the deep shade of coniferous trees, being reported even from dry piney woods.

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*The plant has so little structural resemblance to the genus Anemone that its reference to that genus by Müller is excusable only on account of the crude state of botanical classification at the time at which he wrote. Were it not for completeness, the name, even as a synonym, should be entirely dropped.

†This paper was published in the Proceedings of the Linnæan Society, Vol. VIII., 1807, p. 300.

‡Name derived from κόπτω, *to cut*, in reference to the divided leaves.

§These are Michaux and Bigelow.

‖This was merely an announcement made by Rafinesque (Medical Repository, 2d series, Vol. V., p. 359) of what he proposed to do in a contemplated work styled "Nova Genera et Species Plantarum Boreali-Americanarum." This work, like many other of the projects of this eccentric scientist, never appeared.



MAP SHOWING THE DISTRIBUTION OF COPTIS TRIFOLIA.

EXPLANATION OF THE MAP.

We have endeavored to show the abundance of the plant in four shades:

1st. Light—(The Allegheny Mountain and Northern Ohio and Indiana)—Where the plant is usually absent, but occasionally found in cold swamps.

2nd. Darker—(Lower Michigan)—Where it is more general, but not a common plant.

3rd. Much Darker—(Lower New York, Pennsylvania, etc.)—Where the plant is found in most every locality suitable for its growth.

4th. Very Dark—(Northern New York, Canada, etc.)—Abundant everywhere.

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Northern cedar and spruce and balsam swamps always abound with it. Another favorite habitat of the plant is the cold swamps such as are found in mountain plateaus. It often grows freely in beds of sphagnum and other mosses, especially in wooded swamps.*

Although Coptis is a *swamp* plant, it is not a *mud* plant, but generally selects the dry knolls surrounded by wet soil, or occurring like islands in swamps.

ALLIED SPECIES.—Two other native species of Coptis are found in the Rocky Mountains and extreme Northeastern America.† They are of little interest from a medical standpoint, as the common species, Coptis trifolia, is so very abundant that there will never be any demand nor occasion for collecting either of the Western plants. The rhizomes, however, are bright yellow, contain berberine, and have no doubt the same tonic properties as the eastern species, and it is but proper that physicians and pharmacists of the Northwest should be able to recognize them.

Coptis Occidentalis, Torr. and Gray.—This species has a general resemblance to Coptis trifolia in habit, habitat, and appearance.

Compared with Coptis trifolia, the leaves of Coptis occidentalis are larger and more leathery; the margins are incisely toothed and more or less lobed. The flowers are smaller, and always two—sometimes three—on the scape, which is much shorter than the leaves. The color of the flowers is light yellowish green, and they appear in April, sometimes the latter part of March. In the structure of the

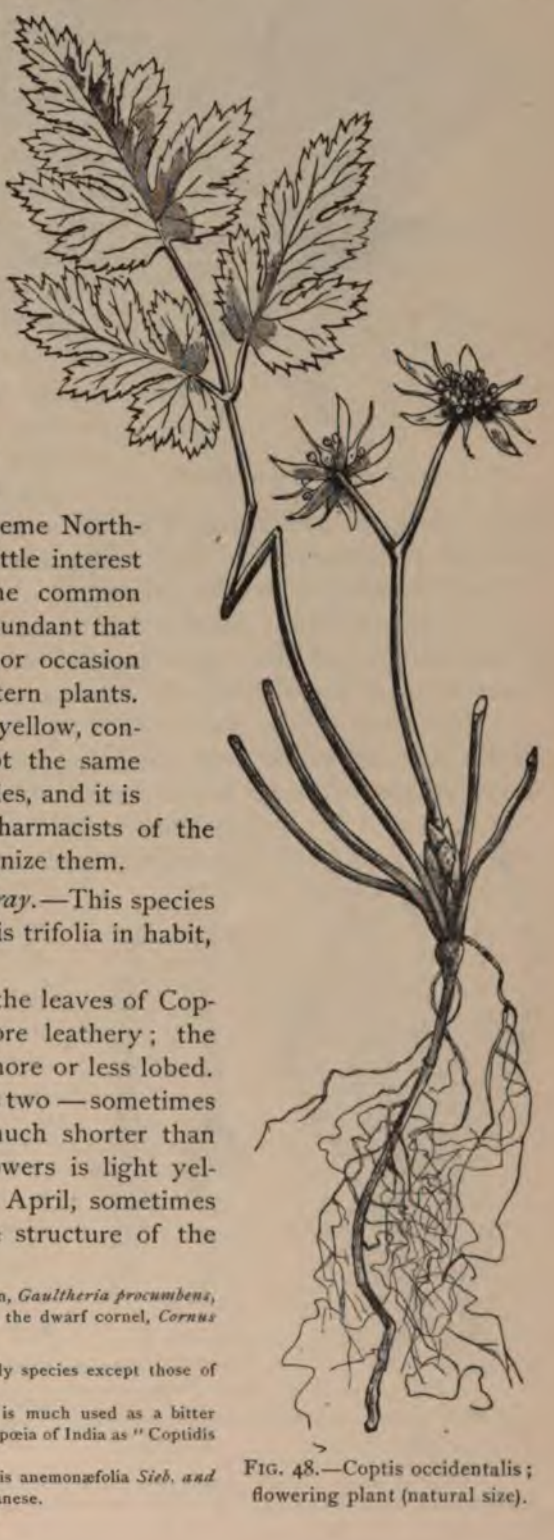


FIG. 48.—Coptis occidentalis; flowering plant (natural size).

* It is frequently associated with the wintergreen, *Gaultheria procumbens*, the creeping snowberry, *Chiogenes hispidula*, and the dwarf cornel, *Cornus canadensis*.

† The genus Coptis is a small family; the only species except those of America are found in Asia..

In India the root of Coptis Teeta *Wallich* is much used as a bitter tonic by the natives, and is officinal in the Pharmacopœia of India as "Coptidis Radix." It grows in the mountains east of India.

In Japan the rhizome of a native species, Coptis anemonæfolia *Sieb. and Zucc.*, is one of the standard drugs used by the Japanese.



FIG. 49.
Flower (magnified) of Coptis occidentalis.

petals, it widely differs from Coptis trifolia (and in like manner from most other petaliferous plants of the tribe Helleboreæ); the petals, instead of being transformed into gland-like or hooded bodies, are flat and similar to the sepals in shape, but are smaller and more slender. They have glandular, disk-like thickenings near the base. This structure is so much in contrast to that of Coptis trifolia that Nuttall, notwithstanding the very close and evident relationship of the two plants, established a new genus for the western species, calling the plant Chrysocoptis occidentalis.

After flowering, the scape elongates and becomes as tall as the leaves. In June the plant matures its fruit, which is a terminal whorl of ten to fifteen dry membranous pods.



FIG. 50.
Fruit of Coptis occidentalis.

In appearance the plant is intermediate between the Coptis trifolia and the Coptis asplenifolia, approaching, however, much more closely the following.

Coptis asplenifolia Salisb.—This species only grows on the northern Pacific coast extending from Washington Territory north through British America to Alaska. The bi-ternate leaves and two-flower scapes characterize it respectively from the two species previously described. (See Fig. 53, on opposite page.) The structure of the petals is somewhat similar to that of Coptis trifolia, being hooded in the middle; but they are much larger and at the apex are attenuated into slender prolongations, as shown in our figure (see Figs. 51 and 52). The sepals are reflexed.



FIG. 51.
Flower of Coptis asplenifolia (magnified).*



FIG. 52.
Front and reverse view of the petal of Coptis asplenifolia (magnified).

The chief character between the two western species is the petals above described. The shape of the leaf is not constant, and intermediate forms are often found. Indeed, the two plants bear such a close resemblance to each other that they would not be distinguished by a casual observer.

The three species which we have de-

* We were unable to obtain a flowering specimen of the plant, and our drawing is copied from the picture in Hooker's Flora Borealis Americana. We suspect that some of the details are exaggerated.

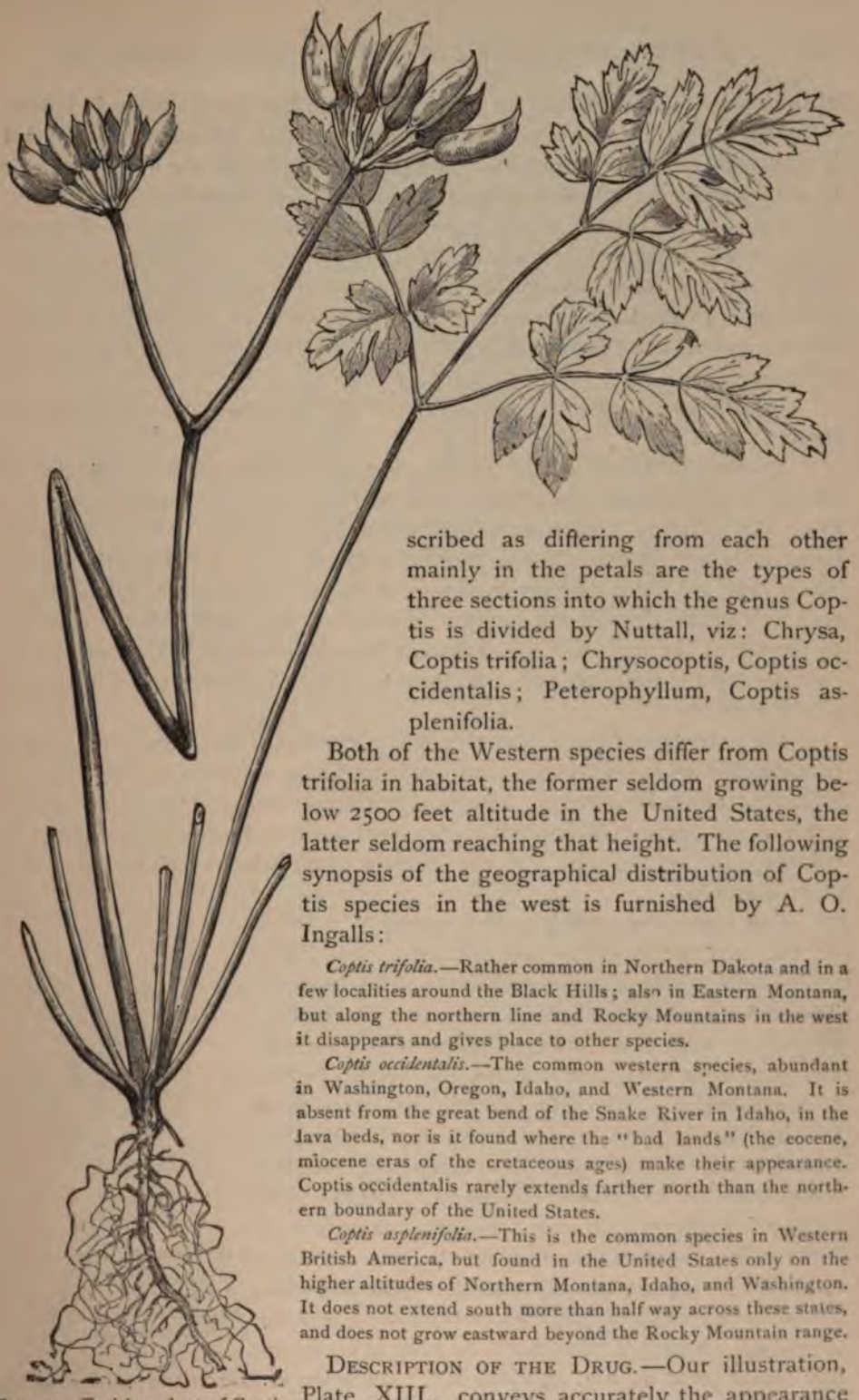


FIG. 53.—Fruiting plant of Coptis asplenifolia (natural size).

scribed as differing from each other mainly in the petals are the types of three sections into which the genus Coptis is divided by Nuttall, viz: Chrysa, Coptis trifolia; Chrysocoptis, Coptis occidentalis; Peterophyllum, Coptis asplenifolia.

Both of the Western species differ from Coptis trifolia in habitat, the former seldom growing below 2500 feet altitude in the United States, the latter seldom reaching that height. The following synopsis of the geographical distribution of Coptis species in the west is furnished by A. O. Ingalls:

Coptis trifolia.—Rather common in Northern Dakota and in a few localities around the Black Hills; also in Eastern Montana, but along the northern line and Rocky Mountains in the west it disappears and gives place to other species.

Coptis occidentalis.—The common western species, abundant in Washington, Oregon, Idaho, and Western Montana. It is absent from the great bend of the Snake River in Idaho, in the lava beds, nor is it found where the "bad lands" (the eocene, miocene eras of the cretaceous ages) make their appearance. Coptis occidentalis rarely extends farther north than the northern boundary of the United States.

Coptis asplenifolia.—This is the common species in Western British America, but found in the United States only on the higher altitudes of Northern Montana, Idaho, and Washington. It does not extend south more than half way across these states, and does not grow eastward beyond the Rocky Mountain range.

DESCRIPTION OF THE DRUG.—Our illustration, Plate XIII., conveys accurately the appearance of the plant, the commercial drug being masses

of the entire plant. While the officinal portion has always been designated as "the root," yet the rhizome has never been separated from the top, and there is really no reason for doing so. The leaf and leaf-stalk are unimportant, and, in our opinion, the officinal designation should have been the plant.

Coptis (Goldthread) accordingly appears in market as masses of the entire plant, in which the bright yellow, thread-like rhizome preponderates, and this yellow color is often perceptible part way up the leaf-stalk. The rhizome is pure bitter to the taste (berberine), and the portion of the leaf-stalk that possesses a yellow color is also perceptibly bitter. The other portions of the plant are insipid.

MICROSCOPICAL STRUCTURE.—(Written for this publication by Louisa Reed Stowell).

Rhizome.—On the outside of the rhizome is a row of epidermal-like cells, having a thick, clear, white wall, thickened on the outer surface, thus resembling the cuticle. Occasionally it surrounds the entire cell. The most of these cells are empty, though a few of them are colored a bright yellow. These cells are quite uniform in size and shape. On a cross section they are round or square, but on the longitudinal section they resemble the cells of the epidermis of the leaf over the midrib or prominent veins. They are long and narrow, and the walls are not of uniform thickness, but covered with irregularly placed nodules.

The outer two or three rows of cells of the parenchyma are smaller, with walls considerably more thickened, than the rest. The walls are a clear white, even glistening like collenchyma. They are frequently empty, sometimes containing a few starch-grains, chlorophyll-bodies (without the chlorophyll), bright yellow coloring-matter, and oil. In the minute inter-cellular spaces occasionally resin is found.

The remainder of this parenchymatous portion of the rhizome is composed of large, oval, thin-walled cells, with numerous small inter-cellular spaces. The majority of the cells contain small, round starch-grains (see Fig. 54). Many of these cells are modified glands or sacs, and contain the bright yellow coloring-matter. The cells forming the rows from the third to the sixth from the outside of these parenchymatous cells are apt to contain oil and the coloring-matter in greatest abundance. Minute particles of hardened albumen are found in some of these cells. Small masses of resin are found between the cells, or attached to the outside of the cell-wall. The majority of these particles of resin are not more than $\frac{1}{2000}$ of an inch in diameter. A mass is occasionally found (as at *m*, Fig. *A*, Plate XV.) much larger and firmer, and even $\frac{1}{1500}$ of

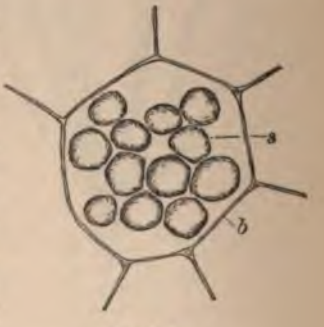


FIG. 54.

A single cell of starch-bearing parenchyma from the rhizome, filled with starch-grains; *b*, parenchyma; *a*, starch-grains. (Drawn with the ⅛-in. objective and the "C" eye-piece.)

PLATE XV.

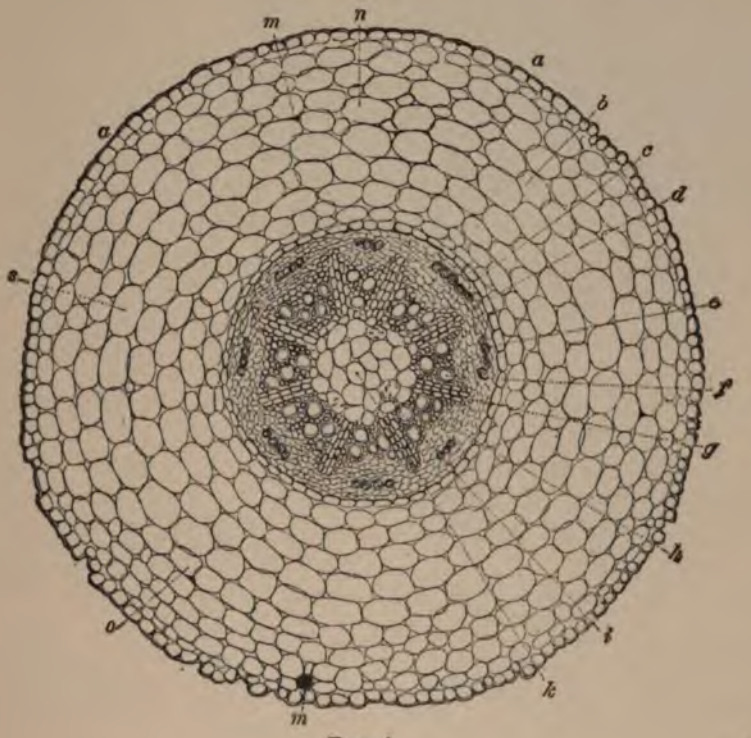


FIG. A.

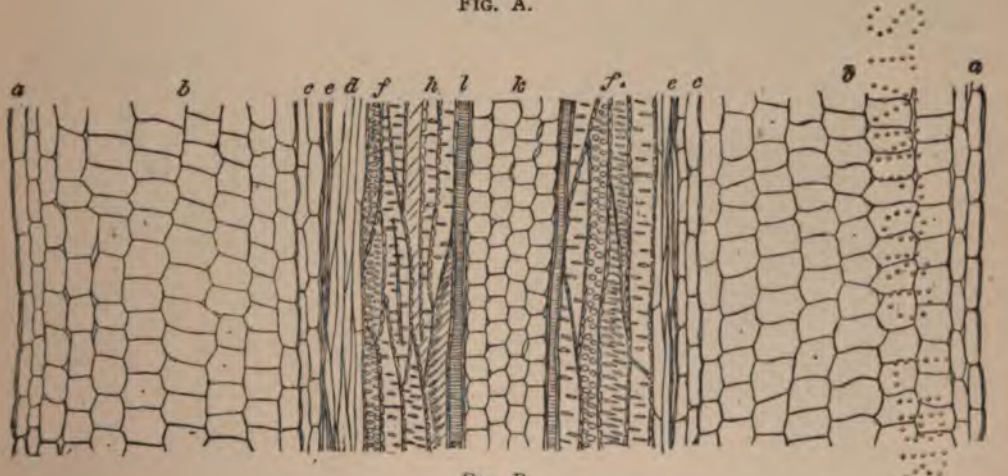


FIG. B.

MICROSCOPIC STRUCTURE OF THE RHIZOME OF COPTIS TRIFOLIA.[a]

A, cross section of the rhizome; B, longitudinal section of the rhizome.

A—Drawn with the ⅔-in. objective and the "A" eye-piece. B—Drawn with the ⅔-in. objective and the "C" eye-piece.

[a] For reference to letters see p. 204.

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an inch in diameter. This resin is not entirely soluble in alcohol, and is turned a blue color by aniline.

Just inside of this parenchyma is the endodermis, loaded with a dark-yellow coloring-matter. On the cross section, the cells are thick-walled, small, oval or square; but on the longitudinal section they are four or five times longer. The endodermis is the dividing-line between the starch-bearing parenchyma and the liber part of the rhizome. There is quite a difference in different rhizomes, both in the size and color of these cells, and they differ even in the same rhizome according to their distance from the leaf-bearing end.

Inside of the endodermis are found simple, thin-walled, hexagonal cells of phloëm, containing protoplasm and albumen. Embedded in this phloëm are clusters of liber fibre, each cluster containing from three to eight small, bright-yellow, hexagonal cells of prosenchyma, having several successive layers of cellulose in their thick wall. These are about $\frac{1}{300}$ of an inch long, and have many radiating lines or breaks, as seen in the longitudinal section.

The woody part of the rhizome is composed of poorly developed medullary rays, wood prosenchyma, and pitted cells, with a few spiral vessels; all colored bright yellow.



FIG. 55.

A single cell from the parenchyma of the pith with reticulated markings. (Drawn with the ⅛-in. objective and the "A" eye-piece.)

The pith in the center of the rhizome is composed of very thin-walled oval cells of parenchyma, loaded with starch-grains. Occasionally a modified cell is filled with coloring-matter. Around the outside edge of the pith are a few parenchymatous cells having distinct reticulated marks (see Plate XV., Fig. A, *i*, and Fig. 55). Many of the cells of the parenchyma, both at the center and the outside of the rhizome, have faint reticulated marks, which show both on the cross and longitudinal sections.

Root.—The root is surrounded by many fine root-hairs, in which is found a small amount of protoplasm. The most of the root is composed of large, thin-walled, oval cells of parenchyma. The most of these contain minute starch-grains (see Fig. 57, on following page), and some of the larger cells contain coloring-matter and oil.

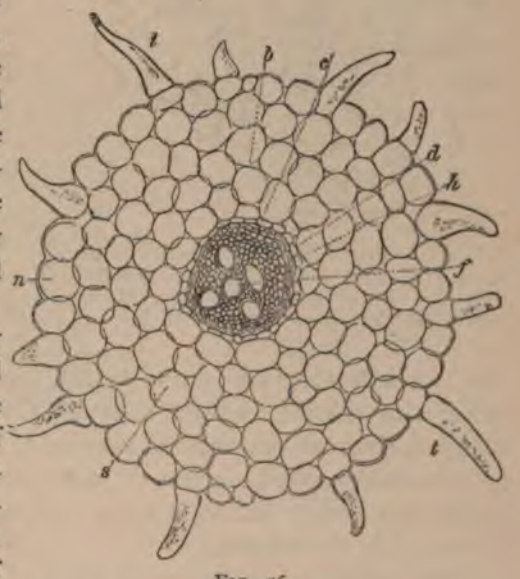


FIG. 56.

Cross section of the root. (Drawn with the ⅛-in. objective, and the "C" eye-piece.

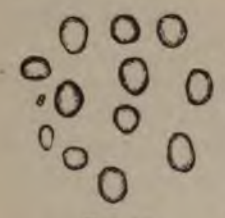


FIG. 57.

Starch-grains taken from the root. (Drawn with the ⅛-in. objective, and the "C" eye-piece.)

In the center of the root is found the usual small woody cord, composed of first the endodermis, then the phloëm, wood prosenchyma and pitted cells. All except the phloëm are colored a bright yellow.

Leaf.— On the midrib of each leaflet, in elogated clusters, towards the base of the leaflet, are short, unicellular, thick-walled white hairs, with minute nodules covering the surface of the hairs (see Fig. 58). Many of these are curved and pointed towards the apex of the leaflet. These hairs contain a small amount of protoplasm, generally dried down in particles, but in the young leaf it is fresh, and exhibits a nucleus. Coloring-matter is not found in these hairs.



FIG. 58.

The epidermal hairs found on the upper surface of the leaves, directly over the prominent veins. (Drawn with the ¼-in. objective, and the "C" eye-piece.)

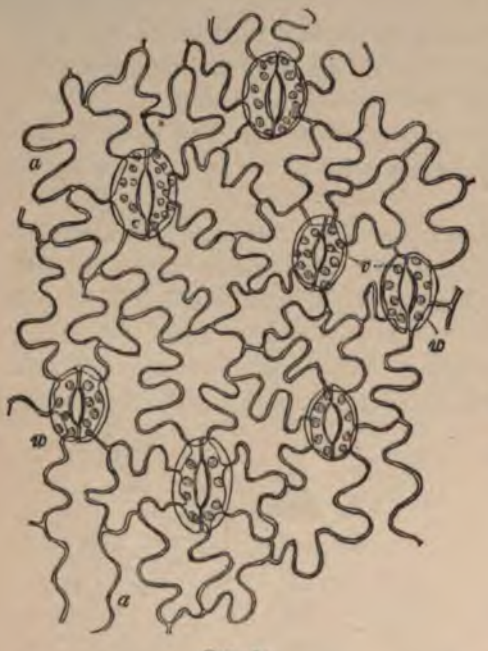


FIG. 60.

Epidermis from the lower surface of the leaf, showing the epidermal cells and the stomates, with the chlorophyll bodies in the guard-cells of the stomates. (Drawn with the ¼-in. objective, and the "C" eye-piece.)

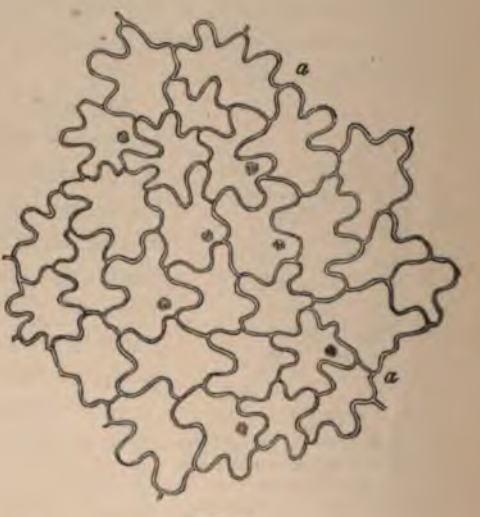


FIG. 59.

Epidermis from the upper surface of the leaf, showing only the epidermal cells and an occasional nucleus. (Drawn with the ¼-in. objective and the "C" eye-piece.)

The entire upper surface of the leaf is covered with a clear, white, thick, firm cuticle. This cuticle is laminated, or composed of five or seven layers of

cellulose placed parallel with the surface. The cuticle on the lower surface of the leaf is more delicate, only about one-half the thickness of the upper.

The epidermis on the upper surface of the leaf is about $\frac{1}{800}$ of an inch wide, and composed of large, quite regular, clear-white, deeply serrated cells; containing in the young, fresh leaves some protoplasm and an occasional nucleus (see Fig. 59). Very few stomates, if any, are present. The epidermis on the under side of the leaves is about $\frac{1}{1600}$ of an inch thick, and composed of thin-walled, empty, deeply serrated cells (see Fig. 60). The numerous large stomates are set a little below the level of the epidermis, and the guard-cells of the stomates are filled with chlorophyll-bodies.

The center of the leaf is composed of the usual palisade cells and loose parenchyma, with numerous large inter-cellular spaces (see Fig. 61). The palisade cells are delicate, not uniformly of the same length, and filled with chlorophyll-bodies, of which many have an oval, rather than the usual round form. The cells of the loose parenchyma contain only a few chlorophyll-bodies and numerous minute starch-grains; also oil and albumen. In many of the cells bordering on the vascular system of the leaf the bright yellow coloring-matter of the Coptis is found. In a few of the small inter-cellular spaces of the loose parenchyma towards the lower surface of the leaf are small masses of resin.



FIG. 61.

Cross section of the leaf, showing none of the framework, but only the fleshy part of the leaf. The section is taken at right angles to the midrib. (Drawn with the ¼-in. objective and the "A" eye-piece.)

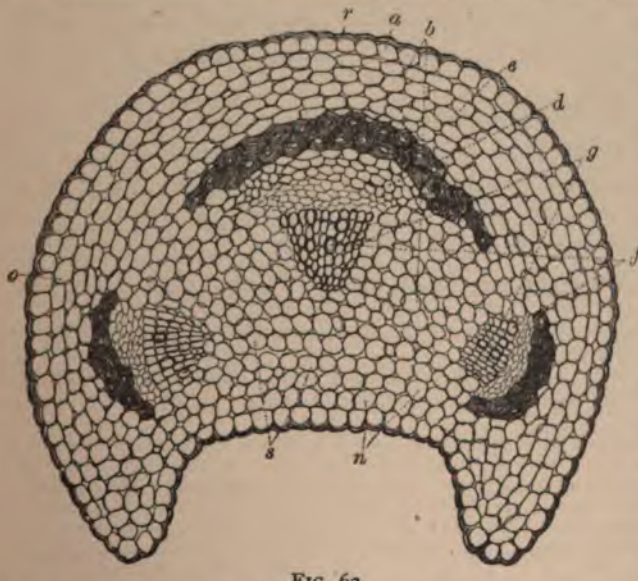


FIG. 62.

Cross section of the stem of the leaf, cut midway of the stem. (Drawn with the ⅝-in. objective and the "C" eye-piece.)

Stem of the Leaf.—The cuticle is thick, laminated,

and in the old stems has taken the peculiar tinge of yellow so common in the plant. It is about $\frac{1}{2400}$ of an inch thick. The epidermis is $\frac{1}{800}$ of an inch thick, and is composed of quite regular cells. These cells are nearly square on the cross section, but on the longitudinal are four or five times longer. Just beneath the epidermis, and especially at the corners of the stem, is collenchyma; thick-walled cells filled with chlorophyll-bodies. The bulk of the stem is composed of simple oval cells of parenchyma, generally filled with starch-grains, a few clorophyll-bodies, and coloring-matter. The coloring-matter is present in nearly all the cells adjoining the liber fibre and the woody bundles. The starch is found in greatest abundance toward the center of the stem. Oil is found in a few special glands or sacs just inside of the collenchyma. The bundles of liber fibre and also the wood prosenchyma and pitted cells are of a bright yellow color. The phloëm is clear white, very thin-walled, and contains protoplasm. In very small inter-cellular spaces in the outer part of the parenchyma resin is found.

LETTER REFERENCES TO PLATE XV. AND FIGS. 54, 56, 59, 60, 61, AND 62.—*a*, epidermis; *b*, parenchyma; *c*, endodermis; *d*, phloëm; *e*, liber fibre, *f*, pitted cells; *g*, medullary rays; *h*, wood prosenchyma; *i*, reticulated cells of parenchyma; *k*, pith parenchyma, *l*, spiral vessels; *m*, resin; *n*, cells filled with yellow coloring-matter; *o*, oil-bearing parenchyma, *p*, palisade tissue; *r*, cuticle; *s*, starch or starch-bearing parenchyma; *t*, root-hairs; *v*, chlorophyll-bodies; *w*, stomates.

COMMERCIAL HISTORY.—Coptis was prominent at one time as an American drug. It was so esteemed in New England that we have it recorded by Dr. Bigelow that "of this article larger quantities are sold in the druggists' shops in Boston than of almost any other indigenous production."* We find in Sanborn's Medical Botany, 1835, that the root of Coptis was at that time worth two dollars per pound by retail. It is now so generally unimportant that, excepting an occasional call for domestic use, it is out of market, and, as a rule, has scarcely an established value.†

PHARMACOPŒIAL HISTORY.—Coptis was not recognized by the first (1820) edition of the United States Pharmacopœia. It was introduced in 1830, and remained officinal until 1880, when it was discarded. Its officinal designations have been "Coptis Trifoliæ Radix," New York edition, 1830; and "Coptis" in all others. The officinal portion has ever been "the root." Coptis was originally (1830) placed in the secondary list of the United States Pharma-

* In connection with this statement it seems strange that "The Pharmacopœia of the Massachusetts Medical Association," published in Boston, 1808, omitted Coptis.

† It is quoted, pressed in ounces, at one dollar per pound Price-list of Allaire, Woodward & Co., Peoria, Ill.) In this connection we present the following interesting letter on the subject, written us by Mr. Chas. A. Peck, of Albany, N. Y.:

"I recall a fact that came under my observation several years ago In a low piece of swampy woods abounding in sphagnum, situated in Rensselaer County in this state New York, there was an abundance of Coptis. The Shakers were then paying 37½ cents a pound for the dried plants, roots and all. The women and children of several families living in the vicinity of this piece of woods spent most of one summer in these woods (which were mostly of spruce and balsam trees), digging Goldthread to sell to the Shakers. They dug it out with their hands only, sitting down by a smudge built to keep off gnats and mosquitoes, while they picked out the 'roots' from among the sphagnum and other mosses among which they crept. They would take their lunch with them and spend the whole day in the swampy woods, and when they had accumulated a wagon load of the dried material, one of the number would start with it for the Shaker settlement at Lebanon, forty miles away."

copœia, and occupied this position through succeeding revisions until 1860, when it was transferred to the primary department, occupying this place until discarded in 1880. When we reflect that Coptis was in more extensive use at an early day than recently, and that it has certainly not been of primary importance within thirty years, we are surprised to find it elevated in 1860 to the primary list of the United States Pharmacopœia. From what we can learn it has always been a cumberer of the pharmacopœial pages, although in local use in domestic medicine, and the committee of revision for 1880 is to be commended for discarding it. The United States Pharmacopœia has never recognized a preparation of Coptis.

CONSTITUENTS.—Bigelow* states that "the constituent with which it most abounds is a bitter extractive matter, soluble both in water and alcohol. It is devoid of astringency when chewed in the mouth, and it gives no indication of the presence of tannic or gallic acid when tested with animal gelatin, or with sulphate of iron." This was the accepted record until Prof. J. M. Maisch † announced that berberine was its bitter constituent, and this was afterward supported by Prof. F. F. Mayer,‡ Mr. E. Z. Gross,§ and Mr. J. J. Schultz.‖ Prof. Mayer announced that the berberine was associated with another alkaloid, and Mr. Gross and Mr. Schultz both obtained it; Mr. Gross giving it the name coptine. These two alkaloids are the characteristic constituents of Coptis. Mr. Gross failed to find starch in Coptis trifolia, but Mr. Chas. W. Burr ¶ detected starch in its root. Mr. Schultz obtained ten per cent. of extractive matter by means of alcohol acidulated with acetic acid.

The Berberine of Coptis trifolia.—Under our direction Mr. J. J. Schultz investigated this subject, announcing the results in the Journal of Pharmacy, 1884, p. 261. It was found that the usual method of separating berberine from Hydrastis was not applicable to Coptis, for neither sulphuric nor hydrochloric acid would satisfactorily precipitate it from aqueous extract or alcoholic tincture of the plant, and that to estimate the berberine it was necessary to use carbazotate of ammonium whereby insoluble carbazotate of berberine was produced. However, as Coptis can not be used economically to prepare berberine, this fact is of little importance. Mr. Schultz obtained an amount equivalent to 0.8 per cent. of sulphate of berberine by using carbazotate of ammonium.

The Second Alkaloid of Coptis trifolia—Coptine.—This exists in very small amount, and possibly is identical with hydrastine, the white alkaloid of Hydrastis canadensis.** It conforms to that alkaloid in chemical properties, and is crystalline. Mr. Schultz under our care obtained only 4.275 grains of the alkaloid from 35,000 grains of Coptis, or but 0.012 per cent.

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* American Medical Botany, 1817, p. 63.

† Buchner's Neues Repertorium of Pharmacie, Vol. XI., July, 1862.

‡ American Journal of Pharmacy, 1863, p. 97.

§ American Journal of Pharmacy, 1873, p. 193.

‖ American Journal of Pharmacy, 1884, p. 261.

¶ American Journal of Pharmacy, 1884, p. 131.

** It is a noticeable fact that berberine is usually, if not always, accompanied by a white alkaloid of which hydrastine is a good representative.

PHARMACEUTICAL PREPARATIONS.—Coptis yields its properties readily to alcohol, or mixtures of alcohol and water, and is easily exhausted by the act of infusion or decoction. The only preparation that has been recorded is a tincture introduced by Bigelow, made by the maceration of an ounce of powdered Coptis in a pint of diluted alcohol. A fluid extract can be made by means of the formula for making fluid extract of Hydrastis (p. 149), substituting powdered Coptis for powdered Hydrastis. This fluid extract has a dark-yellowish, red, or brown color, and possesses the sensible properties of Coptis.

MEDICAL HISTORY AND PROPERTIES.—The various species of Coptis are esteemed as excellent bitters in all parts of the world to which they are native, and are used in domestic practice. Occasionally they are honored by papers from medical writers, some of whom recommend it for intermittent fever, etc., but the record shows that substances equally as effective and cheaper can usually be more easily obtained. Coptis trifolia is typical of the other species, and the thread-like rhizome of this plant has long been used in domestic medicine in the Northern States, especially in New England during the early part of this century. Indeed, there is no evidence to indicate that it was not employed from the time of the settlement of the country. Cullen's Materia Medica,* with additions by Barton, places Coptis and xanthorrhiza together, and recognizes Coptis under the name Helleborus trifolius, remarking as follows: "They are pretty pure bitters, but I am not certain that they possess peculiar virtues." The country people formerly thought, and still contend, that Coptis is valuable in the treatment of aphthous sore mouth, and this was accepted until 1817 by the medical profession. Thus, we extract from an early edition of Coxe's Dispensatory as follows: "They (Coptis rhizomes) possess a considerable degree of astringency and bitterness, and have long been employed by the people in the country as a remedy for aphthous and cankerous sores in the mouths of children, with considerable benefit." In 1817, Vol. I. of Bigelow's American Medical Botany appeared, and, taking issue with all other writers, Dr. Bigelow asserted that "Its reputation, however, in these cases is wholly unmerited, since it possesses no astringent or stimulating quality by which it can act on the ulcerated spots, and when benefit has attended its use it is doubtless to be ascribed to other articles possessing the above properties, with which it is usually combined." This statement of Bigelow was accepted without question by the medical profession, and from that day authorities simply stated that it was a tonic bitter similar to quassia, gentian, and columbo, although its principal constituent, berberine, in our opinion should rather classify it with the species of berberis, xanthorrhiza, and other bitters containing that alkaloid. The first edition of the United States Dispensatory (1833) followed Bigelow, and has continued the subject unchanged until the present day; and the voice of the medical profession is expressed by this paper, which doubtless awards, as follows, to the plant all the credit it merits:

*Cullen's Treatise of the Materia Medica, American edition, by B. S. Barton, Vol. II., 1812, p. 57.

"It is a simple tonic bitter, bearing a close resemblance to quassia in its mode of action, and applicable to all cases in which that medicine is prescribed, though from its higher price not likely to come into general use as a substitute. In New England it is much employed as a local application in aphthous ulcerations of the mouth; but it probably has no other virtues in this complaint than such as are common to all the simple bitters. It may be given internally in substance, infusion, or tincture. The dose of the powder is from ten to thirty grains; of a tincture prepared by macerating an ounce of the root in a pint of diluted alcohol, one fluid drachm."*

THE PHYSIOLOGICAL ACTION AND THERAPEUTICAL USES OF BERBERINE.—(Written for this publication by Dr. J. A. JEANÇON, Professor of Physiology, Eclectic Medical Institute, Cincinnati.)†

Only within the last few years have earnest and scientific researches been made into the nature of the physiological action of berberine upon the animal body. Whilst its chemical properties have been extensively examined, their compositions and reactions thoroughly studied and ascertained, only a few really critical investigators have taken sufficient pains to acquire an exact knowledge of its pharmaceutic, therapeutic, and toxic action. Among those few who have furnished correct data, are Dr. Antoine Curci and Dr. Köhler. The first has published his results in a series of able articles in the *Racoglitore Biologica*, in the years 1879 and 1880. The following are synoptical extracts of the most important of those articles. In the July number of that periodical (which, fortunately, has a highly scientific and at the same time a singularly practical character), Professor Curci, in the article bearing the title "*Ricerche sperimentali sull' azione biologica della berberina*," says: "I found that an aqueous solution of berberine (1:100) destroys amœboid motion of colorless blood corpuscles, reduces their size, causes them to become granular, and makes their nuclei very visible. Colored corpuscles undergo the same change by the action of the solution. In either case no direct contact of the drug with the corpuscles is required; application to the mesentery or equally sensitive parts of a vessel is sufficient to produce hæmostasis in the capillaries at first and subsequently in the veins and arteries, without, however, causing any contraction of the vascular walls. Sulphate of berberine stops the motion of vibriones. A solution of the sulphate applied to voluntary muscles renders their *striæ* more prominent, apparently increases their volume, and the interfibrilar spaces become puffed and have a knotty look. Smooth, muscular fibres seem far less affected by its action. Subcutaneous injections of berberine or its salts produce œdema, extravasation and thrombi in the injected parts; repeated injections in the same locality cause the tissues to become sclerotic and assume a leather-like appearance. No suppuration takes place. Direct

* United States Dispensatory, 1st edition, 1833, p. 252.

† The chemistry of berberine is studied under hydrastis, pp. 95 to 130. The uses of berberine in medicine are appropriately considered with Coptis, which contains it nearly pure, instead of mixed with large amounts of another alkaloid, as is the case in hydrastis.

application to the mucous membrane of the intestines causes at once violent peristaltic contraction of the intestines, with atresia of its cavities, and at the same time discharge of its contents." As a therapeutic agent this author considers berberine very useful in gastro-enteric catarrh; especially the condensing action of the substance upon the mucous tissue, as very valuable in ulceration of the mucous structures of the canal. He thinks a similar action is likely to be exerted upon ulcers of the skin and conjunctivæ.

In his further investigations, the same author, in the April, May, June, and July numbers of the *Racoglitore* (1880), tells of his other experiments: "Subcutaneous application of 0.02 of berberine upon frogs and of 0.06 upon toads, of 0.1 upon moles, and of 0.6 upon rabbits and Guinea-pigs, produces general prostration, muscular fatigue, and subsequent death without actual paralysis. The temperature of warm-blooded animals steadily drops by the action of the berberine sulphate, alternates with an occasional slight rise, and eventually falls again to a fatal extent. The heart's action at first increases, and afterward steadily decreases, until the death of the animal. The pulse becomes at first more frequent, then becomes gradually slower, until it stops altogether, with the stoppage of respiration. Weaker solution than the above-named and smaller doses retard death, and diarrhœa-like discharges from the bowels, albuminuria, accompanied with granular change of the renal epithelium and fatty degeneration of the cortical substance of the kidneys, are then produced. Internally administered, there is equally a fall of temperature, but of shorter duration. Only weakness, loss of appetite, and increased discharges from the bowels, but no diarrhœa nor albuminuria, result." The author looks upon the berberine sulphate as a valuable regulator of the heart's action, by its constant and steady lowering of arterial pressure. Toxic doses certainly cause a fall of the temperature of the body, which he thinks becomes the cause of the death of the poisoned animal. He especially lays stress upon the steady and slow cooling of the body caused by the drug. The animal visibly loses flesh, the forces of the body diminish, and respiration ceases before the heart's action, when the animal dies. The peripheral nerves retain their irritability and electric excitability much longer than the nerve-centers, and the muscular structure longer than the nerves. *Post mortem* the membranes in the serous cavities are found dry; the blood in the cavities of the heart in larger or smaller coagula; the brain somewhat œdematous and hyperæmic. In slow intoxication, the epithelium of the kidneys are found in a state of fatty change; the same is the case with its cortical structures.

The urine voided *intra vitam*, in the poisoned state is always of acid reaction even in herbivora, usually contains albumen and cylinders. This shows that the drug is chiefly eliminated by the kidneys, and but slightly by the intestines and other organs of excretion. The blood of such poisoned animals requires more time for oxydation and reduction of its hæmoglobin than normal blood and is not so readily discolored by sulphate of sodium as usual, the hæmoglobin

seemed more solidly combined with oxygen, from the berberine, than is the case in normal blood. This characteristic action of the berberine exists under all circumstances whether the drug was taken internally, introduced direct into the circulation or subcutaneously. Its action upon the spleen is not very definite. Dr. Julius Kohler, under the direction of Dr Lewin has made a number of experiments with berberine and its salts. He published his results in a dissertation named *Ueber das Berberine, eine Pharmakologishe Studie, Berlin, 1883.*

On page 30, l. c. i., he says, that he used the berberina and its salts also, an aqueous decoction of the *Berberis Aquifolium*, and found that all alike resist the fermentive action of yeast, but exert no action upon peptic digestion of gastric juice unless the substance was administered in enormously large doses. He ascribes the action of the drug upon the intestinal canal as being similar to that of the tannates. He also found that it acted directly upon the blood-vessels, producing contraction (differing from Curci's experiments) and hæmostasis. He does not look upon it as being poisonous. From the few extracts of Curci and Koehler, it is readily seen that berberine and its salts have a limited physiological share of action upon the animal body, The same is found to be the case in regard to their therapeutic agency. To judge from its chemical composition, which ranks berberine with *bioxybenzoles* we may *theoretically* expect that the physiological and partly also remedial action of this substance would resemble the substances of that group of hydrocarbons. Reduction of temperature, especially deleterious action upon the parenchyma of the kidneys, destruction of amoeboid motion of the lower monocellular forms of life, are distinctly characteristic of the reactions of those hydrocarbons upon the animal bodies. However, therapeutic effects are very often exerted in a remarkably similar manner by substances of vastly different chemical compositions. The same may also be said of the physiological properties of bodies, yet the presence of protocatechuic acid and some of its homologous substances in the urine of a dog upon which the writer of this experimented with berberine for some length of time, the same being found in his own urine and in that of other persons after continuous use of berberina for a couple of weeks, led him to believe that a portion of berberine undergoes direct oxydation in the animal body and yields products similar to those brought about by distillation of the substance with alcoholic, potassic hydrate. Several plants containing berberine associated with a number of highly active substances, (hydrastine, podophylin, etc.,) have been for years a very popular remedy in many cases of catarrh of the different mucous surfaces of the body. The older eclectics have very frequently made use of the *Berberis communis*, and the *Hydrastis canadensis* and have established for those plants quite a reputation as an officinal remedy. The trouble only is that until very lately the physiological and even the therapeutic action of berberine separate from the other highly active substances associated with it in the many plants has but little been noticed and this has produced great confusion, and requires a cautious expression of opinion

in regard to its specific biological and remedial qualities. Berberine has been used by the writer of this in place of boracic acid, borax and other so called antiseptic substances in suppurating ulcers and phagedæna of mucous surfaces with no other success than would have been obtained by the use of the substances it substituted. The insolubility of some of its salts, and the fact that they stain permanently the dressings, will very likely retard a free use of these agencies in dressing of wounds and for general local application; on the other hand, being really inodorous, they can readily supplant iodoform as a local application, being more agreeable to use, whilst as an *anti-suppurative* (*sit venia verba*) they in no way yield to iodoform in efficacy.

The writer has lately taken quite a quantity of the substance internally, but must acknowledge that the thermometer has failed to register any great, or even very perceptible reduction of temperature of his own body. The action of the drug upon himself and some other persons who took quite a notable quantity for some time seemed only to be considerable irritation upon the kidneys and the presence of substances having a reaction, similar to that of protocatechuic acid, but no action upon the heart or blood vessels.

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1850.—The Pharmacopœia of the United States of America, p. 49.

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1863.—American Journal of Pharmacy, p. 97.
1863.—Proceedings of the American Pharmaceutical Association, p. 71.
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1879.—The National Dispensatory, p. 457 (and other editions).
1881.—Proceedings of American Pharmaceutical Association, p. 164.
1884.—American Journal of Pharmacy, pp. 131 and 261.
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1884.—A Manual of the Medical Botany of North America, Laurence Johnson, p. 64.

AQUILEGIA CANADENSIS

COLUMBINE.

PART USED.—The entire plant Aquilegia canadensis *Linn.*
Natural Order Ranunculaceæ, Tribe Helleboreæ.

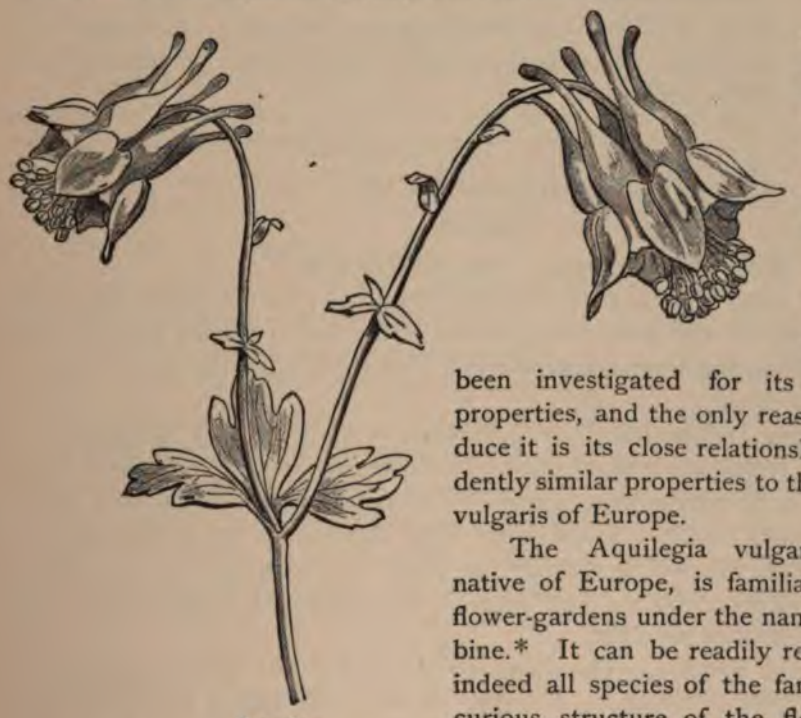


FIG. 63.
Flower of Aquilegia canadensis.

REMARKS.—The subject of this article is not really entitled to rank among the native medical plants. It has never been investigated for its therapeutic properties, and the only reason we introduce it is its close relationship and evidently similar properties to the Aquilegia vulgaris of Europe.

The Aquilegia vulgaris, though native of Europe, is familiar in all our flower-gardens under the name of Columbine.* It can be readily recognized, as indeed all species of the family, by the curious structure of the flowers. The flowers of most of the species are nod-

*Common name derived from the Latin *Columba*, a dove. The five incurved spurs of the petals have been likened to heads of five doves; the sepals to wings. It was a favorite device of ancient artists to represent them in a ring around a dish.

ding. They have five flat sepals, alternating with five equal spurred petals. The spurs are very large and are the conspicuous part of the flower. The flowers of the European Columbine in cultivation vary in all shades of color from blue to white, and are often double with a series of spurred petals.

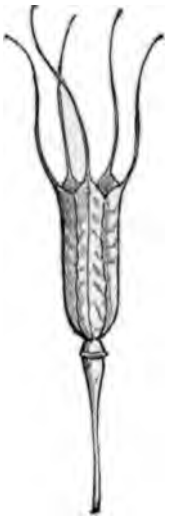


FIG. 64.
Fruit of Aquilegia canadensis.

The native plant, Aquilegia canadensis, is of wide distribution in the United States, and is found generally in rocky situations. It is a much more handsome and more graceful plant than the cultivated species and more worthy of cultivation. The flowers are bright scarlet without, yellow within, and have straight spurs. The fruit consists of five, dry capsules containing numerous black seeds and opening at the apex. The plant can be at once identified by our cut of the flower.

MEDICAL PROPERTIES.—As stated before the medical properties of the plant have never been investigated. They are no doubt analogous to the Aquilegia vulgaris of Europe, which has been used in cutaneous diseases and in jaundice. It is said to be a "diuretic, emmenagogue sudorific, antiscorbutic and aperitive. The seeds are acrid and are taken in vinous infusions for jaundice."

DELPHINIUM.

LARKSPUR.

Natural Order Ranunculaceæ, Tribe Helleboreæ.

INTRODUCTORY REMARKS.—We are induced to give the genus Delphinium a passing notice in this work, not that any of the native species have ever been used in medicine but from the probability that they might be used in place of the imported drug.

The genus Delphinium,* or Larkspur, is a very showy family of herbs found in the temperate regions of the Northern hemisphere. Several species are familiar in flower-gardens, the most common being Delphinium Consolida and Delphinium Ajacis. The flowers of all the species have a peculiar, odd shape (see Fig. 65), which enables the plants of the genus to be easily distinguished. Those who are familiar with the cultivated Larkspur will recognize the wild species on sight.

MEDICINAL SPECIES.—The plant mostly used in medicine is the Delphinium Staphisagria of Southern Europe. It is a tall, coarse herb with an unpleasant odor, and grows wild in the Mediterranean regions. It is known under the English name Stavesacre.

*The name is derived from the resemblance of the unopened flower to the head of a dolphin (*Delphin*), as formerly represented by artists.—Bentley & Trimen.

The part mostly used is the seeds, and their virtues seem to reside in alkaloidal principles (Delphinine, Staphisagrine and perhaps others) that are found in the shell of the seeds. The drug is derived mostly from Trieste. Perhaps the greater part however of the medicine used in this country is the so-called "German tincture," imported from Germany (where the plant does not grow). The drug has been officinally recognized in the last Pharmacopœia under the name of Staphisagria.

Delphinium Consolida is another species that has been noticed considerable in medical works, but has never come into much use. In the Pharmacopœia of 1870 the seed was recognized, but the drug had never been used enough to merit a position, and was wisely discarded in 1880.

The plant is the most common species in flower-gardens, and can readily be distinguished from other species by having only one seed pod to the flower (the usual number is three). It often escapes from flower-gardens and becomes established, for a few years, by road sides and in waste places, but it is not disposed to be a permanent weed. In Central Europe, however, it is considered a troublesome weed in grain fields.

NATIVE SPECIES.—*Eastern Species.*—None of the Eastern species are abundant enough to ever become an important drug, but in the West there are several of the family that deserve investigation.

Delphinium tricorne is, perhaps, the most common species east of the Mississippi. It is a dwarf plant, less than a foot high, with a few petioled leaves at the base, and a long raceme of large, showy blue flowers that appear in early spring. The plant grows from a tuberous root, and is generally found in patches on clayey soil and in open woods. It can be at once recognized by our picture.



FIG. 65.

Flowers of Delphinium tricorne.

Delphinium exaltatum and Delphinium azureum are the only other Eastern species. Both can be readily distinguished from the preceding by their height, which is from two to four feet. They are widely distributed but mostly rare.

Neither of these three species, as we have remarked, has any probability of becoming of any importance as a drug, although all doubtless possess, in the shell of their seeds, the peculiar alkaloids of the genus.

Western Species.—There are a number of Western species all as yet uninvestigated, but most likely to be found active agents; and, as in many places they grow abundantly, they are worthy of attention. It is scarcely necessary to consume our space with the characteristics by which they are distinguished from each other, as one species is as likely to prove valuable as another. They can all be known as Delphiniums at once by the shape of the flower.

The most common species are Delphinium Menziesii, Delphinium decorum, Delphinium azureum, Delphinium bicolor, Delphinium californicum and Delphinium simplex.

In certain localities in the West where cattle are poisoned by eating some wild plant, a species of Delphinium is supposed by some to be the plant that causes the trouble. It is only a supposition, however, and not proven that we can find.* We give, as a note on the subject, a letter received from Wm. C. Cusick, a well known Western botanist.†

MEDICAL PROPETIES.—The native species of Delphinium doubtless possess properties similar to those of the foreign, and as Delphinium Staphisagria is used extensively by Eclectic physicians, we reproduce from Prof. Scudder's Specific Medication, as follows:

"The tincture of Staphisagria has a specific action on the reproductive organs of both male and female; but more marked in the first. It quiets irritation of the testes, and strengthens their function; it lessens irritation of the prostrate and vesiculæ; arrests prostatorrhœa and cures inflammation of these parts. It also exerts a marked influence upon the urethra, quieting irritation and checking mucous, or muco-purulent discharges; it influences the bladder and kidneys, but in a less degree.

"The action of Staphisagria upon the nervous system is peculiar. It exerts a favorable influence where there is depression of spirits and despond-

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* In our opinion the trouble is ascribed falsely to this plant, and we believe that it really belongs to some species of Leguminous plants; probably an Astragalus, several of which have proven to be poisonous to animals, and are called in the West "Loco Plants."—L.

† "Only in certain localities the stock (cattle) are poisoned, although the plant is found everywhere. There is no place nearer than forty or fifty miles of us where it seems to injure stock, and I am but little acquainted with the symptoms of the poisoned animals. The plant is known to botanists as *Delphinium decorum*, Fisch. & Meyer var. *nevadense*. Stock men call it "Larkspur." It seems to poison only cattle, and poisons them only in the early spring when they are first turned on the crop, and it is thought by the cattle men that the animals pull up the plant and eat the roots, which are supposed to be the poisonous part of the plant.

"The symptoms, as well as I can remember, as related to me are: The cattle stagger and fall, soon becoming unable to rise, become wild and dangerous to approach. So long as they are able to go they attack fiercely any person who may approach them. Many of them die, though most recover. I do not know the antidotes, if there are any. It is a query to me if it is really the Larkspur that poisons, for it abounds in our own neighborhood, but never poisons stock here.

"There is this difference, however. In all the neighborhood where the plant is poisonous the altitude is much less than the general elevation, hence the climate is much warmer, and it is possible that the plant that will kill in one place may not be injurious in another. This is only a guess, and perhaps a very absurd one."—WM. C. CUSICK.

ence, in cases of hypochondriasis and hysteria, especially when attended with moroseness and violent outbursts of passion."

In addition, we offer the following synopsis, by Prof. Stillè, of the medical uses of the species, Delphinium consolida and Delphinium Staphisagria, and no doubt our native species will conform in properties.

"They have been used in the treatment of dropsy and spasmodic asthma, generally in the form of a tincture, which has been much employed as a lotion, or as an ointment for the destruction of lice. These effects are due to the alkaloid delphinine."

ACONITUM.

ACONITE.

PARTS USED.—The roots of Aconitum uncinatum *Linn.*, and Aconitum Fischeri *Reich.*

Natural Order Ranunculaceæ, Tribe Helleboreæ.

INTRODUCTORY REMARKS.—The genus Aconitum has been celebrated from the earliest ages on account of the poisonous principle with which nearly all species of the family are possessed.* It is among the first recorded vegetable poisons used, and it is supposed to be that referred to by Pliny as being used for an arrow poison by the aboriginal Gauls. In India where some species are very virulent it is in common use to this day by the natives for this purpose.

To the ancients aconite was considered the most virulent poison, and has a prominent place in their mythology and legends. It was used to poison wild animals; hence the name "wolf's bane," by which it is now commonly known.†

The genus Aconitum is a native of mountainous countries, consisting of about twenty species, mostly found in the mountains of Europe and Asia. The species are specially liable to vary and on this account much confusion exists in their nomenclature.‡

The flowers of Aconite are large and showy, and often an Aconite plant is found in flower-gardens. The color is usually blue, though a few European

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*The Ἀκόνιτον of the Greeks and *Aconitum* of the Romans are held to refer to the identical plant now mostly used in medicine, the Aconitum napellus.

In reference to the derivation of the word aconitum Dr. Chas. Rice writes us:

"The etymology is uncertain, and as there is no ancient name of the plant in other old languages, related to Greek and Latin, in which the same root occurs, we can only make a close guess. Pliny states that its name is derived from the fact that it grows *ἐν ἀκόναις* 'on steep rocks.' Theophrast refers it to the name of the city of Akonai, in Bithynia. Others refer it to *ἀκόνη* (*akonè*), 'whetstone,' 'sharp point.' There is no doubt it belongs to the Indo-germanic root *ak*, 'to be sharp.'"

†"The hunters which seeke after woolfes, put the juice thereof into rawe flesh, which the woolfes devoure, and are killed."—Gerarde (1597).

‡Nearly thirty forms of the common European Aconitum napellus were mentioned by Seringe, in De Candolles Prodromus (1824), the most of which had been previously described as distinct species in Reichenbach's Monograph of the Genus.

species have yellow flowers. The structure is peculiar and the flower of any of the species can be at once recognized by its odd shape. The petaloid calyx consists of five unequal sepals, the upper one (called the galea) much larger than the other, and hood-shaped or helmet-shaped. From this hood-shaped sepal resembling the cowl of a monk, the plant has received the common name Monk's Hood, by which it is generally known in English and American flower-gardens.



FIG. 66.
Section of a flower of an Aconite, showing its peculiar structure.

The root of Aconitum napellus, a common species of the mountains of Europe, was introduced into medicine by Störck, in 1762, and has ever since been a most important drug. Large quantities are imported and used in the United States, but none of our native species have been recognized by either Pharmacopœia or Dispensatory.

NATIVE SPECIES.—With one exception the American species of Aconitum are found so rarely that they can not, excepting as homœopathic remedies, be of any commercial importance. In the Western States, however, we have a species growing abundantly in many localities, and it is not unlikely that some day it may become an important source of the drug.* In the Allegheny Mountains in the East we have two species.

Aconitum Uncinatum Linn.—This is a rare plant, found in rich, damp soil in the Allegheny Mountains. It is rare in Pennsylvania, but more common in Virginia, Maryland and further south. Its most northern station is Chenango county, New York, where it was discovered by Major Le Conte, early in the century, but has not been collected there since.



FIG. 67.
Flower of Aconitum uncinatum (natural size).

The stem is slender, weak and disposed to recline on other plants. It grows from two to five feet long. The leaves are borne on leaf-stalks from one to two inches long. They are smooth, deeply three (sometimes five) lobed; the lobes are acute and coarsely toothed.

The flowers appear late in summer and are bright blue. They are large and showy, and the plant is well worthy of cultivation in flower-gardens. The flowers are borne on peduncles about two inches long, from the axes of the



FIG. 68. *a*
A single pistil of Aconitum uncinatum; *a*, section of the same, showing position of the ovules.

* This plant has heretofore, as far as we can learn, never been investigated from a medical standpoint. The papers accompanying this article by Prof. F. B. Powers, on the chemical constituents, and by Prof. Roberts Bartholow on the medical properties, are made by our request. We trust they will turn attention to this plant, which deserves recognition.

PLATE XVI.



ACONITUM UNCINATUM.
(NATURAL SIZE).

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upper leaves, and are usually in clusters of two or three. They have the characteristic odd shape of the genus. The galea is erect and conical, and beaked in front. The fruit is a cluster of usually three dry pointed pods containing numerous angular, rough seed.



FIG. 69.
Fruit of Aconitum uncinatum (natural size).

FORMS.—This species, in accordance with the habits of the genus, is found in a number of forms. The plant grows in a territory where there are few botanists, and it is not commonly collected. A series of specimens from different localities would no doubt show a number of distinct forms.

De Candolle distinguishes two forms of the plant depending on the shape of the galea, one with the galea pointed, which he calls "var. Linnæanum," the other with the galea obtuse, which he calls "var. Michauxianum."

The most remarkable form of the plant that has come under our notice was collected by Prof. Chickering, in July, 1880, on Little Roan Mountain, in North Carolina. The leaves are laciniately cut, and the flowers have a whitish tinge on the upper part. Prof. Chickering considers the plant Aconitum reclinatum, but as the chief character of that species is the pure white flowers, we can not but consider it a form of Aconitum uncinatum.*

HISTORY.—This plant was known and named by Linnæus in the second edition of the Species Plantarum (1762), and has been fortunate in escaping all synonyms except a single one, Aconitum scandens, a name given it by Muhlenberg.

A plant growing in various parts of mountainous Asia has been decided to be identical with the American plant. According to good authority the Asiatic species furnishes part of the root sold as "Bish," which is a very poisonous drug, and much used in the manufacture of the alkaloids.† If such is

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* The following letter from Prof. Chickering, is of interest in connection with this form:

"In reply to your inquiries respecting Aconitum reclinatum, I have to say that I collected it on Roaring Brook, a noisy little stream running down the side of Little Roan Mountain, at an altitude of perhaps 2,500 feet. It was on July 20, 1880. I had noticed the leaves for some miles along the stream, and at last came upon a clump by the roadside in full flower. The flowering stalks were five or six feet high and made a very beautiful show.

"The main distinction between that species and our common Aconitum uncinatum is in the leaves, which are much more laciniately cut and divided, in the whitish tinge of the upper parts of the flower, and in the general habit and aspect of the plant.

"The botanies speak of it as being found in the high mountains of North Carolina, but I know definitely of no others besides Dr. Gray and myself who have collected it, and I found it in great demand among botanists. I collected perhaps a dozen stalks."

W. P. Conant, in allusion to Prof. Chickering's plant, says:

"We have also in the herbarium (of Department of Agriculture) a specimen collected on Roan Mountain by Prof. Chickering, and labeled Aconitum reclinatum. But the flowers are blue and the leaves seem cut somewhat different from those of Dr. Gray's own specimens."

† Bish, Bis or Bisk, Indian Aconite root, Nepal Aconite, is according to the Pharmacographia, mainly derived from Aconitum ferox, but also from certain other poisonous species of Aconite, viz., Aconitum uncinatum, Aconitum luridum, Aconitum palmatum and Aconitum napellus. The main constituent of Aconitum ferox is a very poisonous alkaloid *pseudaconitine*, more virulent than aconitine.

the case the root of the Asiatic plant differs from our native species, which according to our investigation has the characteristic alkaloid in a very small proportion.*

Aconitum reclinatum Gray.—This species is confined to a very few localities, and is such a rare plant that it can never be of any interest as a medicine. It grows on a few mountain peaks of North Carolina and Virginia, and is found at an altitude of from four to five thousand feet.†

It selects damp and deeply shaded places. The stem is very weak and slender, from five to eight feet long, and when the plant is in flower it is generally prostrated. The flowers are white or cream colored, by which the plant can be at once distinguished from the preceding species. They appear in July.

This plant was discovered by Prof. Asa Gray, on an excursion to the mountains of North Carolina in the summer of 1841, and was described in the following year.‡ There has never been any chemical or clinical investigation made of this plant, and there is no call for them.

Aconitum Fischeri Reich.—This is the only native species that can ever become of any commercial importance. It is abundant in the Rocky Mountains, and as it seems to possess the chemical properties of the imported root it may some day be an important source of the drug.

HISTORY.—There has been great confusion regarding the identity and nomenclature of this species.

The plant was first collected by David Douglas, in 1827, and forwarded by him to the Horticultural Society of London. It was not described until Hooker published his Flora Boreali-Americana (1833), where it was called Aconitum nasutum *Fischer*, being considered the same as a plant figured under this name by Reichenbach, in his illustrations of the genus.§ This plant was

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* A description of the root of Aconitum uncinatum and the result of its chemical and therapeutic investigation will be found after our botanical description of the other native species.

In this connection we call attention to the fact that different species of Aconitum do not exhibit in physiological action the effect that would be supposed to follow their close botanical relationships. Without apparent cause they are variably poisonous. The officinal species differs in virulence with climate and soil. The substance called aconitine varies markedly in value and physiological action as produced by different manufacturers, and as it is crystalline or amorphous. Dr. Charles Rice kindly loaned us the proof-sheets of "A Dictionary of the Economic Products of India," by George Watt, from which we condense the following:

Aconitum heterophyllum of India is largely eaten as a vegetable. The root is pleasantly bitter and is by some considered as a mild antiperiodic and tonic, by others considered inert. The root of Aconitum palmatum "is very bitter, and contains a well defined bitter alkaloid, it has no poisonous properties." In considering these facts we are not surprised to find that Aconitum uncinatum, grown in the Allegheny Mountains of America, is comparatively inert and that the same species in mountainous India is a poison.

† The only habitats recorded are Grandfather and Negro Mountains, in Northeastern North Carolina, and Cheat Mountain in Virginia, though it no doubt grows on adjacent mountain peaks of the Southern Alleghenies.

‡ Dr. Gray first noticed the plant on Negro Mountain July 2, 1884. At that time it was only in bud, and he mistook it for the previously described species. On July 9, he found it growing and in bloom on Grandfather Peak, and the *white* flowers at once attracted his attention to it as a new species. It is described and named in the American Journal of Sciences, April, 1842 (Vol. XLII, 1st series), p. 34.

As far as we can learn Dr. Gray has the honor of being the only botanist that ever collected the plant.

§ Illustratio specierum Aconiti generis, Leipsig, 1823-7.

PLATE XVII.



ACONITUM FISCHERI.
(A SMALL PLANT, NATURAL SIZE).

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brought from Caucasus, Russia, and the name Aconitum nasutum was derived from Fischer's manuscript.

In 1838, when Torrey and Gray published the first volume of their Flora of North America, the plant had been again collected by Nuttall, in his then recent trip across the continent. It was described in the Flora under a name given it by Nuttall, Aconitum columbianum, in his manuscript description of the plant. Although there was doubt, at the time, of its distinction from Douglas' plant, yet it was also described in the Flora as Aconitum nasutum, taken from Hooker's Flora Borealis-Americana. As soon as the identity of the two plants was established, Nuttall's name was dropped, hence the plant has been known as Aconitum nasutum in most works on Western botany.

In very recent years Prof. Sereno Watson has decided that the plant is identical with Aconitum Fischeri, *Reichenbach*, which was figured in Reichenbach's work from a plant of Kamtschatka, and not with Aconitum nasutum of the same work. The close resemblance to the picture of Aconitum Fischeri was noted by Hooker at the time he first named the plant. Hence it is that in Watson's Flora of California and other very recent works the plant is called Aconitum Fischeri.

Aconitum Fischeri.—Description.—This plant is quite common along the banks of streams in the mountains of Western States. It is generally found near the tops of mountains and in mossy or boggy places. It usually grows near the water or in it, but never where the water is not fresh. It grows at an altitude of from 7,000 to 11,000 feet above sea level. The stem is erect and about three or four feet high, although in some favored situations it attains a height of ten feet. The stem is smooth except on the upper flowering portion which is covered with a short pubescence. The leaves are orbicular in outline and deeply three to five lobed; the segments are acute and coarsely and sharply toothed. The leaf stalks are two to six inches long.

The flowers appear in August or September and are borne in a terminal loose raceme. They have the usual odd Aconite shape,* and can be recognized at once. They are usually of a deep blue color, but vary to nearly white in some instances. Sometimes plants are found with bronzed flowers.

FORMS.—The plant is found in a number of forms. These have never been closely investigated, but from what has been written we conclude that it is an extremely variable plant.

Cooper, in 1860, mentions that "two varieties have been collected in Washington," and Watson (1878) notes a small form from Southern Nevada.

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* The helmet is more arched and not quite as flat as shown in the engraving, which was made from a dried specimen. When the difference was discovered the plate had been made, and as the picture is a splendid one in every other particular, and the error a slight one that would only be noticed by a critical botanist, we did not think it would justify us to change the plate.

DESCRIPTION OF THE ROOT OF ACONITUM UNCINATUM.—The tuberous root is of a brown, rusty color. It varies in size from one-fourth to one-half an inch in diameter at the top and resembles an oblique, short radish in appearance. It decreases rapidly in diameter, and tapers into a rootlet in from one-half to one inch from the top, few specimens attaining a greater length. Usually they are cone-shaped, as shown by our engraving, but occasionally are nearly cylindrical and blunt. The tuberous root grows close to the surface of the ground. Its natural position is oblique, as shown in our engraving. The terminal root often extends to a depth of from four to six inches, dividing and subdividing, and often several rootlets the size of a pin strike out from the main root.

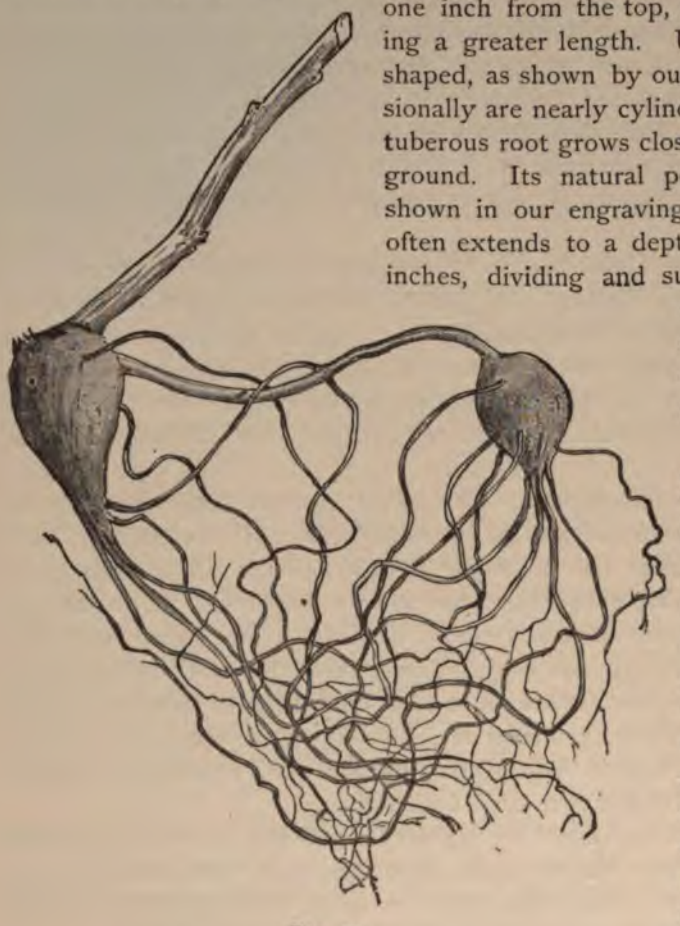


FIG. 70.

Root of Aconitum uncinatum, collected in June.

The method of propagation is peculiar and interesting. The growing stem rises from the top of the oblique root, and in the spring of the year the root sends off near its top, and on the inner side, a runner which attains a length of from one to three inches. At its extremity is produced another tuberous root, which increases until it becomes the size of the parent root, growing obliquely in the same direction. When it has become full size the parent root begins to shrink, and finally it and the connecting runner die, and in the fall decay, leaving a scar on the new root. The new root is provided with a terminal bud, destined to produce the stem next year when the same act of reproduction is repeated.

As the runner is produced in the same direction each year the result is that the plant moves a step each season. Sometimes, though rarely, two offshoots are thrown out by the same plant.

Internally the freshly broken root is white, juicy and succulent; upon exposure of a fresh surface it changes to a pinkish hue. When fresh it is persistently bitter and retains the bitterness upon drying. It does not possess in the least the benumbing properties of aconitine, and as shown by the following chemical investigation it is free from that alkaloid.*

CHEMISTRY OF THE ROOT OF ACONITUM UNCINATUM.—(Written for this publication by Prof. Virgil Coblentz, Prof. of Materia Medica, Cincinnati College of Pharmacy).

To determine the constituents of the root we proceeded in the following manner:

A portion of the tincture made from the fresh root was acidulated with tartaric acid, one-half its bulk of water added, and the alcohol driven off by the heat of a water bath. The aqueous acid solution was then filtered, and this was shaken several times with absolute ether to remove the chlorophyll and fat. The ethereal residues when washed with carbon disulphide to remove coloring matter and waxes and the amorphous residue was found to consist of a bitterish glucoside. The acid solution was then agitated with ether after the addition of magnesium carbonate in slight excess, and after standing was separated, this process being repeated several times. The mixed ethereal solutions when evaporated left a very slight residue accompanied by a little coloring matter, and this was again dissolved in acidulated water and shaken with alkalies and ether. The residue (amorphous and white) was of a bitter and somewhat acrid taste, but entirely devoid of any of the benumbing or tingling sensations that would be caused by the presence of any traces of aconitine. This residue when dissolved in a small quantity of water acidulated with sulphuric acid gave affirmative reactions with the usual alkaloid reagents, but negative results with glucoside tests. The usual color reagents were applied to this (alkaloidal) substance with nothing at all distinctive worth noting. The minute quantity on hand as obtained precluded any further determinations as to its characteristics or proportion.

From these results we infer that the main constituents consist of a glucoside, and an acrid, bitter, amorphous substance of alkaloidal nature existing in minute quantity. Both of these are without distinctive characteristics.

CLINICAL INVESTIGATION OF ACONITUM UNCINATUM.—A tincture of the root of Aconitum uncinatum was made of the strength of officinal tincture of Aconite. This tincture was used in Randal's Island Hospital, New York, by W. E. Hallowell, M. D., House Physician, who prepared a table of the result for our publication. The patients were phthisis cases, in a rather advanced stage. Four patients were treated simultaneously. The commencing dose was two minims, which was increased one minim every two hours during one day, the final dose being seven minims. There was no effect.

The second day the commencing dose was ten minims, which was increased by two minims every two hours, the final dose being twenty minims. There was no effect.

The third day the commencing dose was thirty minims, which was in-

*In our opinion the identity of aconitine is as clearly established by the tongue as by a chemical investigation. We decided that it was absent by taste alone, and were borne out in our opinions by the chemical and clinical investigations.

creased by ten minims every two hours, the final dose being eighty minims; no result.

Observations were made on all the patients every hour, the record showing that no result followed even the large doses.

THE PHYSIOLOGICAL ACTION OF ACONITUM UNCINATUM.—(Written for this publication by Roberts Bartholow M. D., L.L. D., Professor of Materia Medica, General Therapeutics and Hygiene, in the Jefferson Medical College of Philadelphia.)

The preparation furnished by Prof. Lloyd, with which these experiments were made, has the strength of one-half that of official tincture of Aconite. The mode of administration was by sub-cutaneous injection, or by injection into the peritoneal cavity. The first experiments were directed to ascertain the general effects, and from the indications thus afforded, the inquiry was extended to the particular organs or tissues acted on by it. As a similarity of action was supposed to exist between the American and foreign Aconite, an attempt was made to determine this point.

First. The General Effects of Aconite.—Experiment 1.—Frog. Thirty minims of the solution injected into the peritoneal cavity caused apparently some weakness of the muscular system, as shown in the slowness of movements, and feeble jumping. The reflexes, corneal and muscular, appeared to be more active, and on irritation of the sciatic nerve the responses were prompt, the muscles contracting readily. On opening the chest the heart was found to be acting in the usual manner, and continued for the usual time.

Experiment 2.—Rabbit. Two drachms of the solution above given were injected subcutaneously. The effects corresponded to those described in the frog; that is, there were apparently general muscular weakness and heightening of the reflexes; but the circulation and the respiration continued at the normal rate. It does not appear to be at all toxic in these animals.

Second. Action on the Circulation.—Experiment 3.—After division of the medulla, two frogs, of medium size and weight, were placed side by side, their chests opened to expose the hearts. After the effects of the operation had subsided, in one the medicament was injected in the usual way, while the other remained undisturbed, as an experiment of control. Careful comparative observations did not disclose any difference in the rate and character of the cardiac movements. As the dose was sufficient to produce physiological effects, it may be concluded that the action of Aconitum uncinatum does not include the organs of circulation.

Experiment 4.—To ascertain the effect on the blood pressure.

Rabbit of medium size; the carotid connected with the manometer in the usual way. Two doses of two drachms each of the solution were administered subcutaneously. The results were entirely negative. There was no effect on the circulation, beside that due to any alcohol present in the preparation.

Commentary.—The experiments above narrated, are merely examples of a large number, made to ascertain the effects of Aconitum uncinatum. Its affinity to the Aconite of the Pharmacopœia renders it an object of great interest from the physiological standpoint; but it is obvious that it possesses none of the powers of Aconitum napellus, or of Aconitum ferox. In fact it may be regarded as practically inert, although very large doses appeared to heighten a little the cutaneous and corneal reflexes of frogs, but to this result, under the circumstances, little importance should be attached.

The well-known tingling of the tongue and lips, caused by a minute quan-

tity of the tincture of Aconitum napellus, or of Aconitum ferox, especially of the alkaloid aconitine, has been shown by Squibb to be a test of considerable delicacy. No similar impression is made by the preparation of Aconitum uncinatum submitted to examination. Studied with great care and by every available method, I was unable to discover that it possessed any property which can be utilized in medical practice.



FIG. 71.

Fresh root of Aconitum Fischeri, collected in the fall of the year.

DESCRIPTION OF THE ROOT OF ACONITUM FISCHERI.—Our engraving (Fig. 71) represents the average size of the roots obtained by us. It will be observed that they are cylindrical and taper at the lower extremity. They are, as a rule, of greatest diameter about one-fourth the distance below the top, approaching by a graceful curve the constriction that separates the stalk from the root. The parent root produces each season a small tuberous root (sometimes more), at the base of the stalk, which develops and increases during the season until it is of full size; then the stalk dies, the mother root shrinks and decays, the young root forms a terminal bud in anticipation of the coming season and also begins to send out the new root. Our engraving (Fig. 71) exhibits these several phases, the old, contorted, shriveled root being upon the right; the succulent, plump young root, fully developed, in the center, and with its terminal bud; the new root for next season upon the left.

The development of the root of Aconitum Fischeri is the same as that of the European drug Aconitum napellus. Those who are acquainted with the aconite root of commerce will recognize its close resemblance to our figure. It differs from the Aconitum uncinatum which has the young root developed at some distance from the parent root.

The taste of the root of Aconitum Fischeri is bitter, and it benumbs the tongue like the officinal Aconite. Its chemical properties have been studied by Prof. F. B. Power, whose report we introduce verbatim, as follows:

ANALYSIS OF ACONITUM FISCHERI.—(Instituted for this publication by Prof. F. B. Power, assisted by Henry G. Ruenzel).

The material employed for this investigation consisted of the coarsely comminuted root, which was received in a bottle containing a small quantity of alcohol with which it had been digested. The root and liquid were transferred to a flask, about 200 cubic centimeters of alcohol, acidulated with sulphuric acid added and digested on a water-bath for about twelve hours. It was subsequently allowed to macerate for about a day and a half, the alcoholic liquid filtered off, and the root washed upon the filter with about fifty cubic centimeters of alchohol. The residual root, after drying by exposure to the air, weighed twenty-two grams, the original weight of the root being forty-four grams.

The root extracted by alcohol was subsequently digested in the water-bath for twelve hours with water acidulated with sulphuric acid, then allowed to macerate over night and filtered. The filtrate afforded no reaction with alkaloidal reagents, thus indicating that any alkaloid present had been completely extracted by the acidulated alcohol. From the latter liquid the alcohol was removed by distillation and final evaporation, and to the resulting aqueous liquid sufficient water was added to bring the volume to 100 cubic centimeters. This was divided into two equal portions of fifty cubic centimeters each, and having been found to afford an abundant precipitate with alkaloidal reagents, it was treated as follows:

One portion was transferred to a separating funnel, made alkaline with ammonia water, and then shaken with ether. The ethereal liquid upon evaporation afforded a residue which gave the characteristic color reactions for aconitine with concentrated sulphuric and phosphoric acids, although not so decidedly as pure aconitine, which was doubtless to be attributed to small amounts of adhering impurities; when dissolved in alcohol, however, and applied to the tongue, it produced the characteristic tingling sensation and numbness.

The other portion of fifty cubic centimeters of liquid was employed for the quantitative estimation of the alkaloid, and this was accomplished volumetrically by means of a standard solution of potassio-mercuric iodide containing 13.546 grams of mercuric chloride and 49.80 grams potassium iodide in one liter, and therefore 1-20 normal. According to the investigations of Dragendorf, one cubic centimeter of this solution corresponds to 0.0269 gram aconitine,* with acceptance of the formula of Duquesnel $C_{27}H_{40}NO_{10}$.† It was found that 6.3 cubic centimeters of the above 1-20 normal solution were required to completely precipitate the alkaloid, which would therefore correspond to 0.16947 gram of aconitine, or 0.33894 gram in the entire amount of material employed.

This clinical investigation of Prof. Power is almost conclusive evidence that our Aconitum Fischeri contains an alkaloid, or alkaloids, that will prove of therapeutic value. In consequence of the small amount of the drug at our disposal, Prof. Power was unable to identify individual alkaloids as carefully as he would have been pleased to do, and considering the interesting physiological report of Prof. Bartholow, we regret very much that this is the case. Aconitum Fischeri undoubtedly contains the alkaloid aconitine, but it is associated with other proximate principles that, as shown by the physiological investigations of Prof. Bartholow, modify its action in a most interesting manner. The following paper, in his usual thorough manner, presents the results of his work with a portion of the tincture like that sent to Prof. Power.

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* Die chemische Werthbestimmung einiger starkwirkender Droguen, St. Petersburg, 1874.

† Journe de Pharm. et de Chem, (4 ser) , T. 14, p. 94.

A PRELIMINARY NOTE OF EXPERIMENTS WITH ACONITUM FISCHERI, TO DETERMINE ITS PHYSIOLOGICAL ACTIONS.—(Written for this publication by Roberts Bartholow, M. D., L. L. D., Professor of Materia Medica, General Therapeutics and Hygiene, in the Jefferson Medical College of Philadelphia.)*

The preparation used in the following experiments is a tincture made by Prof. J. U. Lloyd, having the strength of the officinal tincture of Aconite. The alcohol it contained was evaporated on a water bath.

Cold-Blooded Animals.—Experiment 1.—Frog of medium size. At 4 P. M. thirty minims were injected into the abdominal cavity. In two minutes the frog gagged violently, opened the mouth widely, and with the fore feet wiped off the tongue repeatedly. At the same time a quantity of mucus was discharged from the mouth. This condition persisted for several hours, the intervals between the acts of gagging growing longer, however, and they, also, lessened in severity. At the end of three hours the frog seemed torpid, and could not clear the surface in attempting to jump. The sensibility and the cutaneous and corneal reflexes were not lessened. Irritation caused prompt muscular movements so long as the power of motion remained.

At 9 P. M. paralysis was complete, and the frog seemed to be lifeless. At 7 A. M., on the following morning, the same conditions existed. At 9 A. M. the chest was opened, and the heart found beating strongly and rhythmically at thirty-two per minute, and continued for some hours longer.

This experiment, several times repeated, yielded uniform results.

Experiment 2.—Frog of medium size. Isolated the sciatic, and ligatured the thigh to cut off the circulation from the limb below. When, after the administration of the solution, the paralysis was complete, mechanical, chemical and electrical irritation of the sciatic, caused active movements of the unpoisoned muscles. Faradic stimulation of the opposite sciatic, and of the muscles at any point, caused active contractions.

From this experiment we conclude that this drug does not impair the irritability of the motor nerves, or the contractility of the voluntary muscles, and that the paralysis caused by it is centric in origin.

That the sensory nerves remain unaffected by it is established by two facts: the frog, in experiment 1, made attempts to get out of the way of an irritation, until the paralysis became complete, and when this condition was reached, faradic excitation of the sciatic caused rapid and stronger action of the heart, when its movements had almost ceased.

Experiment 3.—Frog of medium size. Heart exposed *in situ;* the pneumogastric isolated. Thirty minims of the solution injected as before. When the effects first became manifest, but a feeble response was obtained on Faradic stimulation of the vagus; the heart was slowed but not arrested in movement when a strong current was applied. When the maximum effect of the drug was attained, a strong current did not affect the movements of the heart in any way; in other words, the vagus had lost its irritability—its power of response to irritation.

Warm-Blooded Animals.—Experiment 4.—To determine the general effects of the Aconitum Fischeri.

Rabbit; medium size. Half a drachm of the preparation used in the preceding experiment was thrown into the jugular vein. Paralysis of the extremities followed in a few seconds, the respiration became exceedingly labored, and in five minutes death ensued by failure of the respiratory muscles. On opening the chest the heart was found in strong and rapid action, and continued so for sometime afterwards.

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* Dr. Bartholow desires to thank Dr. A. P. Brubaker, Demonstrator of Physiology and Experimental Therapeutics, for valuable assistance in performing the experiments.

Experiment 5.—Rabbit. The carotid was connected with the manometer and revolving cylinder in the usual way. One drachm of the Aconite solution was thrown into the abdominal cavity. In a minute the characteristic paresis of the respiratory muscles occurred, and at the end of five minutes they were completely paralyzed, and death ensued.

There was no decline of the blood pressure until the failure of respiration. The tracing taken exhibits an increased amplitude of the pulse wave, and the interval between the beats was somewhat lengthened. Faradic excitation of the pneumogastric had no effect on the cardiac movements.

Experiment 6.—Rabbit. The vagus exposed and prepared for faradic stimulation. Injected a drachm of the solution into the peritoneal cavity. The same effects as in the preceding experiment promptly followed. When the maximum action was attained, the vagus was stimulated by a strong Faradic current, but the movements of the heart were not arrested—were not, indeed, in any way affected.

Commentary.—A close correspondence is seen in the effects of Aconitum Fischeri on cold and warm-blooded animals, except as to the rate of movement. It acts more speedily on warm-blooded animals, and also relatively to dose, more powerfully. As respects the character of the actions there is identity. These experiments authorize the following conclusions:

Aconitum Fischeri is a paralyzer of motility, but it does not impair the contractility of muscles, or the irritability of the motor nerves. Its action is central, not peripheral.

It does not affect sensibility or the reflexes until all manifestations of motor activity cease.

It does not paralyze the heart, but by removing the inhibition permits a more active movement of the organ. It paralyzes most completely the vagus so that the strongest stimulation causes no response.

Death ensues by paralysis of the respiration, the heart continuing in action for sometime after respiration has ceased.

Experiment 7.—To determine the effect of the Aconitum Fischeri on the mucous membrane, I placed a large drop near the extremity of my tongue. In a minute the tingling which is so characteristic a symptom of Aconitum napellus was perceived, and it then rapidly increased, but did not attain its maximum for an hour. I then tested the state of the sensibility of the tongue at this point with the aesthesiometer, and found that the perception of the two points was as acute as at the unaffected parts of the mucous membrane. The pain sense was as little affected as the tactile sense. Pricking with the point of the aesthesiometer caused as acute a sense of pains in the area occupied by the tingling as elsewhere. At the end of two hours the tingling was hardly abated in any degree.

Experiment 8.—To ascertain if there be an antagonism between Aconitum Fischeri and strychnine.

Frog; same size as those used in the foregoing experiments. As the action of the agent is comparatively slow in frogs, to save time, I injected one drachm of the solution, being twice the quantity used in the other experiments. The paresis began in fifteen minutes, and at the expiration of an hour paralysis was complete, and all reflex movements had ceased. I then injected one-fiftieth of a grain of sulphate of strychnine.

In one hour after the injection of the strychnine, slight reflex contractions of the legs could be induced by tapping them smartly. Scratching the skin of the abdomen and of the thighs, induced somewhat more active reflex movements. There being no increase in the effects of the strychnine, and three hours after the first dose, a second one of one seventy-fifth of a grain was administered. This distinctly increased the cutaneous reflex, for a little scratching of the skin now caused more prompt and extensive movements. The action of the strychnine did not increase, and after eight hours, no external manifestation of life was apparent, the frog lying limp, extended at full length, and dry on the upper part of the body. The slight impression made by the large quantity of

strychnine given, is the more remarkable, since frogs are exceedingly susceptible to the action of this agent, the one three-hundredth of a grain sufficing to cause active tonic spasms.

Commentary.—That there is an antagonism between Aconitum Fischeri and Strychnine is evident; but the extent of it remains to be determined. That these agents are opposed in the spinal actions of each, would, from *a priori* considerations, be considered probable; experiment demonstrates that such is the fact. That the aconite will antagonize the lethal effects of strychnine rather than the opposite, will, no doubt, be shown by future investigations.

Comparison of the Actions of Aconitum Fischeri and Aconitum Napellus.—Notwithstanding the botanical affinities and, in some respects, the physiological, there are marked and fundamental differences.

Aconitum napellus affects sensibility, and lowers the irritability of the sensory nerves. Aconitum Fischeri does not affect the tactile, or pain sense, although it causes the characteristic tingling, and it does not affect the irritability—the power to perceive and transmit peripheral impressions—of the sensory nerves.

Aconitum napellus paralyzes the end organs of the motor nerves, the trunks, and ultimately the motor portion of the cord. Aconitum Fischeri does not affect the contractility of muscles, or the irritability of the motor nerve, but paralyzes the motor centres of the cord.

Both cause death by paralysis of respiration.

They affect the heart in opposite modes: Aconium napellus stimulates the vagus roots, and slows the heart, while Aconitum Fischeri paralyzes the pneumogastric and increases the force and number of the cardiac pulsations. Aconitum napellus, after a brief, stimulating action, paralyzes the vasomotor center in the medulla, and greatly lessens the blood pressure. Aconitum Fischeri rather stimulates the vasomotor center, and does not lower the blood pressure.

Many points regarding the actions of Aconitum Fischeri remain to be determined. The writer intends to continue his study, but meanwhile submits to the readers of this journal this preliminary note, which contains sufficient facts to stimulate those interested in such work to undertake further investigations. To the practical therapeutist, Aconitum Fischeri offers a most interesting and fruitful subject for investigation of its remedial powers.

ACTÆA.

WHITE AND RED COHOSH.

PARTS USED.—The rhizomes and rootlets of Actæa alba *Bigelow*, and Actæa spicata *Linn.*, var. rubra *Aiton.**

Natural Order Ranunculaceæ, Tribe Helleboreæ.

COMMON NAMES.—The species of Actæa are generally known in this country by a name derived from the Indians, viz. Cohosh,† and are called White Cohosh or Red Cohosh, according to the color of the berries.

In addition to this name the plants have acquired the name Baneberry, from their English relative, and are called White and Red Baneberry.‡

They are called Herb Christopher, Saint Christopher, or simply Christopher, names that have been applied from the earliest time to the English plant.§

The names Necklace Weed and White Beads have been given to Actæa alba in some works, from the resemblance the white berries of this plant bear to a bunch of beads. These names were applied by Eaton in all editions of his Manual, and hence were formerly generally known, but are now seldom used.

We have also seen the name Noah's Ark, and Coral-and-Pearl, given the plant in early medical works.

BOTANICAL DESCRIPTION.—The genus Actæa, proper, consists of but a few species, all closely resembling each other, and is of wide distribution. The typical Actæa spicata is found in Europe, extending over a wide territory, but does not assume any marked varieties. We present a drawing of the flower and berry of this species.



FIG. 71.
A single flower (magnified) of Actæa spicata.



FIG. 72.
A single berry of Actæa spicata.

In America there are three constant forms, and a number that are intermediate. They bear a very close resemblance to each other in habit, leaves and flowers, and only differ markedly in the fruit. Two of these plants are considered as varieties of the European plant; they are the Actæa spicata var. rubra, east of

* In most medical works the two plants are considered as distinct drugs, but as the rhizomes are indiscriminately collected from both species, and afford no distinction, we have placed them under the same head.

† There are four native plants called Cohosh: Black Cohosh, Cimicifuga racemosa; White Cohosh, Actæa alba; Red Cohosh, Actæa spicate var. rubra; Blue Cohosh, Caulophyllum thalictroides.

‡ The English plant, Actæa spicata, has acquired a reputation as a poisonous plant that it seems to us must be in most part unmerited. By old writers the plant was said to grow in dark recesses and to emit a fetid smell, which attracted toads, hence it is called toad plant. The berries were supposed to be poisonous, and the entire plant to poison cattle. Our native plants, which could hardly be distinguished from the foreign, seem to be entirely innocent of poisonous properties, and certainly do not emit any disagreeable odor.

§ In ancient Catholic calendars nearly every day was dedicated to some saint, and a particular flower was connected with each, and usually acquired the name of the saint; thus we have Saint John's-wort, Saint Peter's-wort, etc. Several plants are mentioned in books as Saint Christopher, but Actæa spicata is most generally known under that name. We know of no special reasons why the plant should have been dedicated to this saint.

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the Mississippi, and Actæa spicata var. arguta, of the Western States. Actæa alba is now classed as a distinct species.

As the Actæa alba and the Actæa spicata var. rubra (which are the only forms found over the States east of the Mississippi) bear such a close resemblance that they can hardly be distinguished except when in fruit, we will give a general description that will apply to both.

The rhizome is knotted, horizontal and furnished with numerous fibrous roots. It is not very large, weighing an ounce or two when fresh, and grows within an inch or two of the surface. In the spring it sends up generally a single stem, sometimes two, and often a radical leaf.

The stem is erect, about two feet high, and at the base about the size of a lead pencil. It bears usually two large tri-ternate leaves, on clasping leaf stalks, and above each of these leaves, the thickness of the stem is reduced about one half. The leaflets are oval, acute, veiny, sharply and irregularly cut, toothed on the margins and more or less one or two lobed.



FIG. 73.
A small raceme of Actæa alba (natural size).

The flowers appear in April or May, the white berried plant flowering a week later than the other. They are borne in a short, dense raceme, terminating in a stalk about four inches long. All parts of the flower are white. The sepals which enclose the flower in the bud fall away when it expands. The numerous white stamens are the most showy part of the flower.



FIG. 74.
A single flower of Actæa alba (much magnified).

After blooming, the flower stalk elongates, and when in fruit attains a length of about six inches. The two plants are distinguished by their fruit, hence we will separately describe the fruit of each. The chief characteristic between the two species is the size of the pedicel that bears the berry; in the Actæa alba it is thick and as large as the main stem that bears the bunch; in the Actæa spicata var. rubra it is slender and much smaller than the main stem.



FIG. 75.
Parts of the flower of Actæa alba; *a*, a stamen (enlarged); *b*, a pistil (enlarged).

The Fruit of Actæa Spicata var. Rubra.—This is a cluster of twenty to twenty-four berries. It matures in early July, and when ripe the color is bright, cherry red, the skin smooth and glossy. The bright color will attract



FIG. 76.
The fruit of Actæa spicata var. rubra (natural size).

the attention of the most casual observer when the berries are ripe. They are borne on slender stalks, about an inch long, which when the fruit is ripe are nearly horizontal.

The berries are about the size of large peas and are tipped with small, blunt stigmas, and have sutures running from the base to the apex. They are flattened on the sutured side and attached to the pedicel obliquely at the base. The relative position of the sutures to the main peduncle of the bunch varies with almost every berry, but they usually face the ground. Beneath the skin of the berry is a pure white, pithy flesh, bitter to the taste, and inclosing about twelve angular seeds. These are arranged in two rows and are closely packed together. The berries seem to be specially liable to the attack of small, green worms, which were found in a large proportion of the berries examined by us.



FIG. 77.
A seed of Actæa spicata var. rubra (enlarged).

The Fruit of Actæa Alba.— Actæa alba ripens its fruit in July and August, a few weeks after the red fruited species. It is a bunch of from ten to twenty berries, about the size of a cherry stone. The color of the berries when fully ripe is ivory white, but often they are tinged with red at the apex. They all are tipped with the blunt, black, persistent stigma.

The berries are borne on thick pedicels, about half an inch long, and as thick as the main stalk of the bunch. The pedicels turn red when the fruit is fully ripe; they are horizontal and generally slightly curved (upward), and are thickened or knobbed at the base.

The berries contain usually six smooth, wedge shape seeds, which are arranged in two vertical rows, and completely fill the berry.

In comparison with the fruit of Actæa spicata var. rubra, the fruit of Actæa alba differs as follows: It is borne on thickened pedicels; it is smaller; the tip is larger; the integument is much thicker; there is no pulp; the seeds



FIG. 78.
The fruit of Actæa alba (natural size).

are fewer (six) and larger, and their sides more slanting, and their surface smooth (not roughened).

FORMS OF ACTÆA.—There are good botanists who contend that all the American Actæas are varieties of the same species, and that the "alba" is not sufficiently distinct to be entitled to specific rank. As has been mentioned before, the only prominent distinction is in the fruit; its color, and the thickness of the pedicels. It has been stated that the woody bundles in the pedicel form an unvarying distinction; that they are three in the red-fruited plant and five in the plant with white fruit. At our request, Mrs. Stowell made an examination of a large number of pedicels of both plants, but failed to find any characteristic difference between them. She reports that the "alba" pedicels are much harder, firmer and darker than the "rubra," and that there is a difference in the size of the starch grains, those of the "alba" being much larger. The arrangement of the woody bundles is not alike in hardly any two pedicels of the "alba" nor in any two of the "rubra." The accompanying accurate drawings of a cross-section of a pedicel of each species can not be taken to represent the general appearance of either, because it varies with every specimen examined.



FIG. 79.
An enlarged cross-section of a pedicel of Actæa alba.



FIG. 80.
An enlarged cross-section of a pedicel of Actæa spicata var. rubra.

For more than thirty years it has been noticed by collectors that occasionally plants of Actæa are found with the distinctive character of the fruit directly contrary to the usual form, viz.: white berries with slender pedicels, or red berries with thick pedicels. Several observing botanists have reported these forms to us in the last year. Whether these are hybrids between the two species, or mere sports, we are not prepared to say, but our opinion is that they are the latter.*

Mr. Henry Gillman, who has given the subject of varieties much study, claims that the form with white berries and slender pedicels is quite constant and certainly a good variety, if not a species, for which he would suggest the name *neglecta*. We give his observations in full, as a note.†

Mr. J. S. Merriam, in the "Bulletin of the Torrey Botanical Club" (1872), claims that the two plants "alba" and "rubra" are distinctly characterized and easily recognized by the structure of the pedicel, whatever may be the color of the berries. The "rubra" has "long, green pedicels, hollow, and easily crushed between the thumb and finger. The "alba" has thick, solid pedicels, occasionally having a fine, thread-like hollow at the center, but are never easily crushed."‡

* In this connection it is of interest that in England there have recently been discovered (and an account published in the *Pharm. Journ. and Trans.*) plants of Actæa spicata with white and also plants with red berries. Nothing but black berries had heretofore been known for the English species.

† "Regarding the two forms of Actæa with white berries, that with the slender pedicels is, at least, a strongly marked variety, if not a distinct species. I have made careful examinations and comparisons, sometimes finding both forms in the same locality. I would add that in the variety, the pedicels are green and slender, leaves four-ternately compound, racemes ovate, peduncle longer, berry (white) larger, seeds fewer (about four), and much rougher, and very slightly groved. In the usual form, with thickened pedicels and white berries, the pedicels are red, the leaves three-ternately compound, racemes oblong, peduncles much shorter, berries smaller, seeds more numerous (five to seven), and nearly smooth, with deep groves. The differences appear to me to be specific, and I would suggest for the plant with slender pedicels the name *Actæa neglecta*."—*Henry Gillman.*

‡ Mr. Merriam says: "The small, red berries on thick, short, red pedicels were as clearly of the 'alba' as the white ones. They have every characteristic but color, and that of a very different shape from the 'rubra.' This circumstance has made me doubt the observations on which is made the statement, 'white berries sometimes occur on slender pedicels, and vice versa;' for, in my case, though *vice versa* they were not 'rubra' in any sense."

GEOGRAPHICAL DISTRIBUTION.—In almost all portions of our country one or two species of Actæa can be found. The Actæa alba and Actæa spicata var. rubra grow in most States east of the Mississippi, and the Actæa spicata var. arguta in the Western States. Neither of the species can anywhere be called an abundant plant, although in many places they are common in rocky woodlands and hillsides.

The Actæa spicata var. rubra is a northern species. Its home is the mountains of New Hampshire and Vermont and northern New York, where it is more common than Actæa alba. It extends south as far as the mountains of North Carolina and the States of Tennessee and Arkansas, but is only occasionally found. Over all the territory farther south than the forty-second parallel it is either entirely absent or rare.

Actæa alba is of more general distribution; while it is the common species in the Ohio Valley, it is equally at home on the mountains of Vermont and New Hampshire. A comparison of the two maps herewith presented will exhibit the relative distribution at a glance.

BOTANICAL HISTORY.—The genus Actæa was known to the earliest botanists from a species native of Europe, the Actæa spicata. In the crudest state of botanical classification the plant was included with the Aconites, perhaps from its reputed poisonous properties.

Tournefort called the genus Christophoriana, from the popular name of the plant;* Linnæus, in establishing the genus, called it Actæa.†

The American plants have been designated by a variety of names, according to the specific rank accorded to them by the different writers. Some have considered them distinct species, others varieties of one American species, and others varieties of the European species. At the present time botanical authorities agree that the red-berried plant is a variety of the European species, and the white-berried plant a distinct species.

That there are two kinds of American "baneberry," distinguished by the color of the fruit, was noticed by the earliest observers. Morrison records the fact as early as 1680. Linnæus considered the white-berried plant a variety of the European species, and called it (1753) Actæa spicata var. alba. The red-berried plant he did not designate, although he was aware of its existence from Morrison's reference, which he cites. Aiton referred both plants as varieties of the European species, hence his name Actæa spicata var. rubra still stands.

Pursh (1814) thought them both distinct from the European plants, but forms of the same American species, which he named Actæa Americana, and designated them var. alba and var. rubra. His views seem to have been founded mainly on the fact that in the American plants the petals are shorter than the stamens, while they are equal in the European plant. De Candolle

*See note, on page 232.

†The Greek Ἀκτέα and the Latin *Actæa* are names for the elder. Linnæus transferred the name to this genus, it is supposed, from the resemblance of the leaves to the elder.

PLATE XIX.



MAP SHOWING THE DISTRIBUTION OF ACTÆA SPICATA VAR RUBRA.

EXPLANATION OF THE MAP.

The plant is common only over the territory heavily shaded. Over all the remainder of the shaded portion it is occasionally found, but in most places is very rare if not absent.

PLATE XX.



MAP SHOWING THE DISTRIBUTION OF ACTÆA ALBA.

EXPLANATION OF THE MAP.

The plant is of wide distribution. It is most common over Ohio, Indiana, Kentucky, West Virginia, Pennsylvania and New York, but can be found growing sparingly in almost any locality. It does not end as abruptly as the map would indicate, but it is impossible to determine the exact distribution of a plant.

(1818) adopted Pursh's views, but changed the specific name to express them, calling the plant Actæa brachypetala.*

That the plants are distinct species from the European plant was first proposed by Willdenow, who, in 1813, catalogued the red-berried as Actæa rubra. The white-berried plant was not described as distinct until 1817, when Bigelow included it under that name (Actæa alba) in the second edition of his Flora of Boston. It was adopted at once by Eaton in his next (second, 1816,) edition of the Manual, and in all subsequent issues.

The plants have been described as distinct species by most American botanists, and hence have been generally known as Actæa alba and Actæa rubra. Wood has always classified them as distinct. Gray, in the first edition of his Manual (1848), considered them distinct; in the second (1856) he places them both as varieties of the European plant; and in the fifth (1867), he separates the white-berried plant as distinct, maintaining, however, the red-berried as a variety.

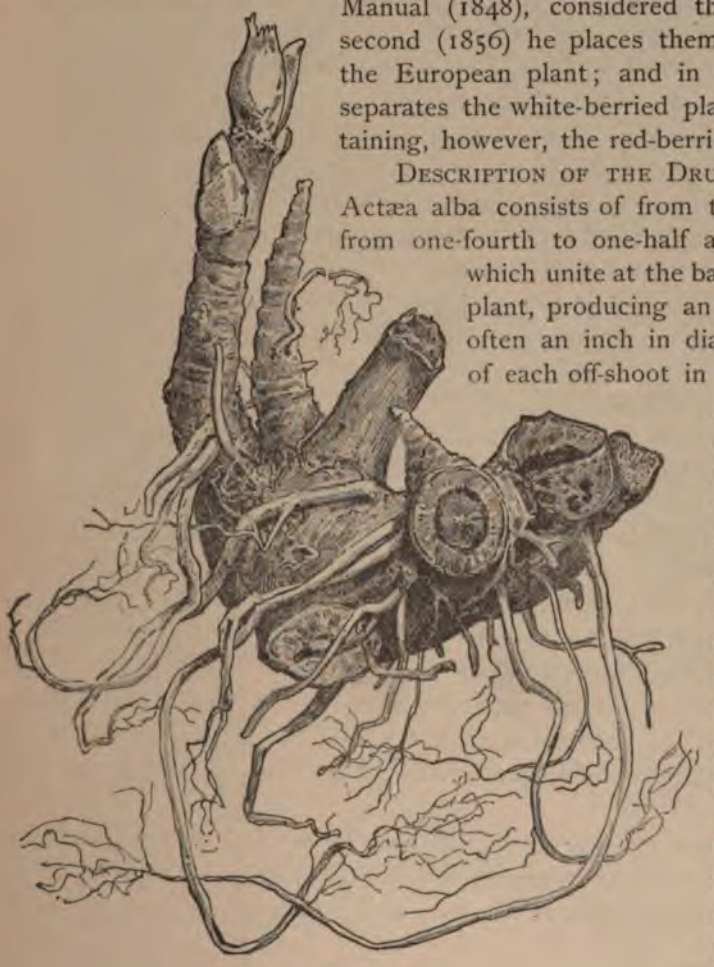


FIG. 81.
Fresh rhizome of Actæa alba (large specimen, natural size).

DESCRIPTION OF THE DRUG.—The rhizome of Actæa alba consists of from two to three shoots, from one-fourth to one-half an inch in diameter, which unite at the base of the stem of the plant, producing an enlargement that is often an inch in diameter. The length of each off-shoot in a large clump, from its connection with the main root, is from three to four inches. When a rhizome attains considerable age and a diameter approaching an inch, it begins to decay and is thus growing in one direction and perishing at another portion.

The lower portion of the stem of the plant has a pink color, and the young buds on the root and base of the stem are also pink. The taste

*VIZ., short-petaled, derived from the Greek βραχύς.

of the fresh, young rhizome is somewhat acrid but distinctly sweet, resembling glycerrhizin, leaving a distinct sweet after-taste. The mature rhizome is of nearly a pure sweet, with but faint acridity, and the sweet impression is persistent. Upon slicing fresh, White Cohosh into alcohol, a faint pink coloration ensues in the woody rays of the root. The roots of White Cohosh are fleshy, and about one-eighth of an inch in diameter. Dried White Cohosh is a shrunken, dark colored representation of the fresh; it is hard, horny and sweet to the taste. One hundred parts of the rhizome lose seventy-five parts by drying.

But little Actæa alba is used in medicine, although in collecting Cimicifuga the root of this plant is indiscriminately mixed with it, but this is unimportant, for undoubtedly they do not materially differ in characteristics.

CONSTITUENTS.—In 1874, Mr. William Dillmore* made an examination of Actæa alba, finding that the aqueous distillate possessed the odor of the root. The infusion and decoction contained the usual constituents of plants, albumen, gum, sugar, starch and extractive, but neither tannic nor gallic acid. He obtained from the alcoholic tincture two resins, one of which was soluble in ether, the other insoluble; both soluble in alkalies. After evaporating the alcoholic tincture and precipitating the resins with water, and filtration, the aqueous liquid was frothy and resembled a solution of saponin.

Our investigations with Actæa alba show it to yield a tincture of a pure, sweet taste, not acrid and not in the least bitter. It contains a resinous body exactly like the purified, resinous substance of Cimicifuga racemosa, and this was neither acrid nor bitter. Since our drug was indisputably the genuine White Cohosh, we think it possible that the bitter character of Mr. Dillmore's product was owing to a sophistication of his drug, and its acrid nature leads us also to think it likely to have contained Cimicifuga racemosa. Chemically the rhizome of Actæa alba differs mainly from that of Cimicifuga in the absence of the acrid principle that is abundant in fresh Cimicifuga, but which mostly disappears when it is dried.

MEDICAL HISTORY OF ACTÆA ALBA.—Early American medical writers distinguished White, Black, and Red Cohosh by name, but presented no authority for a physiological or therapeutical difference in character. We have it from Barton that although the Indians used Actæa in decoction, as an intended remedy in rheumatism, in connection with other herbs, they depended more upon the external application of a decoction of Actæa than its internal application.†

Subsequent writers have made no addition to the medical uses of the plant, although some have confused the supposed poisonous properties of the berries with a probable poisonous action of the root, and others have asserted that it

* American Journal of Pharmacy, 1875, p. 54.

† We quote as follows: "They make a hole in the ground, into which they put a kettle, containing a quantity of the hot decoction. The rheumatic limb is laid over the kettle in such a manner as to receive the influence of the steam. They keep up the heat of the decotion by putting into it, occasionally, hot stones. I presume that the heat, independently of the vegetable employed, has *something* to do in the cure."—Barton's Collections, part 1 (1798), p. 46.

is cathartic. The United States Dispensatory omitted Actæa in its first edition (1833), but mentioned it in the second edition (1834), although nothing of importance has since been added. Prof. King considered White and Red Cohosh together in the first edition of the American Dispensatory, and he accepted the possibility of its being cathartic, for he wrote: "Said to be purgative and emmenagogue."

Frederick Stearns,* 1858, intensified its cathartic properties, as follows: "The rhizome possesses violent purgative power." This is, no doubt, overdrawn, but that both Actæa and its near relative Cimicifuga have cathartic properties, in large doses, is supported by the investigation of Dr. Erick Sattler.†

The facts are: Actæa alba and Actæa spicata var. rubra, together with Cimicifuga racemosa, were used by the American Indians as emmenagogues and parturients, as well as in the cure of rheumatism. Thus they became known to the whites, and by reason of their introduction were employed in domestic practice in the same manner. They accordingly were brought before the medical profession, and while the abundance of Cimicifuga racemosa enabled it to become a common remedy, the relative scarcity of the Actæas kept them from being as well known. There is really little difference, physically, chemically, therapeutically, or physiologically in the the three plants; they are gathered indiscriminately, and doubtless the common plant, Cimicifuga, will naturally always take the precedence. Neither species of Actæa has ever been officinal.

PHARMACEUTICAL REFERENCES TO ACTÆA.

1798.—Collections for a Materia Medica of the United States, Barton, p. 46
1820.—The House Surgeon and Physician, p. 183.
1834.—Dispensatory of the United States (and subsequent editions), p. 1067.
1849.—Elements of Materia Medica and Therapeutics, Kost, p. 235.
1852.—American Dispensatory, King & Newton (and subsequent editions), p. 28.
1858.—Proceedings of the American Pharmaceutical Association, p. 240.
1875.—American Journal of Pharmacy, p. 54.
1881.—Specific Medication, Scudder, p. 58.
1884.—National Dispensatory, 3d edition (and former editions), p. 118.

* "The Medicinal Plants of Michigan," by Frederick Stearns. Proc. Am. Pharm. Association, 1858, p. 240.

† Dr. Sattler's investigations will be found in full under the next plant considered in this work, Cimicifuga racemosa.

CIMICIFUGA RACEMOSA.

BLACK SNAKEROOT.

PARTS USED.—The rhizomes and roots of Cimicifuga racemosa *Elliott.* Natural Order Ranunculaceæ, Tribe Helleboreæ.

BOTANICAL ANALYSIS.—Rhizome knotted and matted, black, thick, branched, marked with scars of fallen stems and leaf stalks. Stem erect, four to eight feet high, unbranched, smooth, furrowed, bearing one or two large leaves near the center. Leaves large, tri-ternately compound, alternate, borne on short, clasping petioles. Leaflets ovate, acute, two to three inches long, thin, smooth, more or less two or three lobed, borne on short stalks; margins sharply and doubly serrate. Flowers very numerous, white, borne in a terminal, branching, spike-like raceme. Pedicels bracted, horizontal, slender, about a fourth of an inch long. Sepals four or five, white, concave, caducous. Petals represented by a few slender two-forked organs, resembling abortive stamens, and easily overlooked. Stamens numerous, showy, with slender filaments, and globular, white anthers. Pistil solitary, white, sessile, smooth; ovary, one-celled, about ten-ovuled; stigma, sessile, on the ventral side of the summit. Fruit, a dry, ovoid follicle, ribbed, dehiscing along the ventral suture, and filled with triangular seeds, arranged in two rows.

COMMON NAMES.—The Pharmacopœia recognizes the name Black Snakeroot as the proper common name for the plant. In the drug trade it is known either as Black Snakeroot or Black Cohosh. The plant was one of the many reported cures for the bite of the rattlesnake, hence the name Snakeroot, and black from the color of the rhizome. The name Cohosh is an Indian name.* The dry pods of the plant, which remain during the greater part of winter, contain loose seed that rattle with the wind. On this account, probably, the plant is called Rattleweed, Rattleroot, and Snakeroot.

The names Rattlesnake Root and Blacksnake Root, as they are sometimes spelled, are probably improper spellings of the names Rattle Snakeroot and Black Snakeroot.

The following names for Black Snakeroot are sometimes found in medical works but should not be used. Bugwort and Bugbane, often applied to the American plant, are borrowed from the European species of Cimicifuga, and are not applicable to our plant.†

Squawroot, sometimes used, more properly belongs to the Blue Cohosh (Caulophyllum thalictroides), to which plant it is referred by the majority of writers.

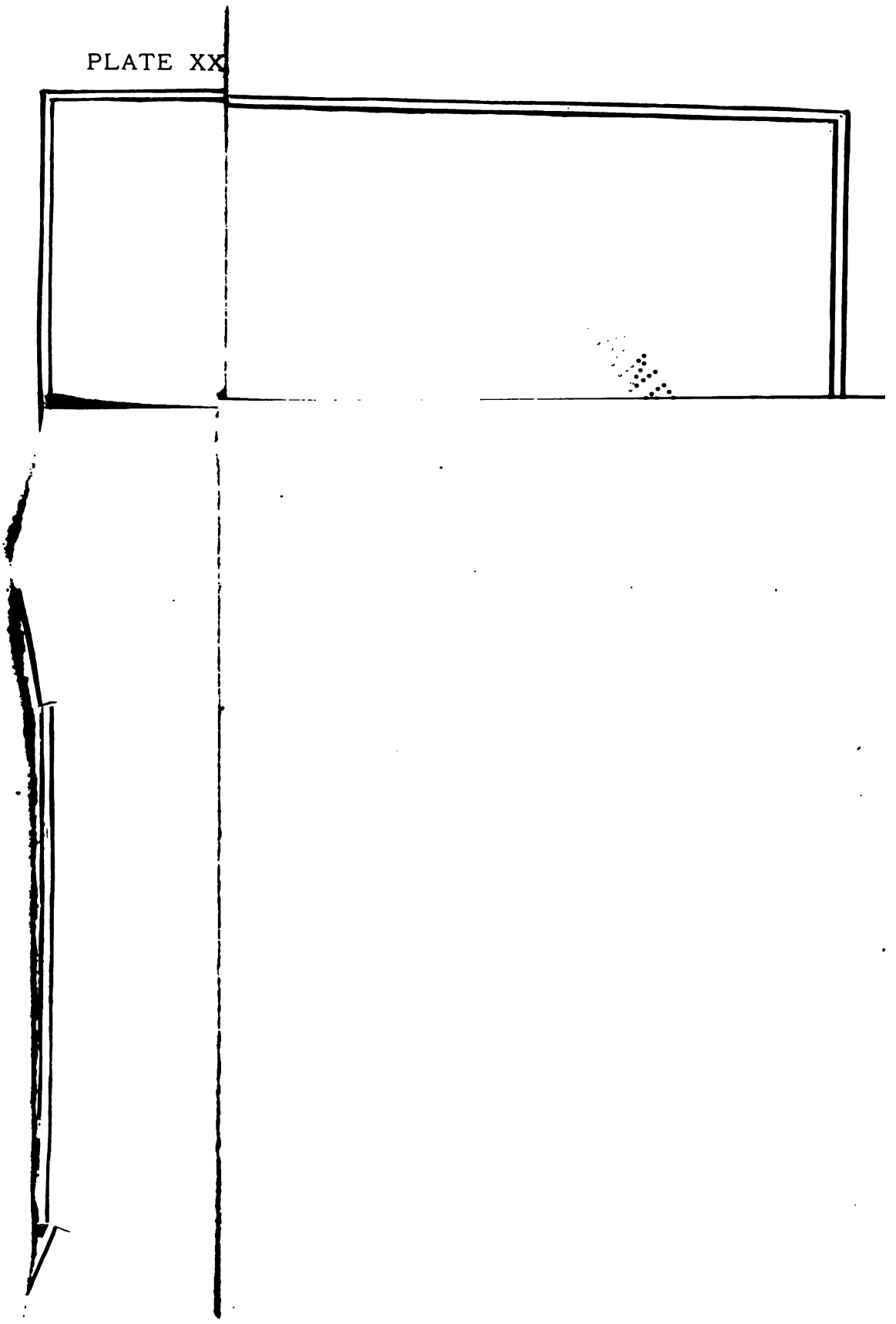
Richweed is a name given to Cimicifuga racemosa as early as 1762, by Gronovius, and is applied to it by some of the very earliest writers. It is now used by botanists to designate a very different plant (Pilea pumila) which has no place in medicine.

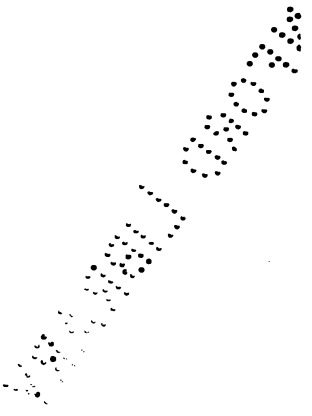
BOTANICAL DESCRIPTION.—Cimicifuga grows in rich woods, generally on hill sides, and is usually abundant. While its natural habitat is shady localities

* The name Cohosh is now applied to four plants (see note, page 232). Its meaning we have so far been unable to ascertain. It seems to have been originally applied by the Indians to Caulophyllum thalictroides, and we hope that we shall be enabled to throw more light on its meaning by the time we come to consider the plant.

† See note * on page 248.

PLATE XX





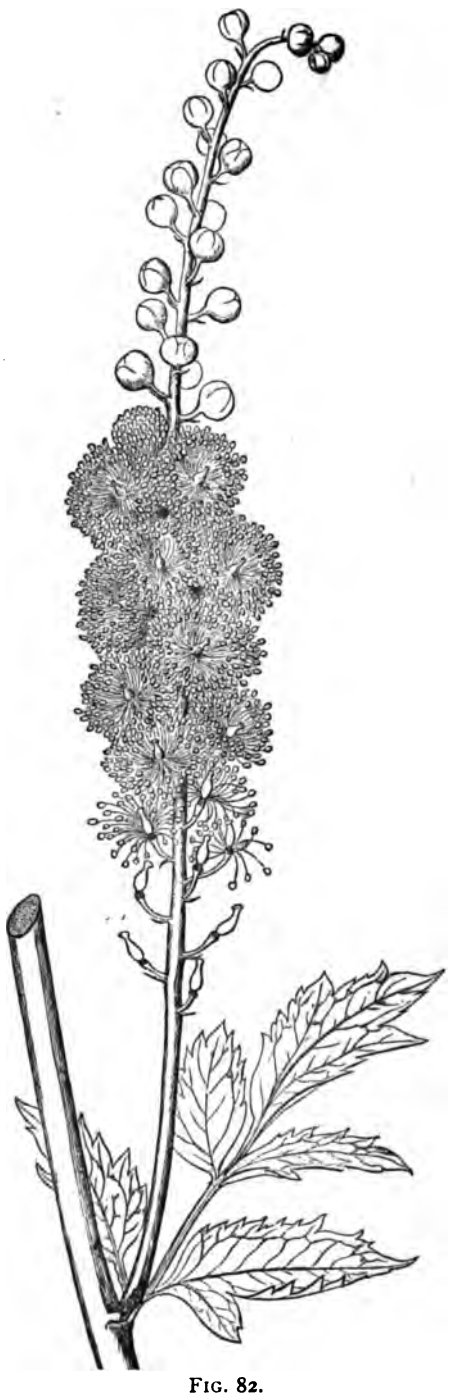


FIG. 82.
A branch of a raceme of Cimicifuga racemosa.

it will remain for a number of years growing in sunny places, such as fence corners of cleared ground and in woodland pastures.

The rhizome is large, knotted, horizontal, and is found from four to six inches below the surface (see Plate XXIII, opposite page 257).

Each rhizome sends up one or two flowering stalks and several large, radical leaves. The leaves are tri-ternately compound and very large; the radical and lower stem leaves are usually two to three feet across. The leaflets are about three inches long by two wide, ovate, acute, and with margins sharply toothed.

The stem is erect, from six to eight feet high, and at the base, half an inch thick. It is smooth, somewhat flattened below, and angular near the top. It does not branch below the flowers. Usually it bears three leaves; a large one on a long stalk from near its base, another large one near the middle; and a small one about a foot below the flower. Our illustration (Plate XXI), represents the stem cut off just below the upper, small leaf.

Cimicifuga blooms from the latter part of June in southern localities to the fore part of August in northern stations. July is the month in which the flowers appear over most of the territory. When in bloom the plant is a most conspicuous and showy object in woods and woodlands; its slender wands of white flowers can readily be distinguished even at a distance.

Each plant ends in a compound raceme of white flowers. The raceme usually has two branches, the lower longer, though in vigorous plants as many as four are sometimes developed.

The branches of the raceme proceed from the main stem an inch or two below the bottom flower, and ascending for three or four inches, they then become vertical and parallel with the main stem, and distant about two inches from it. As in all racemes, the flowers develop upward from the lowest. Fifteen to twenty flowers are expanded at a time.

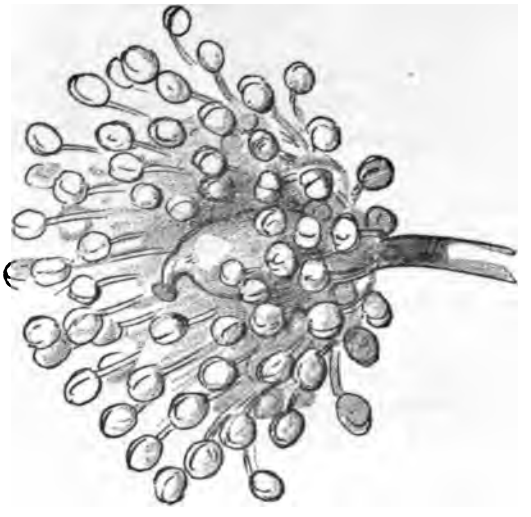


FIG. 83.

A flower of Cimicifuga racemosa (much enlarged).

The individual flowers are about half an inch wide and are placed nearly contiguous though not crowded on the stem. They are borne on slender pedicels which are minutely bracted at the base. The pedicels are a quarter of an inch long and horizontal or slightly ascending.

The flower buds are nearly globular, and on their short but slender pedicels look not unlike large-headed pins. They have five concave, imbricated, white sepals which enclose and protect the stamens in the bud, but fall away as the flower opens.

The expanded flower has no floral envelopes, and consists of a pistil and very numerous stamens.* The stamens indeed are the conspicuous part of the flower, and are almost pure white, both filaments and anthers. The white, ovoid pistil in the center of the flower is about half the length of the stamens. It is rounded at the base and sessile on the pedicel.† After flowering, the short, slender pedicel becomes ascending. The fruit is an ovoid, dry capsule about a quarter of an inch long, with thick, leathery ribbed sides. It opens by splitting down the inner suture at the top. Often the capsule is twisted on its pedicel so that the opening is outward. It is filled with eight to ten angular, brown seed. The dry fruit pods often remain on the dead stalk throughout the



FIG. 84.

A pistil of Cimicifuga racemosa (greatly enlarged), a few days after the stamens have fallen.

* A close examination will detect a few small, slender, claw-shape organs which represent petals, but they are so rudimentary that they need not be mentioned in a popular description of the flower.

† Several of our correspondents have called our attention to the apparent error in both Gray's Manual and Wood's Class Book in describing the ovary as sessile. The meaning is not that the ovary is sessile on the main stalk, but that it is sessile on the pedicel in contra-distinction to the ovaries of other species of Cimicifuga which have stipitate bases.

winter and rattle with the wind, hence one of the common names for the plant is Rattleweed.



FIG. 85. A section of the fruiting stalk of Cimicifuga racemosa (natural size).

BOTANICAL HISTORY. — Cimicifuga is a very conspicuous and showy plant when in bloom, and hence was noticed by the earliest travelers in America,* and carried to the botanical gardens of Europe early in the last century.† It was first described by Plukenet,‡ and rudely figured in his Amaltheum Botanicum, 1705. Several other pre-Linnæan writers mentioned the plant, and all classed it with Actæa, mostly under Tournefort's name, Christophoriana,§ and designated it with specific adjectives indicating its long raceme or spikes.

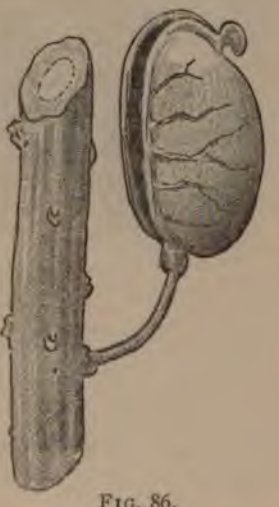


FIG. 86. A single capsule of Cimicifuga racemosa (enlarged).

When Linnæus first specifically named plants, in his Species Plantarum (1753), in common with previous writers, he included this plant with Actæa, to which it is very closely allied in habit, appearance, properties, flowers, etc., and called it Actæa racemosa.

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* A specimen collected by Fisher, in Maryland, nearly two hundred years ago, is still preserved in the Solander Herbarium in the British Museum.

† The first cultivation of the plant in England appears to have been in Sherard's Garden, at Eltham, about 1732. It was described in the first edition of Dillenius' Hortus Elthamensis.

It was growing in the Apothecary's Garden, at Chelsea, as early as 1737. A specimen is preserved in the British Museum which was grown in the Garden and collected in that year.

‡ Plukenet was an ardent botanical collector who lived in the latter part of the seventeenth century. He made a very large herbarium for his time, which in addition to the native British plants, included a large number of foreign specimens obtained by correspondence and from the botanical gardens.

The *Almagestum Botanicum* was a publication intended as a catalogue of his collection, with description of the new plants, and the *Amaltheum Botanicum* was the third volume or rather a continuation of this work.

We are indebted to Dr. Charles Rice for the following lucid explanation of the word Almagestum:

"Claudius Ptolemaeus, the celebrated geographer, astronomer and mathematician of Ptolemais Hermion in Upper Egypt, contemporary of Antoninus Pius (died 161 A. D.), among other important works, wrote a 'Grand Treatise on Astronomy,' μεγάλη σύνταξις τῆς ἀστρονομιας, in thirteen books, which work remained the standard authority up to the middle age. Owing to the gradual decline of general education and knowledge in the time preceding the reformation, the work remained almost unknown, in its original language (Greek), but was duly appreciated by the inquiring and studious Arabic scholars, who, recognizing its great value, translated it, and it is in its Arabic version, and Latin translations from this, that the work first became known in Europe. The title of the work, in Arabic, is Al-majistī, or Al-mjistī, or Al-majustī [best spelled Al-mejistī], the 'al' being the Arabic article, and 'mejistī' being the Arabicised Greek word 'μεγιστη' (megistē) 'greatest, the Arabs having converted the positive 'μεγάλη' *great*, into the superlative 'μεγιστη' *greatest*. Several later Arabic authors, to give some special éclat to their own works, treating of similar subjects, chose the same title '*Al-majistī*.' But when Almagest is mentioned, without reference to other writers, the work of Ptolemy is usually meant. Similarly, many European authors of former times were fond of using the word To them it had gradually acquired the meaning of 'Grand Storehouse [of],' 'Cyclopedia [of], etc., and so we have *Almagestum Botanicum* and other similar works."

As Plukenet lived at the time when new plants were pouring to England from this country, his publications are specially rich in descriptions of American plants. Cimicifuga he classed with the Actæa spicata of Europe, and using the old generic name for this plant called it "Christophoriana facie, Herba spicata, ex Provincia Floridana." He accompanies his drawing with a crude cut of the plant, inaccurate but yet sufficiently true to establish the identity. His original specimen of the plant is still preserved in his herbarium in the British Museum.

§ This is a generic name given by Tournefort to the Actæa spicata of Europe. See page 236.



FIG. 87.
A seed of Cimicifuga racemosa (enlarged).

At that time but two of the species that now constitute the genus Cimicifuga (viz., the plant under consideration, and Cimicifuga fœtida of Eastern Europe), were known. Had Linnæus made a genus for these two he would have had a genus containing two plants belonging to entirely different orders of his artificial system. He did in after years separate the European species from Actæa under the generic name Cimicifuga,* but he did not include our plant in that genus.

The Linnæan name, Actæa racemosa, was retained till the beginning of the present century by all writers excepting Walter, who called the plant Actæa monogyna.†

It was Pursh who first referred it to the genus Cimicifuga which Linnæus had established for the European plant. Michaux had previously referred to this genus, our mountainous species (Cimicifuga americana) which he discovered. Pursh, in addition to this species, having seen our northwestern species (Cimicifuga elata, that he considered identical with the European species, Cimicifuga fœtida), noticed the great similarity of the three plants, and placed them all in a common genus. The plant under consideration he called Cimicifuga Serpentaria.‡

Four years later, Nuttall in enumerating the then known plants of the United States, restored the old specific name, calling it Cimicifuga racemosa. In the same year, Barton (but after the publication of Nuttall's work, as is evident from his mentioning the work,) used the same name, evidently taken from Nuttall's work, but without giving him credit for it.§ Hence De Candolle and several other writers have incorrectly referred the authorship to Barton. It is remarkable, however, that in all the works of both Torrey and Gray, and in most recent works on American botany, the authorship of the name has been credited to a botanist (Elliott) who did not use the name until six years after it was published by both Nuttall and Barton, and that this same error should have been made in the last very carefully prepared edition of the United States Pharmacopœia of 1880.

The following are the distinctive characters between the two genera, Actæa and Cimicifuga, as established by Linnæus. They are drawn entirely from the fruit, as there is no other point of distinction.

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* Derived from *cimex*, the generic name for the bed-bug (*Cimex lectularius*), and *fugare*, to drive away. The European species for which the genus was established is a very fetid herb, and is used to drive away insects just as pennyroyal (Hedeoma pulegioides) is used in this country.

† Viz., one-pistilled.

‡ As this is the first time the plant was referred to the genus where it has finally remained, Pursh's name should be used if the rule of priority alone determined it. Nuttall's name, however, is more appropriate, besides being the specific name used by all previous writers, and it is well that it is adopted.

§ This was not an intentional appropriation of another's ideas. It was not the custom with Elliott, Eaton and several of the old writers to give, in many cases, authority for specific names.

ACTÆA.	CIMICIFUGA.
Fruit, a solitary, fleshy berry.	Fruit, five (or four) dry follicles.



FIG. 88.
Fruit of Cimicifuga racemosa.

It will be seen that Cimicifuga racemosa does not accord with either genus as defined by Linnæus, as the fruit is a dry follicle but solitary. On this account Rafinesque proposed to establish for it a new genus, Macrotrys,* calling the plant Macrotrys actæoides. (Medical Repository, 1808).†



FIG. 89.
Fruits of typical Actæa and Cimicifuga, for comparison; *a*, Actæa; *b*, Cimicifuga.

There is really some structural ground for Rafinesque's genus, because the plant differs from all others of the genus Cimicifuga as follows; but there is, however, such close relationship in every other particular that this difference can not be considered sufficient for maintaining the plant in a separate genus. (See Fig. 88, and Fig. 89, *b*.)

CIMICIFUGA RACEMOSA. (MACROTRYS RAF.)	ALL OTHER SPECIES OF CIMICIFUGA.
Follicle abrupt at the base, solitary, ovoid, seeds smooth, numerous, compressed horizontally.	Follicles five (or four), flattened, stipitate. Seed rough with slender projections.

In 1828 Rafinesque changed his generic name to Botrophis,‡ calling the plant Botrophis Serpentaria.

But one other American botanist has ever followed Rafinesque's generic views. Eaton, in the fourth edition of his manual adopted them, but used Pursh's specific name, calling the plant Macrotys Serpentaria. In subsequent editions he used the old specific name and called it Macrotys racemosa.

Eaton was very positive regarding the rights of the plant to generic rank.§ He spelled the name, however, incorrectly — *Macrotys* instead of *Macrotrys*, an error that was made by De Candolle, from whom Eaton no doubt took it.

About the time that black cohosh was beginning to be used by the Eclectic practitioners Eaton's Manual was the popular text book of botany. Hence it is that his name, Macrotys racemosa, was given to the plant in the

---

* From μακρὸς *large*, and βοτρυς a *bunch*, referring to the large raceme of fruit.—Eaton.

† This was merely an annonncement. See our note, on page 192.

‡ Derived from βοτρυς a bunch, and ὄφις a snake

He gives his reasons for the change, as follows: "The name Macrotrys is delusive and harsh. I have framed a better one, meaning snake raceme, the raceme or long spike of flowers being mostly crooked and like a snake."

§ On this subject he says: "I retain this genus for the species *racemosa*. I yield to authorities in most cases, but in this case I can not submit to the absurdity. No one can be better acquainted with Cohosh than myself." Had Eaton confined the name to this species there would have been some excuse for his method, but to apply it to the other American species as he did was a most glaring blunder.

early medical works, and has persistently clung to it in spite of botanical authority, even to the present day, and will probably always be used.



FIG. 90.

A leaflet of the dissected form of Cimicifuga racemosa, collected by A. Commons.

FORMS.—Cimicifuga racemosa has but little tendency towards variation. Specimens from a number of widely distant stations show a constancy of character.

In central Pennsylvania there exists two plants which are distinguished by root gatherers as the tall and small snakeroots. We are indebted to Kate F. Kurtz for specimens of the tops and rhizomes of both plants. A close examination, however, shows us no difference except in development. The fresh rhizome of the tall plant is much larger and darker colored, and the roots coarser. We can only consider this plant a robust form.

In collecting near Faulkland, Delaware, Mr. A. Commons found a few remarkable specimens, perhaps only sports, growing in a patch of perfectly normal plants. He transferred some rhizomes to his garden where they have since grown, and every year maintain their peculiar characteristics. The leaflets are much divided, in fact pinnatified. The accompanying drawing of a single leaflet will exhibit their peculiarity.

GEOGRAPHICAL DISTRIBUTION.—Cimicifuga is a most abundant plant over the greater portion of the territory east of the Mississippi. The only part



MAP SHOWING THE DISTRIBUTION OF CIMICIFUGA RACEMOSA.

EXPLANATION OF THE MAP.

The centre of distribution is the Ohio Valley. The shading on the map represents very accurately, the occurence of the plant and its abundance.

Duplicate

where it is usually absent, excepting the extreme south, is most of Illinois and Wisconsin and the New England States. The center of its most abundant occurrence is Pennsylvania, Ohio and West Virginia. It extends south throughout all the Allegheny range, and over the States of Kentucky and Tennessee. It becomes scarce in western and northern Indiana, and absent from Illinois, excepting a few southern stations. In southern Missouri it is again found abundant, growing throughout the Ozark Mountains. In the southern half of Michigan it is often found, though not a common plant, and it is scarcer still in the southern point of Ontario. New York has it common in the southern tier of counties bordering Pennsylvania; in the regions of the small lakes it is a rare plant; and in the eastern and northern part of the State it is entirely absent, except a few isolated stations south of Lake Champlain.

In New England it is almost entirely absent. At rare intervals a few specimens are found not a great distance from the ocean, or in the valley of the Connecticut river, or bordering Lake Champlain, but in all instances the number of plants is limited and the find considered of great interest. Not over a dozen stations are known for the plant in the entire New England States.

ALLIED SPECIES.—The two species of Actæa described in the preceding article have such a close resemblance to black snakeroot that there is no doubt that they are indiscriminately gathered by root diggers. Indeed, it takes very close observation to distinguish between the plants by the leaves alone. We have known root gatherers who would not be convinced that Actæa alba was not black snakeroot, and when shown the small flower spikes of the former plant maintained that they were "young plants."

There is no other species of Cimicifuga that is abundant enough to ever supply any amount of the drug that is gathered for black snakeroot. Cimicifuga americana, were it common, would be impossible to be distinguished by root gatherers from the plant under consideration, but it is a very rare plant even to botanists.

On account of the importance of Cimicifuga racemosa as a drug, we give a description of the three other native species of the genus. The two Eastern species are rare, and the Western species has never been investigated, and neither is likely to be ever of any importance.

Cimicifuga Americana.—In the entire list of native plants we do not know of any other two evidently distinct species that bear as close resemblance to each other as Cimicifuga americana and Cimicifuga racemosa. No one but a close observing botanist would ever suspect that they were different plants, and botanists can tell them apart only when in fruit.*

---

*In our experience, trying to obtain the rhizome of Cimicifuga americana for comparison, we corresponded with quite a number of botanists who at first thought they knew the plant, but afterwards found that they had mistaken for it the Cimicifuga racemosa, and in one instance a quantity of the rhizome of Cimicifuga racemosa was expressed us for it. Our rhizomes of the plant were obtained through the kindness of J. Donnell Smith, of Baltimore, than whom there is no more careful botanist nor acute observer. Although he is perfectly familiar with both species, he was compelled to wait until the gynœcium had formed in the bud before he could distinguish the Cimicifuga americana from the other.

The first printed reference we can find to the plant is in Raevschel's Nomenclator Botanicus, published in 1797, where the name "Actæa pentagyna from Carolina," evidently refers to this species. No description of the plant is given, and no authority for the name, and we are unable to find the source of Raevschel's information. Michaux first described the plant in 1803 as Cimicifuga americana, which name it has since retained. De Candolle referred the plant to the genus Actæa and substituted another specific name for it, calling it Actæa podocarpa.*

De Candolle's specific name was adopted by Eaton and also by Elliott, who named it, in accordance with their generic views, respectively Macrotys podocarpa and Cimicifuga podocarpa.



FIG. 91.
A section of a fruiting raceme of Cimicifuga americana.

DESCRIPTION. — Cimicifuga americana resembles Cimicifuga racemosa so closely that our description of the leaves, stem, figures, etc., and our picture (Plate XXI) may almost be applied to this plant.

The stem is more slender and the flowers are smaller and not as closely placed on the raceme as they are in Cimicifuga racemosa. The raceme is also more slender and has usually more branches.



FIG. 92.
Vertical section of a capsule of Cimicifuga americana (enlarged).

In the fruit, however, the two species differ widely. The fruit of Cimicifuga americana consists of (normally five) usually three or four flat, membranous pods. At the apex they are tipped with a slender, subulate style, and at the base they are supported on a stipitate stalk about half the length of the pod. They contain a few, eight to twelve, latterally compressed, roughened seeds. This extremely rare plant, Cimicifuga americana is found only in the Allegheny Mountains. It grows with its allied species, Cimicifuga racemosa, which is everywhere abundant. When in fruit the two plants can be easily distinguished, but otherwise it is very difficult.

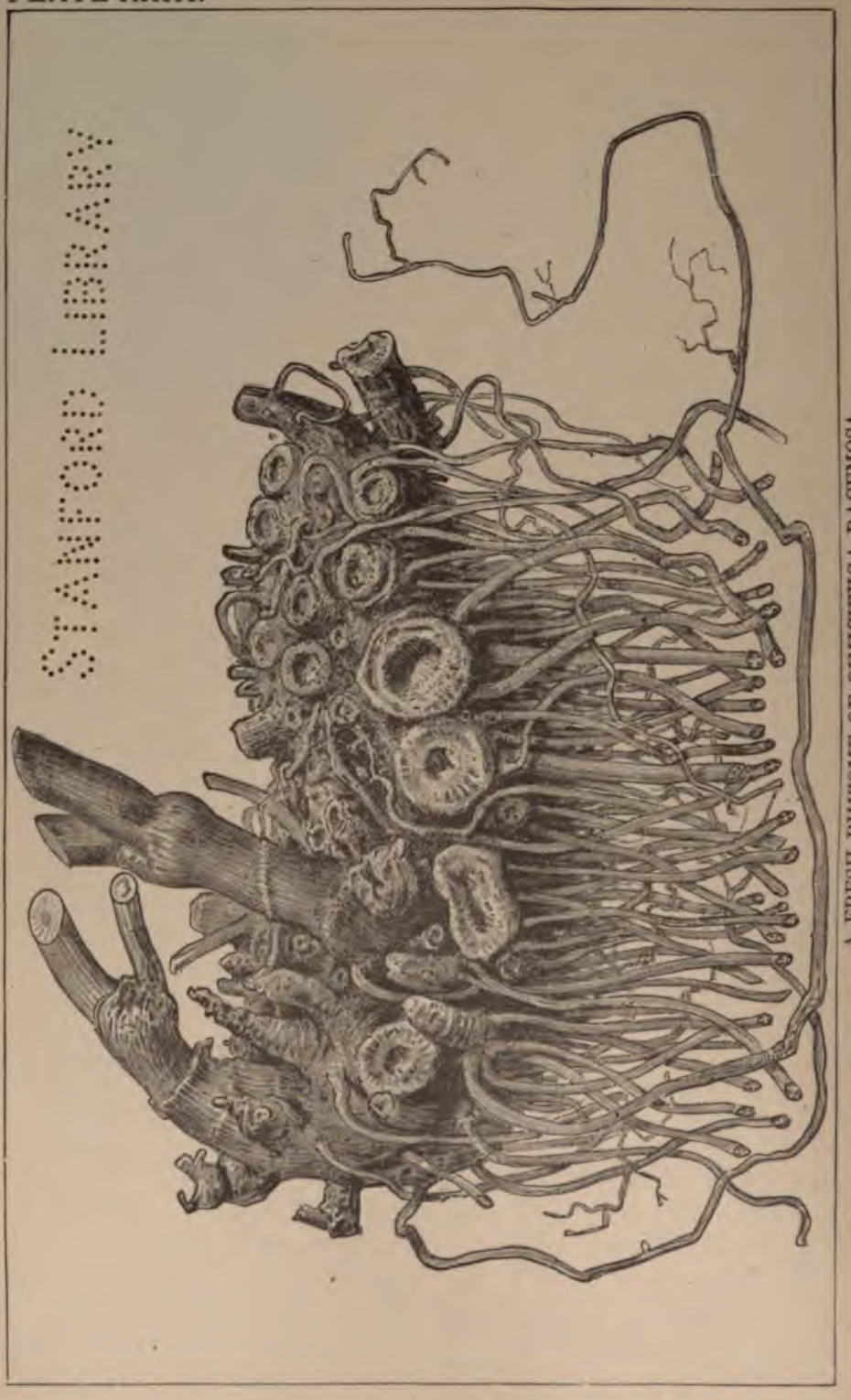


FIG. 93.
A seed of Cimicifuga americana (enlarged).

Cimicifuga Cordifolia, Pursh.—This species is common in certain peaks of the southern Allegheny Mountain, but as it is confined to a restricted territory not much frequented by botanists, it is a rare plant in collections. It does not extend as far north as the Cimicifuga americana.

* The meaning of *podocarpa* is having carpels with a foot or stipitate base.

PLATE XXIII.



A FRESH RHIZOME OF CIMICIFUGA RACEMOSA.
(Natural Size.)

The plant was discovered by Pursh, in 1805, in his trip to the mountains of Virginia and North Carolina and by him named Cimicifuga cordifolia.* It has escaped all synonyms except by De Candolle, who referred it to Actæa as Actæa cordifolia, and by Eaton who called it Macrotys cordifolia. The plant is about three feet high, and has the general aspect of Cimicifuga racemosa, but can be distinguished readily by the leaves which are mostly biternate, and the leaflets which are large, oblique and broadly cordate. In structure of the fruit the plant is closely related to Cimicifuga americana, but the pods are sessile (not stipitate) on the pedicel.

Cimicifuga Elata, Nuttall.—This species is a native of the extreme Northwest (Oregon and Washington). It was first collected by Lewis and Clark (about 1805), and described by Pursh in 1814. Pursh considered it the same as the Cimicifuga fœtida, of Europe, which it closely resembles, and called it by that name. Hooker maintained the same erroneous views, but used Linnæus' name, Actæa Cimicifuga. Nuttall first described it as a separate species, under the name Cimicifuga elata, in a manuscript description published in Torrey and Gray's Flora (1838).

It is a tall plant, with large biternately leaves, thin, prominently three lobed, cordate leaflets, and slender but rather short racemes. The flowers are small and not crowded. The fruit on the lower part of the main raceme is two or three carpeled, but above and on the branches the flowers have only one pistil. The fruit pods are flattened and sessile on the pedicel like the fruit of Cimicifuga cordifolia. We know nothing of the rhizome or its properties.

DESCRIPTION OF THE DRUG.—The fresh rhizome of Cimicifuga racemosa appears in irregular matted clumps, averaging from four to eight ounces in weight. In exceptional cases the rhizome grows much larger, and we have seen specimens weighing over four pounds. The rhizome is horizontal and has numerous short, upward curved branches, which thickly beset the main rhizome, and give it a rough, irregular appearance. These branches are sometimes the remains of former leaf stems, or radical leaves, but for the most part they are undeveloped buds which are produced and grow for a short time, and then become latent. The main rhizome and all its branches are thickly marked with approximate, annular scars, which almost completely encircle them. These scars are left by the decayed bud scales. From the under side of the rhizome proceed numerous fleshy roots, which are from six to ten inches long, and taper from about one-twelfth of an inch in diameter at their place of attachment. These roots are for the most part undivided, but send out several small rootlets.

Fresh cimicifuga rhizome is internally of a white color. It is brittle and breaks with nearly a smooth fracture. It consists of a large central firm pith, surrounded with a circle of concentric, flat, woody rays, and covered with a firm bark. The fresh rhizome is very dark brown, excepting at the base of the

* Viz., heart leaved Cimicifuga, from the shape of the leaflets.

leaf stem, and the young buds which are white and have a pinkish cast.

The dried drug is a shrunken representation of the fresh rhizome. Internally it is dark, excepting the woody rays, which are of a lighter color, and thus prominent in a broken cross-section resembling the spokes in a wagon wheel. The dried roots are very brittle and easily broken; hence, in the commercial drug they are for the most part missing or represented by mere fragments. The larger roots, when broken, exhibit a peculiar structure, which is plainly discernable to the naked eye. It consists of a star or cross formed by the projecting rays of the central woody tissue These rays are from two to five in number, according to the size of the root. When the root dries, the rays, being somewhat firm, prevent the regular shrinking of the root, and it assumes an angular appearance, more marked near the rhizome, as illustrated by figure 94. This peculiar structure is also characteristic of many of the roots of Actæa alba.



FIG. 94.

A cross-section of a root of Cimicifuga racemosa (enlarged), showing the woody rays.

Fresh cimicifuga is acrid and disagreeable to the taste; the odor of the fresh, broken root is penetrating and peculiar. The freshly broken or sliced root is white, but turns pink immediately when covered with alcohol, and imparts a pink color to the liquid, which ultimately changes to yellowish brown, while the final color of the sliced root is a dark buff or gray, occasionally streaked with a green ring beneath the bark. When the fresh rhizome is broken and exposed to the air, it turns dark gray on short exposure, and ultimately nearly black, but does not assume the pink hue.

MICROSCOPICAL STRUCTURE OF CIMICIFUGA RACEMOSA.—(Written for this publication by Louisa Reed Stowell)—*Rhizome.*—Beginning with the outside of the rhizome, there are two or three rows of small, dark brown cells, resembling compressed cork cells.

The remaining structure, except the pith, is in color a light yellow or white. The parenchyma forming the bark is composed of small oval or compressed cells, loaded with starch grains. The walls are somewhat thickened, and occasionally reticulated marks are present.

The woody bundles are numerous, long and narrow, frequently composed of only one row of thick-walled prosenchymatous cells. Seive tissue, or a form of seive opening, is frequent between these cells at their extremities.

These woody bundles are separated by wider and quite regular medullary rays. These cells are tabular in shape and contain starch grains.

PLATE XXIV.



FIG. B.



FIG. C.

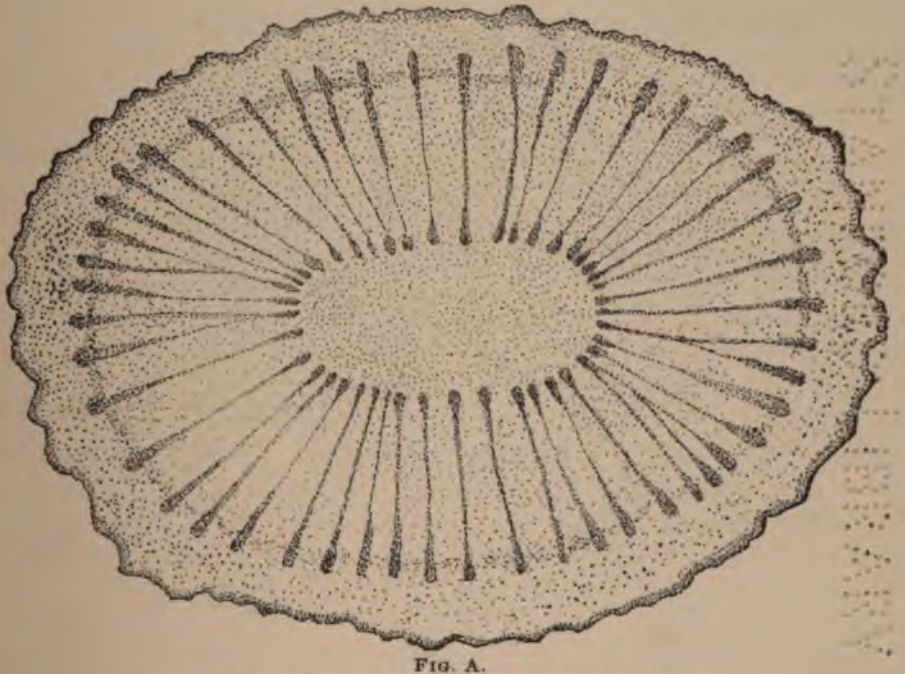


FIG. A.

MICROSCOPIC STRUCTURE OF CIMICIFUGA.

FIG. A.—Rhizome of Cimicifuga racemosa. FIG. B.—Root of Cimicifuga racemosa.
FIG. C.—Root of Cimicifuga americana.

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FIG. 95.
Starch grains from the rhizome of Cimicifuga racemosa (drawn with the ⅛-in. objective and the "C" eye-piece).

A large, dark colored pith is at the center of the rhizome. The cells are larger than those of the bark and loaded with starch grains. There are a few reticulated marks on the walls of these cells.

The starch grains of the rhizome are small, round, and free from any mark or wrinkle over the nucleus. They are more regular in size and appearance than the starch grains of any of the allied species.

Root.—The outer two or three rows of cells of the root, as well as the rhizome, are dark brown, while the inner part is a light yellow. The cortical portion is thick and darker, with much firmer walls than the corresponding part in the rhizome. These are filled with starch grains. The cells of the parenchyma show clearly defined reticulated marks. The walls are thick and firm and show a laminated structure their entire length. They frequently show a double set of lines crossing each other at an oblique angle.

A single row of cells, dark yellow in color, surrounds the woody cord the same as a nucleus sheath.

The woody cord of the center of the root (or rootlet of many writers), is the most characteristic of any of the structures of Cimicifuga racemosa. It is composed generally of four distinct woody bundles arranged in the form of a cross. These are separated by four wide, prominent medullary rays, composed of thin walled, rectangular-shaped parenchyma.

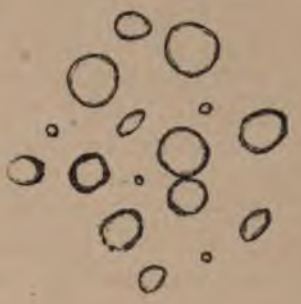


FIG. 96.
Starch-grains from the root of Cimicifuga racemosa (drawn with the ⅛-in. objective and the "C" eye-piece).

Cimicifuga Americana.—Rhizome and Root.—The rhizome is composed almost entirely of parenchyma filled with starch grains. The woody bundles are short, only about one-eighth the length of the radius of the rhizome. They are fewer in number and more irregular in shape and position than those of Cimicifuga racemosa. In the bark parenchyma between the medullary rays are occasionally found bundles of bright yellow prosenchyma.

The starch grains are larger and more regular than the starch grains of Cimicifuga racemosa. They have very much the peculiar appearance of corn starch, angular, depressed on some of the faces, and with frequent crosses or stellate marks in the center of the faces.

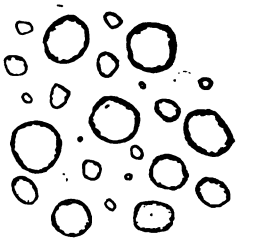
The outer row of cells of the root are regular, with walls thickened and colored a dark red, the rest of the structure to the central cord is composed of regular parenchyma loaded with starch grains. These starch



FIG. 97.
Starch grain from the rhizome of Cimicifuga americana (drawn with the ⅛ in. objective and "C" eye-piece)

grains are smaller than the starch grains of the rhizome and are free from any markings. They are generally round.

The central woody cord is not conspicuous and sometimes has several rays.



FIG, 98.
Starch-grain from the root of Cimicifuga americana (drawn with the ⅛-in. objective and "C" eye-piece).

CONSTITUENTS. — The first analysis of this plant was by Dr. G. W. Mears, in 1827.* He obtained tannin, extractive matter, gallic acid, resin, gum, starch, and a bitter (acrid) substance. He endeavored to find an alkaloid, being convinced that such a substance ("alkali") was present, but failed.

In 1834† Mr. John H. Tilghman made an analysis of the rhizome, and endeavored to produce a crystalline substance similar to that which he states was then sold by a pharmacist of Philadelphia as being obtained from cimicifuga.‡ He failed to make it, however, and then he investigated the crystalline substance of the pharmacist and found it to be a calcium compound. He identified in cimicifuga, gum, starch, resin, tannin, wax, gallic acid, sugar, an oily body, chlorophyll, extractive, and salts of iron, calcium, magnesium and potassium. He sums up, "These experiments have not led me to any decided conclusion as to the nature of the active principles of cimicifuga."

Mr. J. S. Jones‖ next investigated the plant, and again obtained the bodies that Messrs. Mears and Tilghman had previously found.

In 1861§ Mr. Geo H. Davis made a careful examination, and obtained albumen in addition to those already named, and he split the resinous body into two substances, one soluble in both ether and alcohol, and another soluble in alcohol, but insoluble in ether. He found salts of silica in addition to the inorganic bodies the others had named.

In 1871¶ a paper from Mr. T. E. Conard appeared on "A Neutral Crystallizable Principle in Black Snake Root." This was obtained by extracting the fresh rhizomes with alcohol; adding solution of subacetate of lead to precipitate the resin, tannin, etc.; passing sulphuretted hydrogen into the liquid to free it from lead; filtering; evaporating the filtrate to dryness; washing the residue with

* Philadelphia Med. [illegible] Surgery Sept. [illegible] pp. [illegible]
† American Journal of Pharmacy [illegible]
‡ We can find no reference to this material in any work at our command.
American Journal of Pharmacy [illegible]
American Journal of Pharmacy [illegible]
¶ American Journal of Pharmacy [illegible]

ether to remove fat; and dissolving it in sixteen times its weight of alcohol to form a "saturated solution."* This solution was mixed with aluminium hydroxide and agitated for twenty-four hours, and then evaporated to dryness. The residue was extracted with hot alcohol and filtered, from which filtrate, by evaporation of the alcohol, "there remained a crystalline substance of a light yellow color, not of a very regular or decided shape, but of a massy appearance, resembling almost exactly the crystals of sulphate of aluminium on a small scale." This substance was nearly tasteless, but its alcoholic solution was acrid and sharp. It dissolved in chloroform, dilute alcohol, slightly in ether, insoluble in benzine, turpentine and bisulphide of carbon. It fused by application of heat, then took fire, and finally was entirely dissipated. It refused to affect litmus or to unite with acids, and did not evolve vapor of ammonia with caustic alkalies, (all of which applies to resin of cimicifuga.—L.)

In 1876† Mr. L. F. Beach reports an examination of commercial resin of cimicifuga (cimicifugin), in which, by following Conard's process, he obtained a crystallized principle that formed in the hexagonal system. In 1878‡ Mr. F. H. Trimble endeavored to obtain this crystalline body, but failed, although his work seems to have been very carefully performed. In 1884‖ Mr. Milton S. Falck published a paper, stating that from the juice of the fresh plant, he obtained by Conard's process a substance that in some respects resembled the mass Conard obtained, and which also appeared to be crystalline. In alcoholic solution it was neutral to litmus paper, and yielded alkaline fumes when fused in a test tube with caustic potash, and it gave a precipitate with some alkaloidal reagents whereby Mr. Falck suggested that it be of alkaloidal nature. However, in many respects it is different from the substance described by Mr. Conard. It will be seen from the literature on the subject, that the only important point of difference is the crystalline body reported by Mr. Conard, and, taking the medical history of the plant into consideration, supported by its chemistry, it is evident that the resins are the important constituents. From the first analysis (1827) to the present day, every examination gave the resin. Until Mr. Conard announced a crystalline body, such a substance was unknown, excluding inorganic salts, and it is desirable that Mr. Conard's claims should be substantiated or disproved. On this subject we have the written records of Mr. Beach and Mr. Falck, in which the substance is claimed to have been found, and that of Mr. Trimble, who failed to produce it; and we will further add that we have never seen it obtained from the commercial drug.

In this connection we would call attention to certain features of the report of Mr. Conard, with our experience with dried cimicifuga:

* This will not make a *saturated* solution.—L.
† American Journal of Pharmacy, 1876, p. 385.
‡ American Journal of Pharmacy, 1878, p. 468.
‖ American Journal of Pharmacy, 1884, p. 459.

1st. The amount of solution of subacetate of lead he used (three fluid ounces), will *not* precipitate the resin from two pints of tincture of cimicifuga. Indeed, subacetate of lead will not precipitate this resin at all.* The astringents are thrown from solution by the lead and a certain amount of resin is precipitated by the water of the lead solution.

2d. The residue from Conard's evaporated tincture (after passing sulphureted hydrogen through it) is mostly resin and sugar.

3d. The washing with benzine is unnecessary, as nothing of importance is removed.

4th. The extracting by water of this residue (after washing with benzine), separates only sugar and such bodies as are found in most plants and are classed as extractive matters.

5th. The resin left from these experiments will not saturate sixteen times its weight of alcohol. It is very soluble in alcohol.

6th. This resin is not rendered insoluble by digestion with alumina. The only effect that we have observed from this manipulation, is the separation of minute amounts of coloring matter.

7th. This resin has never in our hands assumed a crystalline form.

To sum up, in our opinion Mr. Conard's plan of procedure does not separate the well known resin of cimicifuga, but purifies it from many extraneous substances. If it assumed a crystalline form (and he is not very positive, saying, "not of a very regular or decided shape, but of a massy appearance"), it was an unusual occurrence. We have worked some thousands of pounds of cimicifuga for the resin since Mr. Conard's paper appeared, and have often endeavored to obtain a proximate crystalline substance by his process, and have in every instance failed; and we feel satisfied that the product of Mr. Conard's examination with the officinal drug, is simply a purified resin.†

However, in order to produce other evidence, we interested Prof. Robt. R. Warder in the subject, and he spent a couple of weeks in our laboratory and carefully investigated the matter. He reports as follows:‡

THE ALLEGED "CRYSTALLIZABLE NEUTRAL PRINCIPLE" OF CIMICIFUGA RACEMOSA.—(An investigation instituted for this publication by Robt R. Warder, Professor of Chemistry in Purdue University, Lafayette, Ind.)—This well known plant was examined more than fifty years ago by Tilghman,‖ and later by Jones§ and by Davis.¶ These authorities show it to contain starch, sugars, tannic acid, gallic acid, oils, coloring matters, resins, etc. The most prominent feature of the alcoholic extract is a resinous mixture of bodies, easily precipitated by the addition of water, known in unofficinal pharmacy under the name of cimicifugin, macrotin or macrotyn.

In April, 1871, Mr. T. Elwood Conard,** after a tedious investigation,

* Mr. T. H. Trimble decided (1879 that the portion precipitated by subacetate of lead yields a crystallizable acid. —*Nat. Disp.*

† It is not always easy to decide as to the crystalline nature of an evaporated liquid. Sometimes it leaves a substance that appears to be semi-crystalline, but which is really devoid of any crystals. Again, an amorphous, glossy like layer of residue will contain well defined crystals, nearly invisible while surrounded by the amorphous substance in which they are imbedded, but which become distinct when this envelope is removed by an appropriate solvent. In this connection we will say, that often we place too much stress upon a *crystalline* body. While it is true that many of our most valuable principles are crystalline, it is also true that many uncrystalline substances are equally valuable. The characteristic principle of cimicifuga is a resinous amorphous principle.

‡ Prof. Warder repeats part of the historical portions already introduced, but which, however, renders his paper more complete.

‖ Journal of the Philadelphia College of Pharmacy, 1834, pp. 14, 20.

§ American Journal of Pharmacy, 1843, pp. 1, 5.

¶ American Journal of Pharmacy, 1861, pp. 391, 396.

** American Journal of Pharmacy, 1871, pp. 151, 153.

announced the discovery of a crystallizable neutral principle, obtained from the perfectly fresh root, by a circuitous process. Beach* obtained this principle from macrotin by the same process; and he states that the crystals belong to the hexagonal system. Trimble† precipitated the resin by water, purified it by benzine, and separated it by chloroform into a soluble and an insoluble portion. Each of them was separately treated with subacetate of lead (the latter also with alumina), yielding only a resinous mass, similar in properties to Conard's principle, but amorphous. Quite recently, Falck‡ has again announced Conard's crystalline substance, as found in extract of the fresh drug.

The following experiment was made to isolate the "crystallized principle," if possible, and to make a fuller examination of it; for there is no record of analyses, nor even of the melting point, and therefore no evidence that a pure substance was obtained:

Ten pounds of the dry and powdered drug were moistened with alcohol and carefully exhausted by percolation. One-half of the percolate was treated with six fluid ounces of solution of subacetate of lead, and a bulky precipitate of dirty yellow color was filtered off. The filtrate was again treated with the same quantity of subacetate, yielding about one-fourth as much precipitate as before, and of a lighter color. Conard expressly states that his subacetate of lead "completely precipitated the resin, tannin, etc., and most of the coloring matter," and it was my intention to follow strictly the process indicated. The filtrate would now remain clear for a few moments on the addition of a small quantity of lead acetate, but a larger proportion of water produced an immediate precipitate of resin, and an addition of lead solution caused a gradual separation of white, curdy precipitate, which was believed to result from the simple decomposition of the subacetate or from diluting the alcoholic solution of resin. Sulphuretted hydrogen removed a large quantity of lead from the solution; the alcohol was distilled off, the residue evaporated at about 80° C. with constant stirring, and solidified on cooling to a sticky, resinous, flexible cake. This was removed from the evaporating dish and pulverized in a mortar with the aid of benzine; repeated washing with this menstruum removed a small quantity of pale yellow oil. The residue, when freed from benzine by drying, weighed four ounces. This was repeatedly washed with water, first by trituration in a mortar, then on a filter, with the removal of a half ounce of crude glucose and extractive matter of very dark color. The residue obtained by these series of operations had all the usual appearance, taste, and physical aspects of the resinous substance precipitated by water from the alcoholic extract, except that it was a little paler. This was completely dissolved in twelve fluid ounces of cold alcohol and shaken at intervals with freshly prepared moist alumina, which showed little tendency to combine with the remaining coloring matter. The fluid was evaporated to dryness in contact with the alumina, as in Conard's process; the mass was again dissolved in alcohol, filtered from the alumina, and again exposed to spontaneous evaporation; but only an amorphous product was obtained, as in Trimble's experiment; and this resembled ordinary cimicifugin in color, taste, and tenacity, and in solubility. In fact, the lead had served to precipitate tannin with part of the coloring matter, and benzine removed only traces of impurity, while simple dilution of the original extract would seem to accomplish nearly the same purpose with far less delay.

It is difficult to understand how Conard obtained any crystals free from fixed matter, by the course he describes, or how Beach determined the system of crystallization. The testimony of Trimble, that crystals are not obtained by similar processes, was fully confirmed, so far at least as the dried material is concerned. Some crystalline substance may yet be obtained among the con-

* American Journal of Pharmacy, 1876, p. 151.
† American Journal of Pharmacy' 1878, p. 468.
‡ American Journal of Pharmacy, 1884, p. 459.

stituents of the resin, or derived by a partial decomposition of those constituents; but the study of this subject had previously been undertaken by Prof. Coblentz.*

THE FRESH JUICE†.—Expressed from the green rhizome, this has a sweet taste and the odor of the rhizome. It contains glucose in abundance, but no resin, or at least but traces of it. It is reported by Mr. Falck that by following Conard's process, from this juice he obtained a crystalline body.‡ We expressed a quantity of the juice, and could not do so. After the final washing of the extractive matter by benzol and water, all of it had disappeared. Glucose is the main constituent of the juice.

THE GREEN RHIZOME.—This was used by Conard. We went through the process carefully, with negative results. When the lead and aluminium compounds are separated, an amorphous resin remains.

To sum up, by referring to our statement regarding the resin of cimicifuga and to the paper of Prof. Coblentz on this substance,|| it will be seen that all our endeavors to obtain crystals from that body were ineffectual. We are convinced that cimicifuga does not contain a crystalline proximate principle, and that the gentlemen who thought to have obtained it, either mistook a salt of lead or aluminium for a product of cimicifuga, or were mistaken as regards the crystalline structure of the substance they observed.

PHARMACOPŒIAL HISTORY.— Cimicifuga was not officinal in the first (1820) edition of the U. S. P. In the Philadelphia edition, 1830, it was introduced under the names Cimicifuga racemosa *Nuttall*, and Cimicifuga Serpentaria *Pursh*, (radix, *the root*), and in the New York edition of same date it was recognized (Cimicifuga radix) under the names Actæa racemosa and Cimicifuga Serpentaria. The common name in both instances was Black Snakeroot.§ The edition of 1840 designated it as Cimicifuga, "the root of Cimicifuga racemosa, *Torrey and Gray, Flora of North America*," and this description remained unchanged in the subsequent revisions of 1850, 1860, and 1870. In 1880 we have "Cimicifuga (Black Snakeroot), the rhizome and rootlets of Cimicifuga racemosa, *Elliott* (Nat. Ord., *Ranunculaceæ*)." It has always occupied a position in the primary list of the U. S. P.

PHARMACOPŒIAL PREPARATIONS.—*Fluid Extract of Cimicifuga.*—There were no recognized officinal preparations of Cimicifuga until 1860, when a fluid extract was introduced, as follows:

"EXTRACTUM CIMICIFUGÆ FLUIDUM.—(*Fluid Extract of Cimicifuga.*)—
Take of Cimicifuga, in fine powder, sixteen troyounces;
Stronger Alcohol,¶ a pint and a half,
Diluted Alcohol, a sufficient quantity.

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* See page 269.

† We return our thanks to Mr. C. S. Ashbrook for valuable assistance in a line of these examinations.

‡ See page 265.

|| See pp. 268, 269.

§ In the Philadelphia edition it was spelled Black Snake Root.

¶ "Alcohol Fortius," Stronger Alcohol. Spirit, of the specific gravity 0.817, U. S. P. 1860.

Moisten the Cimicifuga with four fluid ounces of the Stronger Alcohol, introduce it into a conical percolator, pour upon it the remainder of the Stronger Alcohol, and, when the whole of this has entered the powder, gradually add Diluted Alcohol until a pint and a half of tincture have passed. Set this aside, in a shallow vessel, until reduced by spontaneous evaporation to twelve fluid ounces. Continue the percolation with Diluted Alcohol, until two pints more of tincture have been obtained. Evaporate this, by means of a water-bath, at a temperature not exceeding 150°, to four fluid ounces; then add the tincture first obtained very gradually so as to avoid precipitation, allow the mixture to stand for twenty-four hours, and filter through paper."

The foregoing formula was defective from the use of two menstruums. As a consequence, the evaporated hydro-alcoholic final percolate refused to yield an extract soluble in the reserved portion that was produced by stronger alcohol. Then, too, the water in the creamy extract left from the evaporation of the final percolate altered the reserved percolate, and when it was added, precipitation of resinous matter resulted, and the operator vainly tried to "add the tincture first obtained very gradually so as to avoid precipitation." Hence we find the Pharmacopœia of 1870 directs as an improvement the use of stronger alcohol throughout the entire operation, sixteen troy ounces of cimicifuga being used to produce a pint of fluid extract.

The process of the Pharmacopœia of 1880 is practically that of the preceding revision, excepting that one hundred grammes of powdered (No. 60) cimicifuga are employed to produce one hundred cubic centimeters of the finished product; Alcohol of s. g. 0.82 being employed throughout.

Tincture of Cimicifuga.—This (1880) revision introduced also a Tincture of Cimicifuga, made as follows:

"Cimicifuga, in No. 60 powder, *twenty parts*,
Alcohol, a sufficient quantity to make one hundred parts.

Moisten the powder with *fifteen* (15) *parts* of alcohol and macerate for twenty-four hours; then pack it firmly in a cylindrical percolator, and gradually pour alcohol upon it until *one hundred* (100) *parts* of tincture are obtained."

There have never been any other officinal preparations of cimicifuga, and, in our opinion, either the tincture of 1880 should have been omitted, or, it should have been directed to be made extemporaneously. This could have been accomplished practically, and when called for, by the admixture of one part of fluid extract of cimicifuga and four parts of alcohol.

UNOFFICINAL PREPARATIONS.—Of these, the resin of cimicifuga is most important. It has always been a favorite with the Eclectics, and represents the active principles (or most of them) of dry cimicifuga. (See page 268.) A few of the others are of sufficient importance to be recognized by Eclectics, and have thus earned a place in the American Dispensatory. The rest have been used more or less in private practice, and have finally wandered into print and are occasionally referred to. The larger number of these mixtures are nearly obsolete and should not be revived. However, our work would be less complete should we exclude them, and as pharmacists occasionally have a demand for these old preparations, we feel that they should all be placed on record in this publication.

Resin of Cimicifuga (*Cimicifugin, Macrotyn*).—Preparation.—Take of powdered cimicifuga, any convenient amount, prepare it for percolation and exhaust it with officinal alcohol, evaporate the tincture to a creamy consistency and pour it into twenty times its bulk of cold water, stirring constantly. Collect the precipitate, wash it well with cold water and dry it by exposure to a cool atmosphere.

It dries slowly, owing to the partial melting of the outer surface, which forms a coating that prevents the escape of vapor from within, for which reason the vitrious mass must be often crushed. During the exposure it darkens considerably, sometimes being almost black.

History.—We recognize under the above name the substance that precipitates when the residue of an evaporated alcoholic tincture of cimicifuga is precipitated in water.

Cimicifugin was first made and used in medicine by Prof. John King, in 1835, who called it to the attention of physicians in 1844, and again in the "Western Medical Reformer" of 1846.*

In 1849 Mr. Wm. S. Merrill contributed a paper to the "Eclectic Medical Journal," in which he gives a process of making "Macrotyn" by precipitation of an alcoholic tincture of cimicifuga (Macrotys) with water. In 1856, Grover Coe assails the "macrotyn" as not representing the plant, and he asserts that the value of cimicifuga depends on three principles—resin, alkaloid and neutral. As usual, however, with that writer, he rests his proof with an unsubstantiated statement. From that time until the present, this substance under the name Cimicifugin, or Macrotyn,† has been an important drug with many Eclectic physicians and is consumed in considerable amounts. It contains the principle of the rhizome that produces the disagreeable symptoms (see medicinal properties), and is of considerable interest therapeutically. Although this is a mixture of substances, we shall refer to it as a resin, in accordance with the generally accepted view of the writers.

Properties.—Freshly precipitated cimicifugin is of a light yellowish color, and imparts a sweet taste to water. Upon drying, it darkens, and becomes deep brown, nearly black when in mass. Upon triturating this, a brownish or yellowish powder results. The odor is like that of the fresh rhizome and very strongly marked, somewhat like smoke. The taste is at first sweet (resembling glycerrhizin), and upon prolonged chewing becomes disagreeable and acrid, imparting a burning or smarting sensation to the throat.

Solubilities.—This substance, being a mixture, is partially soluble in several menstruums and entirely soluble in none. It is almost dissolved by both ethyl and methyl alcohols. Boiling water extracts small amounts of the sweet principle, leaving the acrid substance. It is about one-half dissolved by ether

* See American Dispensatory.

† The word was originally spelled Macrotin, but we know of no reason for changing the *y* of Macrotys into *i*.

and but in small amount by chloroform, benzol and benzine, and it is nearly dissolved in a solution of caustic alkali. It is, really, a mixture, one constituent of which is an acrid resin (soluble in ether and alcohol), and this imparts most of the acridity to the rhizome. Another is a resin that is soluble in alcohol and nearly insoluble in ether. Neither of these substances is crystalline.

Mr. L. F. Beach* reports that by following Conard's process with commercial cimicifugin,† he obtained crystals of the hexagonal system.‡ As we have never succeeded in obtaining crystals from it, we submitted some of the pure precipitate to Prof. Virgil Coblentz, with a request that he obtain these crystals for us, and to otherwise report on the substance. We herewith submit the result of his investigation:

EXAMINATION OF CIMICIFUGIN FOR THE DETECTION OF A CRYSTALLINE SUBSTANCE.—(By Virgil Coblentz, Professor of Chemistry in the Cincinnati College of Pharmacy.)—"The alcoholic solution of the cimicifugin was colored greenish black (no precipitate) by ferric chloride. After prolonged boiling in an excess of water, about forty per cent. of the substance was dissolved, which solution readily reduced Fehling's solution. The undissolved residue was a brownish colored resin (brittle), which retained the acrid taste and peculiar odor characteristic of the drug. The portion soluble in the boiling water possessed a sweetish taste free from acridity, and gave a slight precipitate upon the addition of an acid, it *possibly* being due to a principle, similar to glycerrhizin in its nature; gummy and mucilaginous principles were also present in this aqueous solution. The resinous residue remaining after treatment with boiling water possessed an acrid and slight bitter taste, and on resolution in alcohol and precipitation in water, became of much lighter color. The original principal (cimicifugin) was subjected to Conard's process (see page 262). It was found that decolorization with alumnic hydrate was unnecessary. As the alcohol slowly evaporated, a clear, pale yellow brittle resin separated upon the sides of the beaker. It was inodorous and of an acrid taste, requiring for solution a large excess of ether. The operation was repeated several times, with larger amounts of material, with same results as before. This resinous-like substance, after prolonged boiling with water acidulated with hydrochloric or sulphuric acid, was split into sugar and another substance which separated as a gray amorphous mass. This was washed and dried. It was soluble in alcohol; insoluble in ether, chloroform, turpentine, carbon disulphide, benzine or baryta water. Its alcoholic solution is not colored by ferric chloride When warmed with sulphuric acid (dilute) it gives a purple color; other acids and iodine do not affect it. The following may be inferred to be the composition of the so-called resinoid:

Portion soluble in water	Gum; coloring matter; a sweet principle (reducing Fehling's solution); mucilage.
Insoluble in water	A resinous-like substance possessing acrid taste of drug, that splits into sugar and another substance on treatment with dilute acids.

The result of my investigation was entirely negative in my attempt to obtain a crystalline principle from the so-called cimicifugin."

Fluid Extract of Cimicifuga.—Prof. Wm. Proctor first recommended a formula for making this preparation in the American Journal of Pharmacy, 1854, p. 107, and next Prof. J. M. Maisch suggested a process in the American Journal of Pharmacy, 1859, p. 313. Both these processes were defective from the fact that ether was unnecessarily used, and that water was a large constituent of the final liquid. One of the processes employed sugar. Hence, Prof. Proctor recommended to the American Pharmaceutical Association, 1859, that alcohol only be used, a process that has not been improved upon to the present day. (See Pharmaceutical Preparations, p. 266.)

* American Journal of Pharmacy, 1876, p. 375.

† This is indefinite. Commercial cimicifugin is of questionable composition.

‡ See pp. 264, 265, 266.

Extract of Cimicifuga.—A hydro-alcoholic extract was directed to be made by Dr. King (Eclectic Dispensatory) in 1852, by percolating the cimicifuga first with alcohol, then with water, mixing the percolates and evaporating to an extractive condition. This process is objectionable, and we commend the following:

Take of Fluid Extract of Cimicifuga, any convenient amount. Evaporate until reduced to the condition of a soft extract.

Compound Fluid Extract of Cimicifuga.—

Take of Fluid Extract of Cimicifuga.....one ounce.
Fluid Extract of Wild Cherry.....one ounce.
Fluid Extract of Ipecac.....one-fourth ounce.
Fluid Extract of Liquorice.....one-fourth ounce.
Fluid Extract of Senega.....one-half ounce.
Mix them together.

These ingredients are in accordance with Tilden & Co.'s Book of Formulas, 1861. The proportions are in accordance with the Druggists' Circular, 1872, p. 143. No uses given for this mixture.

Compound Enema of Cimicifuga.—

Take of Powdered Cimicifuga.....two ounces.
Powdered Geranium.....two ounces.
Water.....four pints.

Mix them together, make a decoction, and strain. This is an astringent preparation, employed as an injection in leucorrhea, etc. Formula of Dr. Y. T. Morrow, from the American Dispensatory.

Infusion of Cimicifuga—

Cimicifuga.....two ounces.
Boiling Water.....one pint.

Pour the boiling water on the crushed cimicifuga, and when it becomes lukewarm, strain it. This is the strength Sanborn states (The Sick Man's Friend, 1855) was used by the Indians, who drank two or three swallows of it at a time during the day. This infusion was afterward made one ounce to the pint, but we think that if a deviation is made from the original strength, the officinal proportion, one to ten, should be employed.

Cimicifuga Mixtures.—For Rheumatic Affections and in Anasarca.—

Take of Tincture of Cimicifuga.....one ounce.
Iodide of Potassium.....two drachms.
Syrup of Ipecac.....one ounce.
Water.....two ounces.

Mix together. Teaspoonful three or four times a day. (Journal of Materia Medica, 1860.)

For Chronic Bronchitis and Early Stages of Phthisis.—

Take of Tincture of Cimicifuga.....one ounce.
Tincture of Sanguinaria.....one ounce.
Sulphate of Morphine.....two grains.
Syrup of Acacia.....two ounces.

Mix together. Give a teaspoonful when the cough is troublesome. (Journal of Materia Medica, 1860.)

For Dropsy.—

Take of Tincture of Cimicifuga.....one ounce.
Tincture of Myrrh.....six drachms.
Laudanum.....one drachm.
Tincture of Capsicum.....one drachm.

Mix together. Take thirty or forty drops three times a day. (Journal of Materia Medica, 1860.)

Compound Pills of Cimicifuga.—

Take of Solid Extract of Cimicifuga.....one drachm.
Solid Extract of Scutellaria.....one drachm.
Valerianate of Quinine.....thirty grains.

Make 60 pills. Dose.—One every two or three hours. Used in nervous diseases, cholera and fevers, attended with wakefulness and restlessness. (Tilden & Co.'s Book of Formulas, 1861.)

Syrup of Cimicifuga.—

Take of Fluid Extract of Cimicifuga.....three ounces
Simple Syrup.....six ounces.

Mix them together. Dose, 30 to 60 drops. Used in rheumatism and wherever cimicifuga is indicated. (Tilden & Co.'s Book of Formulas, 1861.)

Compound Syrup of Cimicifuga.—

Take of Compound Fluid Extract of Cimicifuga.....two ounces.
Simple Syrup.....one pint.

Mix them together. Dose, three to six fluid drachms. (Tilden & Co.'s Book of Formulas, 1861.) No ascribed value to this mixture.

Tincture of Cimicifuga.—

Take of Cimicifuga.....three ounces.
Proof Spirits, or Wine.....one quart.

Mix and let it stand a few days

This is Beache's formula, of 1833, given in his work (American Practice of Medicine) as "Tincture of Cohush." An officinal formula for making Tincture of Cimicifuga was introduced into the Pharmacopœia in 1863 (see page 267).

Tincture of Colchicum with Cimicifuga (Compound Tincture of Colchicum), *King*.—

Take of Tincture of Cimicifuga,
Tincture of Colchicum, equal amounts.

Mix them together. (American Eclectic Dispensatory, King & Newton, 1852.) Used in inflammatory rheumatism and in gout.

Compound Tincture of Cimicifuga.—

Take of Tincture of Cimicifuga.....four parts.
Tincture of Sanguinaria.....four parts.
Tincture of Phytolacca.....one part.

Mix them together. Alterative, expectorant, and used in pulmonary affections. (American Dispensatory.)

MEDICAL HISTORY AND PROPERTIES.*—The important papers of early medicine were contributed to medical journals, and from them our authors derived the most of their information. Schalpf (1785) mentions the plant, but evidently knew little of its uses. The next reference we can find is that of Barton† (1801) in which he speaks of it being used by the Indians—"our Indians set a high value on it." He ascribes to it astringent properties, stating that it was used in decoction as a gargle in putrid sore-throat, as a cure for the itch, and as a drench for the murrain in cattle. He gives it the Indian name "squaw root," a name that denotes one of its uses with the Indians, for they applied it in diseases of women. In 1820 we find that Hand‡ states that a tea "promotes perspiration and produces sleep," is used in rheumatism, hysterics, colic, fevers and debility from nervous prostration. Bigelow (1822)§ states that Dr. Tully found it, in addition to the foregoing, diuretic, tonic, and useful in dropsy.

Dr. J. S. Gardner‖ (1823) published a paper in which he commends it highly in pulmonary affections, speaking of his own experience as follows: "Shortly after commencing the use of this remedy, the hectic paroxysms, which had attended me some time previously, were entirely checked, the nocturnal evacuations from the surface of the body began to diminish, the expectoration of a fluid from the vessels of the lungs and bronchia, resembling pus in appearance, was speedily arrested; the cough became less troublesome and frequent. My pulse, which for some time before was never lower than from 100 to 120 pulsations to the minute, was reduced to the minimum standard; the pain in my right breast and side left me, my strength and appetite began to improve, and I speedily abandoned the use of all medicines or other means. A period of twelve months or more had elapsed, from my primitive ill health to the time of using this medicine. It certainly possesses the power in an eminent degree of loosening arterial action, and at the same time imparting tone and energy to the general system."

Ewell¶ (1827) devotes considerable space to this plant, but aside from certain combinations that he recommends to be made of it, nothing new is produced. In 1827** Dr. G. W. Mears published a paper on the therapeutical uses of cimicifuga, together with an excellent lithographic figure of the plant and a chemical examination of the rhizome. His medical work was mainly a record of cases in which he had used it.

Rafinesque†† (1828) states that "This is one of the numerous Indian cures for the bites of snakes; they use the root chewed and applied to the wound," and in 1830‡‡ he adds, "used for all rheumatic pains, diseases of languor and squirrous tumors, in tincture or decoction, by the Cherokees and Southern tribes." He refers to its uses in many of the other diseases named by us, and adds that it is a favorite remedy with the Indians generally. The most complete résume on the subject to that date, appeared in 1829 as an addition to Edwards and Vavasseur's Materia Medica, by Togne and Durand. It was quite a creditable paper, but nothing new was developed

* This article was written independently of the following excellent paper by Dr. Sattler, and naturally many points will be repeated. On this account we have thought best to place this in smaller type.

† Collections for a Materia Medica, Part II.

‡ House Surgeon and Physician, p. 236.

§ Sequel to the Pharmacopœia of the United States, p. 125.

‖ Medical Recorder.

¶ The Medical Companion or Family Physician, p. 748.

** Philadelphia Monthly Journal of Medicine and Surgery, Sept. 1827, p. 748.

†† Medical Flora of the United States, Vol. I., p. 85.

‡‡ Medical Flora of the United States, Vol. II., p. 201.

Smith* states that "The Indians cure the ague by sweating with this root," meaning, perhaps, that they employed it in their fashion of steaming the patient in a close tent. He also asserts that "The yellow fever has been speedily cured by it, the bile having been first evacuated by an emetic." Howard† (1832) records that "It is likewise said to be a valuable remedy in small pox, and, in addition, he states that "repeated experiments (of others) left no doubt on the minds of our informants, that rattle-root may be regarded as a specific against the effects of the small pox poison," and he refers to the paper of Dr. G. W. Mears, in which it cured "intermittent fever which had resisted for six weeks the ordinary treatment," and adds, "Rattle-root has, however, acquired the greatest celebrity as a cure for coughs and consumption."

Beach‡ asserts that "a strong decoction mixed with slippery-elm bark, makes a good poultice for every kind of inflammation. A decoction is also used for the purpose of arresting hemorrhage. A syrup of the root is good for coughs. It also makes an excellent gargle for quinsy." The first edition (and subsequent issues) of the United States Dispensatory recognized cimicifuga, ascribing to it more or less of the values previously recorded. Dunglison§ (1843) places cimicifuga with the "special sedatives," but he states that "cimicifuga, in large doses, unquestionably belongs to the division of acro-narcotic poisons; but the author has had difficulty in deciding as to what class of therapeutic agents it ought to be referred"; and, considering the preceding literature on the subject, we are not surprised to find even Prof. Dunglison somewhat cautious. He accepts that "Cimicifuga unites, with a tonic power, the property of stimulating the secretions, particularly those of the skin, kidneys and pulmonary mucous membrane." The most carefully revised communication on the properties of this plant, however, to that date (1848), ‖ is by Dr. N. S. Davis, Chairman of the New York section of the committee on the Indigenous Medical Botany of our country. He decides that cimicifuga is a valuable remedy, but asserts that "the prevailing opinions in regard to its action on the system are entirely erroneous." He cites the statements of the authorities he recognizes—Wood, Griffith, Lee, Williams, Chapman, Payne, and the U. S. Dispensatory, and says "none of these opinions accord with our own experience.

"We have never known it to produce a perceptible increase in any of the secretions of the system, nor has it the slightest stimulating qualities. But, we have uniformly found it to lessen the frequency and force of the pulse, to soothe pain, and allay irritability. In a word, it is one of the most purely sedative agents we possess, making its impression chiefly on the nervous system of organic life. In large doses it produces vertigo, dimness of vision, and a depression of the pulse, which remains for a considerable time," and to sum up, adds, regarding its use in rheumatism, "Its curative powers being dependent entirely on its *sedative* action (as we believe) through the nerves of organic life, it can only prove effectual when given in the early stages before the occurrence of these fibrinous deposits around the ligaments and parts affected, which so generally occur in the later stages of protracted acute cases, and in all the more chronic forms of the disease. It is only in the acute form of rheumatism that its own complete curative power is exhibited. *The more acute the disease, the more prompt and decided will be the action of the remedy.*"

In 1852 the Eclectic Dispensatory appeared, and Prof. King gave to cimicifuga an unusual prominence. Inasmuch as he had long looked upon that plant as one of our most valuable indigenous remedies, and always recommended it highly, it naturally came into general use among the Eclectics, and is still a great favorite with the practitioners of that school of medicine. King excluded many of the reputed uses of cimicifuga, as in his opinion they were unsupported by evidence sufficient to entitle them to credence, but he made the plant conspicuous in all his writings.¶

It is a curious coincidence that, in 1872, we again have revived the statement of Howard,** that cimicifuga is an antidote to the small pox, or a preventive to it. After forty years, we find Dr. G. H.

* Botanic Physician, Elisha Smith, p. 427.

† Improved System of Botanic Medicine, Vol. II., pp. 183, 300.

‡ The American Practice of Medicine, Vol. III., p. 30.

§ General Therapeutics and Materia Medica, Vol. II., p. 194.

‖ Ives' Report of the Committee on Indigenous Medical Botany, Am. Med. Assoc. Report, 1848.

¶ The students are familiar still (1885) with Prof. King's "favorite remedy," as is shown by his teachings to the present day.

** Howard wrote several pages to support the value of cimicifuga in this disease. See his "Improved System of Botanic Medicine," 1832, Vol. II., pp. 183, 184, 185 and 300.

Norris, states at a meeting of the Alabama State Medical Association, 1872, that "during the prevalence of small pox in Huntsville, certain families, at the instance of some one unknown, had resorted to the free use of the tea of Cimicifuga racemosa, or black snakeroot of the United States Pharmacopœia, as a preventive of small pox. In the families using the Cimicifuga there occurred no case of the small pox, though some were exposed to the disease. In the same families Dr. Norris vaccinated the members, but without effect, so long as they continued the use of the Cimicifuga; after ceasing to use the tea as a prophylactic he again vaccinated them, when the specific effects of the vaccine virus were produced. He submitted the results in these cases as new,* and not without interest to the profession."

Prof. John Scudder is an ardent admirer of Cimicifuga, and we reproduce, as follows, from his "Specific Medication," a few of his terse sentences regarding that drug: "Like all other direct remedies, it (Cimicifuga) may be employed in any case, no matter what name the disease may have in our nosological classification, if the condition of the nervous system calls for it. The heavy, tensive, aching pains are sufficiently characteristic and need not be mistaken. So prominent is this indication for the remedy, in some cases, not rheumatic, that I give it with a certainty that the entire series of morbid processes will disappear under its use. For years I have employed Macrotys† as a specific in rheumatism and with excellent success. Not that it cures every case, for it does not; neither would we expect this, for this would be prescribing a remedy for a name. Macrotys influences the nervous system directly, relieves rheumatic pain when not the result of inflammation, and probably corrects the diseased condition (formation of lactic acid) which gives origin to the local inflammatory process. Thus in the milder cases, where the disease has not localized itself as an inflammation, Macrotys is very speedy and certain in action. Where rheumatism has localized itself in an inflammatory process, all the benefit we obtain from it is that we remove the cause, and hence the reason for a long continuance of the inflammation. It is a remedy for all pain of a rheumatic character, and for these we prescribe it with the best results. Those cases which go under the name rheumatic neuralgia are very speedily relieved by it. In some cases the pains of week's duration disappear in a single day."

At the meeting of the Chicago Gynæcological Society, 1885, Dr. J. Suydam Knox read a paper, "The Influence of Cimicifuga racemosa upon Parturition," in which he gives the results of its use in one hundred and fifty cases of labor, in which he decides that it is a valuable remedy, but in the discussion that followed, his views were criticised by Dr. Jaggard and others.

This brings us to date, and, as will be seen from our brief synopsis, Cimicifuga as a drug, occupies a position that has been of interest to the medical profession from a very early day in American medicine. It is conspicuous for its many recommendations and its uncertain position with many prominent therapeutists. In this connection the following special papers from representatives of the various bodies of medical men will be of interest.

THE MEDICAL HISTORY AND PHYSIOLOGICAL ACTION OF CIMICIFUGA RACEMOSA.—(Written for this publication by Dr. Eric E. Sattler, Demonstrator of Anatomy and Clinical Lecturer on Diseases of the Nervous System in the Miami Medical College of Cincinnati.)

This native American plant, about which there exists such a diversity of opinions and results, well deserves our attention and scrutinizing study.

History of its Uses.—The aborigines of America already discovered medicinal virtues in this plant; finding it, as they did, growing in various parts of the country, they soon learned to use and value it highly for a variety of complaints, chief among which were rheumatism and amenorrhœa. In rheumatism they depended much more on a decoction of the roots externally

* If the Doctor had been familiar with the early literature of that part of the medical profession outside the regular branch, he would doubtless have found his entire experience recorded, and the origin of its use in that disease would not have been unknown. Many country people are familiar with these old works.

† Prof. Scudder uses the term Macrotys, see our botanical history.

than internally. A hole was made in the ground, into which they put a kettle containing a quantity of the hot decoction. The rheumatic limbs were placed over the kettle in such a manner as to receive the influence of the steam. It is probable that the effect of the heat had considerable to do in subduing some of the more annoying symptoms of rheumatism. In facilitating parturition and as an emmenagogue it was also highly esteemed by the Indian women, whence its name—*squaw-root.** It was also used by the Indian doctors for ague and fevers, which it cured by profuse perspiration. As an antidote for the bite of snakes (the chewed roots applied externally to the wound), it also had some renown. These accounts are interesting to us only in an historical way, and not as the basis for scientific deductions. The Indians were probably not any too careful in their collection of plants, and the resulting product was often times a promiscuous decoction of numerous plants.

Benj. S. Barton† (1801) was probably the first writer to describe the plant. He classed it under the head of "astringents," the root of the plant having the astringent properties. He mentions the fact of a strong decoction of the roots having been used as a gargle, with great benefit, in an epidemic of putrid sore-throat which prevailed in Jersey many years ago. A decoction was also believed to be a sure cure for the itch.

In 1823, the attention of the profession was called to an article in the "American Medical Recorder," by T. S. Garden,‡ on the "Use of Actæa racemosa" in Phthisis pulmonalis. Dr. Gardner used it on himself when he was suffering from what he called "incipient phthisis."‖ He found it especially useful in checking the hectic paroxysms, diminishing night sweats, improving cough and expectoration, reducing an excited pulse and allaying irritation through its sedative properties on the nervous system and circulation. He found it to possess in an eminent degree the power of lessening arterial contraction, and believed it to have a tonic influence on the system. In 1850 Dr. Garden § asserts that thirty years' continued use of the drug has fully corroborated and confirmed his first favorable anticipations.

Chapman ¶ (1825) classified the drug with the "expectorants." He never found it astringent to any degree, but says it is "expectorant, narcotic, antispasmodic, diaphoretic, and in large doses emetic." In popular practice, at this time, it was reputed in pulmonary diseases, especially in asthma and consumption. In consumption it was said to lessen the frequency of the pulse, to allay cough, to quiet the mobility of the nervous system and to subdue hectic fever.

C. R. Rafinesque (1828) refers to it under the name of "Botrophis ser-

* I am informed by one of the able editors of this journal that the term squaw-root should be applied properly not to the *black* cohosh, but to the blue cohosh.

† Collections for an essay towards a Materia Medica for the United States, 1801.

‡ On the use of Actæa racemosa in Phthisis pulmonalis, American Medical Recorder, 1823.

‖ In all probability Dr. Garden's case was not one of incipient phthisis, but rather a subacute bronchitis with considerable expectoration. At least the term "incipient phthisis" must be accepted with considerable hesitation.

§ Treatise on Therapeutics and Pharmacology, G. B. Wood, M. D. Letter to the author.

¶ Elements of Therapeutics and Materia Medica, N. Chapman, M. D.

pentaria" (black snake root).* Its properties, according to this authority, are diuretic, sudorific, anodyne, repellent, emmenagogue and subtonic. It is valuable as a gargle, in dropsy, hysteria, and as an auxiliary in acute and chronic rheumatism. In veterinary practice it was largely used, according to this and other authors, in the treatment of murrain, a decoction being employed which purged the cattle, expelled their worms and thus cured the disease.

Young† (1831) first called attention to the efficacy of this drug in the treatment of St. Vitus Dance, although Dr. Garden claimed to have called attention to its medicinal powers in Chorea originally in 1832. Dr. Young relates the history of four severe cases of Chorea, that had failed to be benefitted by other remedies, in which the administration of cimicifuga was followed by signal benefit and cure.

Hildreth‡ (1842) speaks of it as valuable in incipient phthisis. He used it with benefit in asthma instead of lobelia, also in Chorea. Its narcotic properties he mentions as being similar to those of colchicum, veratrum and digitalis.

R. E. Griffith‖ (1847) found it to act like a stimulant tonic and capable of increasing the secretions from the skin, kidneys and lungs. The action of the drug on the uterus he claims unsatisfactory and doubtful. In affections of the lung and in rheumatism he found, on extended trials, good reasons to believe in its efficacy.

The committee of the American Medical Association (1848), N. S. Davis, Chairman,§ were satisfied that the prevailing opinions in regard to the action of cimicifuga on the system were entirely erroneous. No two opinions agree, for while by some it was classed under the expectorants, by others it was termed a tonic, or narcotic, or diuretic, emmenagogue, etc. The committee never found it to produce any perceptible increase in any of the secretions of the system, nor have any stimulant properties. They uniformly found it, however, to lessen the frequency and force of the pulse, to soothe pain and allay irritability. In a word, they held it to be the most purely sedative agent we possess, producing its impression chiefly on the nervous system of organic life.

G. B. Wood¶ (1856) classified the drug under the "nervous sedatives." He found it very serviceable in Chorea, and thought it should be considered among the standard remedies for this complaint. Although the value of this drug was first publicly made known to us by Dr. Jesse Young, of Pennsylvania, Dr. Isaac Hays, in a note, stated that ten years before the publication of Dr. Young's article, Dr. Physick had informed him that he had used the same remedy with good effect, in chorea, in 10 grain doses every

* Medical Flora and Manual of Medical Botany of the United States, by C. R. Rafinesque.
† American Journal of Medical Sciences. Remedial Powers of Cimicifuga in the treatment of Chorea.
‡ American Journal of Medical Sciences, Vol. IV., 1842, on Cimicifuga and Iodine in Phthisis pulmonalis.
‖ Medical Botany, R. E. Griffith, M. D.
§ Transactions of the American Medical Association, Vol. I., 1848.
¶ Treatise on Therapeutics and Pharmacology, by G. B. Wood, M. D.

two hours. Dr. Young gave ℥i. of the powdered root three times a day. Dr. Wood also employed the remedy in epilepsy, but found it no material benefit.

J. D. O'Connor* (1858) used it successfully in rheumatic and neuralgic pains. He used it in chorea with as much confidence as he did quinine in intermittent fever. Dr. Simpson, of Edinburgh, in his own case, found it repeatedly to cure an attack of lumbago with wonderful rapidity.

Dr. F. N. Johnson† found it extraordinarily efficient in acute rheumatism. In twenty of the worst cases "the results were satisfactory in the highest degree, every vestige of the disease disappearing in 2, 8 or 10 days, without inducing any sensible evacuation or leaving behind a single bad symptom." An equally enthusiastic follower says, "We have no more doubt of the efficacy of cimicifuga in the early stage of acute rheumatism than we have of the power of vaccine as a preventative of variola."

H. C. Wood‡ (1874) classed it under the antispasmodics, and says it is of undoubted value in simple chorea as it occurs in children. In inflammatory rheumatism it is at present rarely, if ever, used.

The preceding presents the important points culled from the literature concerning cimicifuga, and does not by any means exhaust it. A number of articles on the subject, being in the main, however, only repetitions of what has been said, will be found scattered throughout the pages of medical journals.‖

Clinical Investigation with the Fluid Extract of Cimicifuga Racemosa.—In order to test the value of cimicifuga in medical practice and furnish reliable indications for its use, Prof. J. U. Lloyd kindly placed at my disposal the Fluid Extract of Cimicifuga racemosa. The writer regrets to say that owing to the limited time at his disposal, his investigations were not as extensive as could be wished, but he hopes that the results obtained in his investigations at his Clinic for Nervous Diseases, Miami Medical College, and in his private practice, will enable the profession to pursue investigations with this no doubt valuable but somewhat discarded drug.

Physiological Action.—10 to 20 drops of the Fluid Extract, taken internally, do not sensibly affect the system. On September 21st I took ℥i. of the Fluid Extract. In twenty minutes a sickening feeling at the stomach and some dizziness was felt, accompanied by a sense of fullness in the head and temples. Thirty minutes from the time of taking the first dose ℥i. was again taken. In fifteen minutes my head began to swim and I became nauseated.

* Corbis Segminis. Cincinnati Lancet, 1858.

† Treatise on Therapeutics and Pharmacology, by G. B. Wood.

‡ Treatise on Therapeutics, H. C. Wood, 1874.

‖ 1827, Philadelphia Monthly Journal of Medicine and Surgery, Vol. I.; 1845, Southern Medical and Surgical Journal, Vol. I.; 1855, Columbus Medical Counsellor, Vol. I.; Pharmaceutical Journal, March, 1861; 1861, Chicago Medical Examiner, Vol. II.; 1867, Medical and Surgical Reporter, Philadelphia, Vol. XVII.; 1868, Medical and Surgical Reporter, Philadelphia, Vol. XVIII.; 1869, Medical and Surgical Reporter, Philadelphia, Vol. XX.; 1872, Atlanta Medical and Surgical Journal; 1876, Chicago Medical Times, Vol. VII.; 1876, West Virginia Medical Student, Vol. I.

The dizziness was great and accompanied by the most intense headache, which persisted fully eight hours. A slight diarrhœa also set in, but did not amount to more than a relaxation of the bowels. A drowsy feeling came over me, although the sévere headache prevented my sleeping any. Pulse, when first dose was taken, was 80. It diminished in frequency and became fuller in force gradually, until thirty minutes after taking the second dose it was 62 to the minute. The experiment was repeated several times with almost uniform results, and it was noted that when the drug was taken on an empty stomach its action was at least twice as marked and the retching more intense than when taken on a full stomach. In several of my cases I noted similar conditions after the administration of the Fluid Extract of Cimicifuga in doses of from 20 to 50 drops. In several cases headaches developed which prevented the further use of the drug. In others, a diarrhœa set in and became annoying. In others again, dizziness or nausea in varying degree was present. For these reasons it is well to begin with small doses and gradually increase them from day to day. I have found the administration of smaller doses frequently repeated to give better results than large doses at longer intervals. It is also well to bear in mind that the medicine is best administered after food.

Clinical Investigations.—My observations have been especially directed toward a certain class of Nervous Disorders in which cimicifuga was claimed to be efficacious, although as occasion presented I have not hesitated to use it in cases that I thought might derive some benefit from its use.

Chorea.—Five cases. It would have given me great pleasure and satisfaction to have used this remedy in some thirty cases of chorea that I treated a year and a half ago in an endemic during the months of March, April and May, but unfortunately the opportunity was not afforded and these cases had the benefit of treatment with Fowler's Solution with uniformly good results. In the five cases observed, I have found it efficacious in four; the fifth only yielded to large doses of arsenic. The cases came to my Clinic after they had undergone all kinds of treatment. Two cases had been treated three months outside, with no improvement. I prescribed 10 drops Fluid Extract of Cimicifuga racemosa every two hours, and on my next Clinic day (three days after) a noticeable improvement had taken place, and in the course of two weeks no trace of choreic movements were able to be perceived. The other cases progressed similarly favorable.

Epilepsy.—Although I tried this remedy in at least ten cases of epileptic convulsions, the convulsions seemed rather aggravated than diminished. In only one case, still under observation, of petit-mal in a boy aged 12 years, is an improvement manifested.

Hysteria.—It is of undoubted benefit in this disease. I generally prescribed it in combination with bromide of potassium, and sometimes it acted like a charm. In one case of hysterical mania I administered 40 drops every two hours with marked benefit.

Cephalagias.—In nervous headaches and those accompanied by congestion of the brain, it was found to be of decided benefit, seeming to quiet the nervous system and diminish the flow of blood to the head.

Phthisis pulmonalis.—It is simply a palliative remedy in this disease, acting as a sedative to the circulatory system. It is of unquestionable value in the hectic fever accompanying this trouble, its soothing influence being soon felt by a diminution of the number of heart beats and its calming effect on the nervous system. As a means of allaying cough, it seems to possess no value.

Rheumatism.—Although greatly lauded in this affection, a trial was not made of its efficacy, as the profession are in no need of a more certain remedy than the salicylate of sodium.

At the request of the editors of this journal, Prof. Joseph Eichberg, M. D.* employed samples of macrotyn (the resin principle of cimicifuga) in a number of cases of muscular rheumatism, and vague, indefinite pains in various parts of the body. Dr. Eichberg reports as follows:

"It was given in two-grain doses, repeated every four or six hours, and was administered either in powder, pill or capsule. In only one case was I able to satisfy myself of any favorable action exercised by it on the course of the trouble. In nearly all the cases, the remedy had to be discontinued very soon because of a severe and persistent headache which is set up. This symptom made its appearance within eight hours after the administration of the first dose. It may be that the quantity selected for trial was too large, two grains at a dose, and I shall test it farther in smaller doses."

Febricula.—In these slight (idiopathic) forms of fever not characterized by any definite organic lesions, to which the name of Febricula is given, the cimicifuga will be found of great service and benefit, never failing of attaining the desired result of rest to the nervous and circulatory system.

Emmenagogue.—I have had no opportunity of testing the remedy as to its value as an emmenagogue. In one case of hysteria, under treatment with cimicifuga, the flow of blood, which was rather profuse, was stopped each time by the administration of the Fluid Extract of this drug.

Indications.—The Fluid Extract of Cimicifuga, then, will be found of undoubted use in chorea (of childhood), in hysteria and nervous cephalagias, in hectic fever, and Febricula. It should be classed under the head of "Nervous Sedatives."

THE HOMŒOPATHIC USES OF CIMICIFUGA RACEMOSA.—(Written for this publication by Edwin M. Hale M. D., Emeritus Professor of Materia Medica and Therapeutics in the Chicago Homœopathic College).

Cimicifuga racemosa is one of the most important of all the indigenous remedies. Its range of action is quite extensive; it has been quite thoroughly

* Professor of Physiology and Clinical Laryngology in the Miami Medical College, Cincinnati.

proven; the clinical experience with it is already large; and it has great possibilities for future development.

Sphere of Action.—It is essentially a cerebro-spinal remedy. The brain and spinal cord are directly under its influence, upon which it acts primarily as a depressing irritant. Its action on the muscular system is probably not direct, but a result of its effect upon the spinal cord. It differs from nux and ignatia in that they are exciting irritants of the spinal cord. Cimicifuga indirectly affects the vegetative system—the functions of digestion and assimilation. It has but few symptoms of gastric or intestinal derangement not due to reflex irritation.

It has become one of our most potent remedies in disorders of the mental sphere, namely in melancholy and aberration of mind. The characteristic symptoms indicating its use are: "Great melancholy; the patient feels grieved, troubled with sighing; sensation as if a heavy black cloud had settled all over her, and enveloped her head; as that all was darkness and confusion, while at the same time it weighed like lead upon her heart. She was suspicious of everything and everybody; would not take medicine if she knew it; indifferent, taciturn; takes no interest in household matters; frequently sighs and ejaculates; great apprehensiveness and sleeplessness."

These symptoms are always promptly removed by cimicifuga. I have treated many cases of profound melancholy, even from disordered liver, with this medicine, and can truthfully assert that it has cured the majority, and even when the disorder of the mind depended on incurable physical disease, its palliative effect was remarkable. One keynote to be remembered is sleeplessness. Many physicians have informed me that if, in cases of melancholy, sleeplessness was present, cimicifuga nearly always cured.

In delirium tremens cimicifuga is indispensable. When there is nausea, retching, dilated pupils, heavy, pressing out headache, trembling of the limbs, incessant talking, changing from one subject to another, obstinate sleeplessness, imagines strange objects on the bed, with quick hard pulse, and a peculiar wild look in the eyes, the third dilution frequently repeated, aided by a good diet of milk, wine, whey, mutton broth, etc., will soon restore the patient.

A lady patient of mine who was taking five drops of the first dilution for rheumatism, was annoyed by an allusion of a mouse running from under her chair. This illusion disappeared upon suspending the medicine, and recurred when taking the same doses.

The nerves of sensation are very unfavorably affected by massive doses. It causes a pure neuralgia, and what the older authors called neuralgic rheumatism. The neuralgia is not confined to any particular set of nerves, as is the case with some remedies. Its depressing irritant action seems to be universal. The pains are aching, pressing, remitting, and are attended with great restlessness, and a weak exhausted feeling. It seems to affect the sensory nerves of

the left side most. The nerves of motion are profoundly irritated. In the words of Dr. T. C. Miller, whose experience with it for fifteen years enabled him to judge of its powers: "It is one of the most remarkable remedies in all diseases of the ganglio-spinal system, particularly when the motor side is excited, and yet in the whole prevails atony in the muscular and nervous system."

This statement of its pathological action gives us the clue to its wonderful efficacy in chorea. It is indicated in many kinds of chorea, whether arising from rheumatic irritation of the cord, from uterine disease, or from purely psychical causes. The symptomatic indications are chiefly abnormal movements, uncontrolled by the will, in all those parts of the body supplied by motor nerves which affect both voluntary and involuntary muscles. The motions consist of twitching, jerking, twisting actions. They are sometimes attended by pains like neuralgia or rheumatism. The movements abate or are absent during sleep. They are aggravated by emotions, at the menstrual periods, or are caused by suppressed menses. They are attended by depression of spirits and sleeplessness, and often by mental derangement.

Cimicifuga is useful in many kinds of tremors which resemble St. Vitus' dance, but due to functional derangement of the nerve centers. If they are caused by structural changes this remedy is useless, or if they are caused by mercurial or other mineral poisoning. I do not think cimicifuga will be found very useful in convulsions of any kind, unless they resemble chorea; consequently it will not be available in ordinary puerperal convulsions or epilepsy. It bids fair to become a prominent remedy in cerebro-spinal meninitis and possibly myelitis.

Cimicifuga, in the lower dilutions, is indicated in the three grades of cerebro-spinal diseases, namely: cerebro-spinal meningitis; cerebro-spinal congestion; cerebro-spinal irritation. The following are the indications for its selection: delirium, like mania-a-potu, with nausea, retching, dilated pupils, tremor of the limbs, quick full pulse, and wild look out of the eyes.—Headache, pain over the eyes, extending along the base of the brain into the occiput.—Brain feels too large for the cranium, a pressing from within outwards, or a sense of compression in the temples.—Excruciating pain in the forehead and in the eyeballs, vertex, nape of the neck, and occiput, with fullness and throbbing, as if the top of the head would fly off.—Dull pains in the occiput, with shooting pains down the back; the head is jerked backwards.—Intense pain in the eyeballs, with black specks before the eyes, dilated pupils, double vision, congested conjunctive, and lachrymation.—Intense throbbing pain, as if a ball were driven from the neck to the vertex with every throb of the heart.—Tongue swollen, breath offensive, pharnyx dry, dysphagia, roughness and hoarseness of voice.—Nausea and vomiting attend pain in the head.—Pains in the back, of a drawing, tensive character, or dull and heavy, with tenderness on pressure.—Alternate tonic and clonic spasms, night and day.—Spasmodic

jerkings, like chorea.—Rigidity of the muscles of the neck and back.—Intense aching pains in the neck, head and all the joints of the extremities, like the pains which accompany the fever of variola.—Eruption of white pustules on the face and neck; sometimes large, red and papular.

In inflammatory muscular rheumatism cimicifuga has always had a deservedly high popularity, both with physicians and laymen. The rheumatic fever, for which it is specific, is marked by several very characteristic symptoms, namely, the suddenness of its onset, the severity of its manifestation, and its location in large muscles. In such cases it often acts with surprising rapidity, relieving the fever, pain, soreness and restlessness in a few days. It differs from Rhus in not acting on the tendons, or terminal attachments of muscles, and from colchicum, bryonia and asclepias, in not acting on serous tissues, at least I do not think it has that affinity for serous tissues which is possessed by other well known medicines. I would not give the impression that cimicifuga is not useful in chronic rheumatism, for some of its most brilliant achievements have been in that direction. But in such cases the location of the disease has been in the belly of the muscle, *i. e.*, its longest or middle portion, and its inception was originally sudden and severe.

Cimicifuga has made some surprising cures of acute and chronic inflammation of the cervical and lumbar muscles ("stiff neck" and lumbago), in chronic inflammation of the muscles of the upper and lower extremities and intercostal rheumatism.

The febrile symptoms of cimicifuga are more erethistic or irritative (reflex or sympathetic) than inflammatory or synochal. It will be rarely useful in fevers, except as an intercurrent remedy. I have found it useful in the myalgic troubles which often follow scarlet fever. It relieves those intolerable pains in the back and limbs, the stiff neck and muscular cramps which are such painful sequels of that malady.

Night sweats, when not due to suppuration or anemia, but to some fault in the proper supply of nervous energy to the skin are readily arrested by this drug.

In the provings it is observed that cold sweat is quite a common symptom, especially after 3 A. M., sometimes lasting all day, with weak, irregular pulse, and pain under the left breast. Also that these symptoms are very common in women, and sometimes men, whose nervous system has been weakened by long illness, trouble or care; and in all such cases, cimicifuga in the third to the sixth dilution will prove an admirable restorative.

No drug in our materia medica uniformly causes such severe pain in the head, both internal and external. Internally it causes passive congestion or anæmia, according to the constitution of the prover. Externally it causes pains in the muscles and the nerves supplying them.

The character of the pains and distress are:

Internally, "a sensation in the head as if the temples were compressed,"

dullness and heaviness in the head, as he had been on a "spree"; head felt as if it had been pounded, full of something heavy; moving the head or turning the eyes causing a sensation as if the cranium was opening and shutting; head feels if he had been without sleep for a long time; brain feels too large for the cranium, pressing from within outwards; severe pain in the forehead, extending to the temples and vertex, with fulness, heat and throbbing; when going up stairs, a sensation as if the top of the head would fly off; excruciating pain in the eyeballs. Nearly all the pains in the head extend to the eyeballs; they are aggravated by movement, relieved by the open air; attended by faintness and "sinking" at the pit of the stomach.

Externally—it has severe pain over the right or left eye, extending into the eye, and back into the base of the brain; pain over the eyes, extending along (around) to the base of the brain and occiput, and nape of the neck; pain in the occipital region, with shooting pains down the back of the neck; dull, boring pain over the left superciliary ridge, at 10 A. M.; pains in the occiput extending to the vertex.

Cimicifuga is indicated in headache resulting from loss of sleep, night watching, and abuse of alcoholic drinks; from mental strain and worry of mind, and from exposure of the head to draughts of cold, damp air. It is useful in the following kinds of cephalagia: congestive headache (passive, perhaps active); nervous headache (periodical or remittent); rheumatic headache (in the muscles—catarrhal); hysterical and menstrual headaches (at change of life); cerebro-spinal headaches.

In the cerebral irritation of children during teething, when they are fretful, feverish, sleepless, the sixth or thirtieth dilution has a soothing effect.

The eyes are severely acted upon by cimicifuga. Few drugs cause such intense and persistent pains in the eyeballs. The pains are chiefly aching, extending to different portions of the head. Many of the pains, however, seem fixed in the center of the eyeball, and simulate the rheumatic and neuralgic affections of the eyes. In some cases the eyelids become inflamed. One characteristic of the eye affection is that in the majority of cases no redness of the eyeballs exist; in other cases, as in Dr. Hill's proving, the "eyes were congested, so as to attract the attention of every one, although there was no disagreeable feeling in them." This discrepancy is probably owing to some difference in the constitution or idiosyncracy of the prover.

Thé action of cimicifuga on the stomach seems to arise from its depressing effect on the solar plexus and its sympathetic nerve connections. It resembles the action of sepia, digitalis, murex and ignatia, all of which produce, like cimicifuga, that peculiar sensation of faintness, sinking and emptiness which attended all the provings. This sensation is sometimes attended with nausea and vomiting. This faint sensation alternates during the same day with a sensation of fulness or repletion, both sensations resulting from a depression of the same nerve. In the nausea and vomiting of drunkards, tea drinkers and preg-

nant women, when attended by the above morbid sensations, it will act curatively.

It increases the quantity of urine, which is pale and limpid. Take the symptoms in connection with the general nervous depression, sinking at the stomach, etc., and we have good data for prescribing it in nervous diabetes, or that condition which frequently precedes or follows nervous attacks of various kinds, hysteria and the like.

Cimicifuga is one of our most important remedies in many of the diseases of women. In amenorrhœa, or delayed appearance of the menses in young girls, from deficient nervous energy in the ovaries, and when the abnormal nervous influence is directed to other organs, giving rise to chorea, hysteria, nervous headaches, etc., cimicifuga will restore the functions of the reproductive organs to a normal state. Should there be at the same time, with the above conditions, a chlorotic state, helonais or ferrum should be alternated with this remedy. In retarded menstruation, when pulsatilla or senecio are not indicated, and when at the usual menstrual period the discharge does not appear, but in its case comes a pressive, heavy headache, melancholy, palpitation of the heart, and other reflex symptoms, in these cases cimicifuga will restore the normal condition of the system and cause a regular return of the menses.

In suppression of the menses from a cold, mental emotions, or febrile conditions, when rheumatic pains in the limbs, or intense headache, or uterine cramps are present, this remedy will be found very useful. In dysmenorrhœa cimicifuga has been used successfully by all schools. I have treated many cases of difficult and painful menstruation, arising from various causes, and while in all there was improvement, in many the morbid condition seemed to be permanently removed. I consider the following symptoms as indicating its use: Before the menses the peculiar headache similar to that caused by this medicine; during the menses aching in the limbs, severe pain in the back, down the thighs and through the hips, with heavy, pressing down, labor-like pains, weeping mood, hysteric spasms, cramps, tenderness of the hypogastric region, scanty flow of coagulated blood, or profuse flow of the same character; between the menses, debility, nervous erethism, neuralgic pains, tendency to prolapsus, etc.

As a parturifacient it was in general use among the Indians in the early settlement of this country. Bigelow speaks of it as an active agent in facilitating parturition, and Tully says he has known many cases where it has produced abortion in pregnant women when prescribed for a cough. The evidence on this head is far more full and satisfactory in regard to its emmenagogue properties. Prof. Lee says: "It is believed to exert a specific influence on the uterine contractions, lasting longer than that of ergot, and followed by less torpor and greater susceptibility and capacity for action in the uterus than before its employment. After-pains are often readily relieved by small

doses of cimicifuga, second or third, or cimicifugin third. I have used it with signal benefit in those cases which seemed to be kept up by a neuralgic disposition, or mental and nervous irritability, and the patient was sleepless, restless, sensitive and low spirited.

Suppression of the lochia is treated successfully with this remedy. It is also useful for the relief of those bearing-down pains, indications for prolapsus, which women frequently suffer from after confinement. It is eminently homeopathic to a tendency to abortion. It has been successfully used in instances of "habitual abortion" with the result of preventing the usual miscarriage in the second and third months.

Sterility when not due to extensive ulceration, or other structural changes in the uterus, may be cured by cimicifuga.

Prolapsus uteri is often removed by this remedy, especially when occurring in nervous, melancholy subjects, and is the result of abortions, cervical congestion, or defidient nerve inervation. Two key-symptoms indicate it in prolapsus, namely, melancholy and "sinking" at the pit of the stomach.

Ovarian disorders, of a nervous rather than inflammatory or structural character, will often find a specific in cimicifuga. Ovarian neuralgia is perhaps as often cured by it as by any other remedy. In this affection it is specially indicated when the ovarian pains are reflected or change their location to other portions of the body, as the leg of the same side, the region under the left breast, or extend up the whole side to the shoulder. As ovarian disorder is usually attended with abnormally depressed states of mind, cimicifuga is as often indicated as platinum, with which it affiliates in many respects.

Dystocia is one of those abnormal conditions which come clearly under the domain of homeopathic medication. It is useless to cling to the antiquated superstition that a woman must suffer the "pangs of childbirth." Dystocia is always the result of an abnormal condition of the tissues concerned in the functions of childbearing. I do not wish it understood that a majority of cases of painful labor can be remedied by medicines. I have attended very many women who did not suffer to any degree. They expressed themselves as caring very little for the pains. Nor were these women all healthy. But this abnormal phase was somehow absent or nearly so. I have also attended many women whose previous labors had been very painful, almost unendurable without ether, but owing to the administration of cimicifuga, during the last weeks of pregnancy, they suffered very little. So many of these cases have occurred in my practice and in that of my colleagues that it is not proper to affect skepticism or unbelief. As a rule first labors are painful and protracted, while subsequent ones are less so. But if five or six are very painful, and each one seems to be more painful than the last, we can not expect the seventh to be painless, except from medicinal interference. Now, if in such cases cimicifuga is given, and the next labor is easy, what is the inference? Evidently that the medicine affected a change of condition from abnormal to normal. In such

cases cimicifuga should be given at least two weeks before the expected date of labor, in doses of one to ten drops, two or three times a day, the doses repeated oftener as the date approaches.

In irritable uterus, that condition once described by Gooch, and lately declared by Hewitt to be a condition of flexion, cimicifuga is an admirable remedy when the pain seem like those of rheumatism or neuralgia.

Mammary pains of a reflex character, occurring during pregnancy, with dysmenorrhœa, or at the climateric, and even after confinement, are also included in the curative sphere of this medicine.

For those obstinate reflex pains in the left side, occurring in women, generally the unmarried, this remedy is as nearly a specific as can be.

Diseases of the heart are cured or greatly palliated by cimicifuga. It is useful in: endocarditis, especially idiopathic or rheumatic; pericarditis, in alternation with aconite, spigelia, or bryonia; cardiac myalgia, which is often mistaken for true angina pectoris; cardiac debility, characterized by irregular palpitation, with intermitting and weak pulse. Its symptoms are so similar to digitalis that it is often impossible to select between them. The history of the case will decide. If the symptoms of cardiac debility are primary, *i. e.*, arising from nervous atony, cimicifuga is primarily indicated.

It is useful in chorea of the heart, a disorder now admitted to exist even when no other choreic symptoms appear. It is characterized by tumultuous, irregular, unexpected and strange motions of the heart, aggravated by emotions and subsiding during sleep.

I ought to add that I consider Actæa alba and rubra to be very similar to cimicifuga (once called Actæa racemosa) in many respects. I have frequently substituted the former for the latter species, especially in uterine disorders, with good results. Dr. Winterburne, of New York city, recently gave favorable experience with Actæa alba in nervous and uterine disorders.

THE USES OF CIMICIFUGA RACEMOSA IN THE ECLECTIC SCHOOL.—(Written for this publication by Prof. John King M. D., Professor of Obstetrics and Diseases of Women, in the Eclectic Medical Institute, Cincinnati).

The following is a concise statement of the therapeutical value of black-cohosh root, as determined in my own practice, and when its employment was not alternated nor combined with other medicines. I have prescribed this agent since 1832, at which time, as far as I am aware, very few practitioners had any knowledge of it as a medicine. A saturated tincture has always been, and is still preferred, prepared with stronger alcohol; and next to this, the alcoholic extract.

These preparations, when administered internally, lessen the action of the heart and arteries, diminish nervous irritability, and remove abnormal conditions of muscular tissues, as well as of certain glandular organs, while at the same time a mild narcotic influence is experienced in numerous instances. In

inflammatory rheumatism, when given in the first attack, the tincture has not only removed the disease, but has likewise appeared to so change the rheumatic tendency, that a second attack is seldom to be anticipated; to effect this the tincture should be administered in doses of from ten to sixty minims, repeated every two hours until the patient's head becomes affected, after which the intervals between the doses should be sufficiently increased so as to continue and keep up this action upon the brain for several days, or until the disease has completely disappeared. In chronic rheumatism it has proved useful, diminishing the severity of the pain, and lessening the duration of the disease, but nothing more, unless in combination with other agents.

In conjunctivitis and in sclerotitis, in doses of from ten to sixty minims, repeated every hour or two, it has effected a complete recovery in a few days. It has also been attended with excellent results in relieving the more active symptoms attending the early stages of phthisis, in which disease a further investigation of its action is highly desirable, as well as in catarrhal affections of the respiratory organs.

In chorea this is the principal agent upon which I have relied for the last fifty years, preferring, however, in this malady, the alcoholic extract. Without entering into particulars, it may be stated that this agent has been successfully employed in neuralgic affections, in uterine leucorrhea attending endometritis, as well as congestion of the uterus, also in those affections of the female reproductive organs in which the menstrual function becomes deranged, as manifested by amenorrhea, dysmenorrhea, menorrhagia, frigidity, sterility, etc.

It is an ecbolic, as several instances are known in which the tincture, having been taken every three hours by pregnant women, effected the desired abortion; it undoubtedly exerts a very positive influence upon the generative organs of women. As an accelerator of labor, in cases of uterine inertia, the tincture or the powdered root proves a substitute superior to ergot, in the majority of cases arousing the uterus to contractions more nearly resembling the normal ones, and without any risk to the fetus, or impairment of uterine sensibility to its influence upon subsequent administration; though, as with ergot and similar agents, it occasionally fails in its action. Immediately subsesequent to a protracted or severe labor, the tincture will allay any nervous excitement that may be present, will relieve severe after-pains, and will favor uterine involution. In subinvolution of the uterus, accompanied with menorrhagia, the tincture or the extract will be found an efficient remedy.

When the tincture is exhibited in sufficient doses to keep up a slight effect upon the brain, it proves a very remarkable remedy in certain forms of malarial disease, also in neuralgia. Gastric acidity undoubtedly interferes with its remedial action in all instances. The root is said to contain tannin, but no decidedly astringent effect has been observed from its use.

Although a large dose is given herein, yet it must be remarked that some care and watchfulness is necessary in its administration, as I have met with

several instances in which two or three drops of the tincture, repeated every hour, have, after a few doses, occasioned symptoms closely resembling those of delirium tremens; indeed, in one case, the administration of but one drop was invariably followed by these symptoms, and its further employment had to be omitted. Black cohosh is one of the most peculiar agents met with in the vegetable kingdom; it appears to exert a remedial influence upon both the serous and mucous tissues of the system when in abnormal conditions, and consequently has proven a superior remedy in numerous chronic diseases.

The specific tincture of the root, as prepared by Messrs. Lloyd Brothers, appears to have nearly, if not quite, all the remedial influence of the saturated tincture, more especially in rheumatic and neuralgic affections, and in abnormal conditions of the principal organs of reproduction in the female. The fluid extract and the infusion of the root are less active in effecting the therapeutical influences just described; however, they will be found more especially beneficial in small pox and other exanthema, both as a prophylactic and a remedy. It will simply be remarked here, that in alternation or combination with other medicines, not only is the usefulness of black cohosh increased but its field of operation greatly enlarged.

The resin of cimicifuga, improperly called "cimicifugin," was first prepared by myself in 1835; then, having subsequently tested its therapeutical virtues for about ten years, I called the attention of practitioners to it; but, it did not come into general use until about 1850. This resin does not appear to possess exactly the same properties as the tincture, its narcotic influences being less decided. Alone, I have found this resin very efficacious in maladies of the female reproductive organs, as in chronic ovaritis, endometritis; menstrual derangements, as amenorrhea, dysmenorrhea and menorrhagia, frigidity, sterility, threatened abortion, uterine subinvolution, and to relieve severe after-pains. In alternation or combination with other medicines, it has exerted efficacious results in many diseases not necessary to name here. Other practitioners have related its employment in nervous, rheumatic and gastric affections, with much benefit, as well as in certain acute maladies.

The dose of the saturated tincture of black cohosh varies according to its effect upon the patient, from one minim to sixty minims, to be repeated three or more times per day; of the specific tincture, from one minim to ten minims, repeated every two or three hours; of the alcoholic extract from one-fourth to one grain; of the resin from one-half of a grain to three, and even six grains, three times a day; of the powdered root, from ten to sixty grains, as may be required.

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PLATE XXV.



XANTHORRHIZA APIIFOLIA.

(FLOWERING PLANT, NATURAL SIZE.)

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1883.—Proceedings American Pharmaceutical Association, p. 128.

XANTHORRHIZA APIIFOLIA.

SHRUB YELLOW ROOT.

PARTS USED.—The rhizome and roots of Xanthorrhiza apiifolia *L'Her.* Natural Order Ranunculaceæ, Tribe Helleboreæ.

BOTANICAL ANALYSIS—Rhizome, growing several inches below the surface, branched, woody, cylindrical. Stem erect, woody, unbranched, two or three feet high, bearing leaves and flowers only on the upper portion, marked with scars of fallen leaves. Leaves, alternate on the upper portion of the stem, odd-pinnate, erect; leaf-stalk long, abruptly dilated at the base, bearing five approximate sessile leaflets at the extremity; leaflets oval or lanceolate, wedge-shape and sessile at the apex, veiny, deeply incisely, two or three cleft or parted, margins incisely serrate. Flowers numerous, small, dark purple, racemosely arranged in a drooping, few-branched panicle, appearing in early spring. Sepals five, purple, petaloid, spreading, acute, equal. Petals five, small, erect, two-lobed, gland-like organs raised on a short claw. Stamens five, alternate with the petals, or sometimes ten. Pistils five or ten, sessile; ovary one-celled, with a tapering style, containing two ovules attached to the middle of the ventral suture. Fruit a cluster of small, membranous, gibbous, follicles, each containing a solitary, minute seed suspended from its apex.

COMMON NAMES—From the bright yellow color of the rhizome the plant is known as Yellow Root. In most medical works, to distinguish it from Hydrastis canadensis also called Yellow Root, Xanthorrhiza is designated as Shrub Yellow Root, but in the Southern States, its place of growth, where Hydrastis is mostly absent or rare, the plant is known to the people simply as Yellow Root.

In European works the plant is often called American Shrub Yellow Root; in botanical works it is usually designated as Parsley-leaved Yellow Root; and in the drug trade is generally known as Southern Yellow Root.

The name Yellow-wort is also applied to the plant instead of Yellow Root, in many works, and is modified by all the before mentioned adjectives.

BOTANICAL AND GEOGRAPHICAL DESCRIPTION.—Shrub Yellow Root, is a very common plant along the streams in the mountains and hilly portions of the Southern States. It grows in clumps or patches abundantly along the sandy banks of streams and in shady situations rather than in the sun. It extends northward along the mountains to Pennsylvania, and has been found in a few localities in New York. Mr. J. H. Sears reports that it has been introduced and is rapidly spreading in Essex county, Massachusetts.

The rhizomes grow horizontally several inches below the surface and are branched and often densely interwoven. They send up at intervals of several inches, stems that are usually branched below the surface, the branches arising erect and parallel and appearing like separate stems.

Above the ground the stems are erect, simple and seldom (if ever) branched. They grow from one to three feet high and are about the size of a lead pencil in diameter and nearly uniform in thickness throughout. The leaves are borne all in a terminal cluster and the whole aspect of the plant, its simple, unbranched, uniform stem and terminal bunch of leaves remind one of a palm tree on a small scale.

The bark is externally of a light gray color,* especially on the new wood, and bright yellow beneath. It is marked at intervals of one to two inches with scars of fallen leaves. The stem grows six to nine inches, from a terminal bud, each year, and the base of each year's growth is shown by a number of approximate scars. The woody zone is of a light yellow color and has a large number of medullary rays which can be plainly seen in a cross section. A white pith in the center of the stem has one-third the diameter of the stem.



FIG. 99. Cross section of a stem of Xanthorrhiza apiifolia.

The leaves are deciduous and hence are found only on the new wood or upper portion of the stem. They are alternate, and grow erect at a very acute angle with the stem. The base of the leaf-stalk clasps and nearly encircles the stem with a peculiarly abrupt dilation.

Each leaf consists of five, sessile, pinnate, approximate leaflets borne near the top of the long slender leaf-stalk. The leaflets are about two inches long, ovate, cuneate at the base, veiny, glabrous, and incisely lobed; the margins are doubly and incisely, cut toothed.

The flowers appear in early spring, together with the partly grown leaves. They are small, brownish purple, numerous, and arranged in lax, racemose, few-branched, drooping panicles from the axis of a (fallen) bud scale.†

* The statement in Wood's Class Book and other works that the plant has a yellow bark is incorrect.

† Not from the axes of the lower leaves, as stated by Bentley and Trimen.



FIG. 100.
A flower of Xanthorrhiza apiifolia (enlarged).

The individual flowers are borne mostly two or three together,* and on bracted pedicels. They consist of five brownish purple, spreading sepals, five small, gland-like petals, five (sometimes ten) stamens and five (or more) sessile pistils. The ovary contains two ovules attached about the middle of the inner suture. Only one of these ovules matures, and as the ovary grows it develops unequally, the ovary bearing portion becomes the summit of the pod and the original stigmatic apex becomes deeply dorsal (see figs 103 and 104). The fruit is produced in a branching panicle borne on the stem at the base of the leaves. It consists of very small inflated light yellow, or straw-colored membranous pods, tipped on the back with the persistent short stigmas and containing each a minute dark seed suspended from the apex of the pod.



FIG. 101.
A flower and petal of Xanthorrhiza apiifolia (enlarged).†



FIG. 102.
A section of an ovary of Xanthorrhiza apiifolia (enlarged).



FIG. 103.
A section of a fruit of Xanthorrhiza apiifolia (much enlarged).



FIG. 104.
The fruit of Xanthorrhiza apiifolia (enlarged).

BOTANICAL HISTORY.—The plant was discovered by John Bartram‡ in Georgia, about 1760.‖ He transferred the plant to his

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*Our criticism of the engraving of Xanthorrhiza in Gray's Genera (plate 17) would be that the pedicels are not simple as those mostly shown, also the absence of bracts.

†This figure, taken from Baillon's History of Plants, represents ten stamens. The usual number is five.

‡J. Bartram was one of the pioneer botanists of America. He was born in 1701, of Quaker parents, his grandfather having been one of the famous settlers who came over with William Penn in 1682. Bartram early manifested a love for natural sciences, especially botany, and made many excursions through what was then the English provinces in quest of new plants. He established at Kingsess on the banks of the Schuylkill, about five miles from Philadelphia, the first botanic garden in this country and filled it with native plants, collected on his various trips. Bartram labored under great difficulties on account of his isolation from the working botanists of his day and the delay and trouble in communicating with them. He was in correspondence with the foremost botanists of Europe at that time, Linnæus, Dillenius, Catesby, Sloane, Sherard, Fothergill, Gronovius and others, and furnished many new plants for European botanical gardens. We find record of his sending plants to Sherard as early as 1728. Bartram's industry in the pursuits of science secured for him fellowship in the leading learned societies of Europe and he was appointed "American Botanist" by King George III. He was not the author of any work on botany, but a journal of his travels in Florida, containing many botanical notes, was published by William Stock about the time of his death. Bartram died in September, 1777, in his seventy-sixth year.

‖We have no record whatever of the year the discovery was made. The only reference we can find is Woodhouse, who states (1802) that it was brought to Philadelphia "about forty years since."

botanical garden at Kingsess where it continued to flourish luxuriently for a number of years. We are unable to find the name that Bartram applied to the plant. His son, William, called the plant Marbosia tinctoria,* in honor of M. de Marbois† and it is probable that he received the name from his father.‡

All writers agree that the plant was introduced into Europe in 1766, by John Bush, who probably obtained it by purchase from Bartram. As it was easily propagated it became established in a number of botanical gardens, but was overlooked by botanical writers for twenty years. In 1784‖ L'Heritier§ described and illustrated it with a beautiful engraving in his work entitled "Stirpes Novæ aut Minus Cognitæ."¶ He called it Zanthorhiza apiifolia.**

In 1785, Humphrey Marshall, a Philadelphia horticulturist, published his Arbustrum Americanum, or catalogue of American trees and shrubs, and described the plant as Xanthorhiza simplicissima,†† and in our opinion this is the prior name and should be adopted.‡‡

In 1802,|||| Dr. James Woodhouse figured and described the plant and

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*Barton gives the name Zanthorhiza Marbosia, *Bartram* as one of the synonyms for the plant. We do not know where this name was published, but it was probably in one of the horticultural catalogues issued by William Bartram, after the generic name *Xanthorrhiza* had been established by Marshall and L'Heritier. It is evident that Marbosia was the original generic name given the plant by the Bartrams.

† The Marquis de Marbois, whose proper name was François Barbe de Marbois, was an eminent French statesman and literator who was born at Metz in 1745. He was prominent in French politics and wrote several works, one a history of Louisiana. For the French nation, he negotiated the sale of the tract, formerly known as Louisiana, to the United States. He was not a patron of botany and we do not know why Bartram should desire to commemorate his name by a genus of plants.

‡ We have searched in vain for the original reference for this name, Marbosia tinctoria, by William Bartram. The only work of importance published by him was his Travels in North and South Carolina, printed in 1792, but we do not find any reference to the plant in this work, and had he mentioned it, he would have probably used the name Xanthorrhiza, which was by that time well established and known. John Bartram and after him William, his son, were horticulturists and sold plants to the gardens of Europe, They issued a "sheet catalogue, published by John and William Bartram, botanists in Kingsess; containing the names of Forest Trees and Shrubs growing in, or near, their garden" (see Marshall's Arbustrum, page xx. of the introduction). It was in this catalogue, no doubt, which we have not been able to obtain, that the name Marbosia tinctoria was printed.

‖ Although dated this year, it is probable the work was not issued for several years afterwards. See note ‡‡ below.

§ Charles Louis L'Heritier was a wealthy French botanist, who resided in Paris. He began the study of botany as a pursuit to fill his leisure hours, about 1770, and died in 1800, murdered by his son. He was an ardent admirer of Linnæus, and as at that time French botanists were strongly opposed to the Linnæan system and in favor of that of their own countrymen, Tournefort and Jussieu, L'Heritier met with bitter opposition at home. In order to establish his own views, having wealth and leisure, L'Heritier began the publication in fascicles of an expensive work, elegantly illustrated, called "Stirpes Novæ aut Minus Cognitæ," and Xanthorrhiza was one of the plants described in this work.

¶ Viz., plants new or little known.

** The generic name Xanthorrhiza is derived from ξανθός *yellow* and ῥίζα *root*, from the color of the rhizome. The specific name Apiifolia is from *Apium*, the former generic name of the Parsley and *Folium*, a leaf, from the resemblance of the leaves of this plant to those of the Garden Parsley (now Petroselinum sativum, formerly Apium sativum).

†† Viz., most simple, a prominent characteristic of the unbranched stems.

‡‡ A careful consideration of all the evidence on the subject convinces us that the generic name Xanthorrhiza was originated by Marshall, and that L'Heritier deliberately stole the name, ante-dated his publication, and received unmerited credit as its author. It is evident that one copied from the other and it seems very strange that Marshall, a comparatively obscure American botanist, should have been familiar with an expensive French work issued by L'Heritier only a year previous, and on a subject not confined to American plants. Besides Marshall distinctly states that "he imposed the name (Xanthorhiza) before he heard of Bartram's name (Marbosia)." That L'Heritier was guilty of ante-dating some of his fascicles was charged and proven by a Spanish botanist, Cavanilles, whose work on the Mallow family was seemingly forestalled by L'Heritier.

‖‖ Medical Repository, 1802, p. 159.

proposed the name Xanthorrhiza tinctoria,* but the article not appearing in a botanical work, writers on plants have mostly overlooked it and few have used the name, even as a synonym.

In most botanical and medical works L'Heritier is credited with naming the plant, and his name and spelling Zanthorhiza apiifolia has been generally used.

ORTHOGRAPHY.—The generic name of the plant has been spelled in a variety of ways by botanical authors. *Zanthorhiza* is the usual manner, but we find on search the following spellings: Zanthorhiza, Zanthoriza, Zanthorrhiza, Zanthorriza, Xanthorhiza and Xanthorrhiza. Marshall spelled it Xanthorhiza and L'Heritier, Zanthorhiza. The correct spelling, as now accepted by Watson, and to which attention was specially drawn by W. H. Leggett, in 1870,† is Xanthorrhiza.

As far as we can find, Sprengel is the only botanist who has spelled it correctly; most writers follow L'Heritier, and make the two-fold error of beginning with an initial *z* and not doubling the *r*.

BOTANICAL AFFINITIES.—The genus Xanthorrhiza consists of only the one species described in this article and is confined to the Southern Allegheny range. In botanical affinities it stands between the two orders Ranunculaceæ and Berberidaceæ, and while by all systematists it has always been included in the former, our belief is that it belongs to the Berberidaceæ and will finally be placed there. We would not, however, assume to make that change in this work contrary to all authorities however strong our convictions may be.

In general aspect the plant resembles some evergreen species of Berberis, especially Berberis nervosa, so closely that it cannot but be noticed at once, and the yellow color of the wood and chemical constituents are almost identical with those of all species of Berberis. No other species of Ranunculaceæ (excepting the abnormal genus Clematis, which agrees with the order in most other particulars) has a *woody* stem at all and none have the prominent constituent of the Berberidaceæ (Berberin) in such quantity.

The woody rhizome of Xanthorrhiza is so nearly like the root of Berberis repens and Berberis Aquifolium that they could be substituted in commerce.

Xanthorrhiza agrees with Berberidaceæ and differs from all other Ranunculaceæ in having definite stamens. The principal reason why Bentham and Hooker refer it to the latter seems to be that these stamens (and other parts of the flower) are five, instead of three or a multiple of three; also because they are alternate with the petals. Baillon has shown that they are often ten and in this case alternate ones are opposite the petals, a position rare among plants generally, but common in the Berberidaceæ.

The peculiar glandular petals of Xanthorrhiza are not found in other Ranunculaceæ, but are found almost identical in size and appearance in several genus of the Berberidaceæ.

Other points might be shown to prove, as we claim, that the genus Xanthorrhiza is wrongly classed.

THE MICROSCOPICAL STRUCTURE OF XANTHORRHIZA RHIZOME.—Written for this publication by Louisa Reed Stowell.—Forming the external part of the rhizome are nine or more layers of tabular, or brick-shaped cells of parenchyma, closely resembling cork.

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* Dr. Woodhouse proposed the name because, as he states, "the stem is sometimes branched, hence the name *simplicissima* is not appropriate, and the leaves do not sufficiently resemble those of Parsley to be called *Apiifolia*."

† On this subject Mr. Leggett says: The English Z is never an equivalent for the Greek ζ, and with the exception of Zanthoxylum all other botanical names beginning with ζ in Greek are spelled with an X, quite a number commencing with this same syllable *Xantho*. Lindley and the English botanists generally seem to prefer the X, but on the continent Z prevails."

"In this connection we are reminded of another point in which inaccuracy is frequent. The word is composed of two elements *xantho* and *rhiza*; now it is an invariable rule in Greek compounds that when the first part ends in a vowel and the second commences with an *r* that the *r* must be doubled. We therefore submit that the correct spelling should be Xanthorrhiza."—Wm. H. Leggett, in Bulletin of Torrey Botanical Club, 1870.

Next to this structure are found the usual oval cells of parenchyma, so closely resembling the green layer of the bark. These cells contain a few small starch grains. This structure is bright yellow in color, which deepens as it approaches the wood. The cells of the inner part of this structure are much smaller than those of the outer part.

The woody zone of the rhizome has generally eighteen clearly marked medullary rays. The prosenchymatous cells of the wood are thick-walled and firm. This structure is bright yellow in color.

The pith parenchyma, or the central part of the rhizome, is slender, and composed of thin-walled, delicate cells, containing a few small starch grains. Many times these cells have disappeared leaving an open space in the center of the rhizome.



FIG. 105.
The rhizome of Xanthorrhiza apiifolia, dried (natural size).

DESCRIPTION OF THE DRUG.—As found in commerce Xanthorrhiza consists of the woody rhizomes of the plant—in sections from four inches to a foot long. The main rhizome is about one-third of an inch thick and it sends off numerous branches, which are slender and nearly uniform in thickness, being about a sixth of an inch in diameter. These branches form the greater bulk of the commercial drug. The rhizome, when fresh, is covered with a bright yellow bark, which, on drying, becomes light brown. When dry it is brittle and easily separated from the woody portion and is wrinkled longitudinally. The woody portion of the drug is of a uniform light yellow color; it breaks with a brittle fracture and exhibits numerous medullary rays. The pith in the center of the rhizome is quite distinct, especially in the branches, occupying at least one-half their diameter. Xanthorrhiza is intensely bitter, owing to the berberine, which is its prominent constituent.

CONSTITUENTS.—Dr. Woodhouse made an examination of the drug and thought to have discovered a resin and gum, both bitter. This was correct, as far as the resin and gum are concerned, but the bitterness was due to the berberine. That Xanthorrhiza contained berberine was first announced by Mr. G. Dyson Perrins in the Pharmaceutical Journal and Transactions, May, 1862. This was indicated independently of the publication or this paper, however, for, May 3, 1862, Mr. Wm. S. Merrell, of Cincinnati, in a letter addressed to the Publishing Committee of the American Journal of Pharmacy states that "hydrastia closely resembles berberine, the alkaline base of Berberis vulgaris, and also we think that of Xanthorrhiza apiifolia."* Mr. Perrins positively demonstrated both by reactions and analysis that the yellow coloring matter of Xanthorrhiza was berberine, and he was the first who proved it.

It is a matter of record that in many (perhaps most) berberine yielding plants a colorless alkaloid accompanies berberine.

In order to determine if this is also true of Xanthorrhiza, under our direction Mr. J. Schultz investigated the subject in our laboratory. All endeavors to identify a second alkaloid were fruitless, and berberine only was obtained.

The berberine of Xanthorrhiza is more difficult to separate than that of Hydrastis canadensis, and, although hydrochlorate of Berberine is nearly insoluble in water and in alcohol, the addition of hydrochloric acid to excess, either in the alcoholic or aqueous percolate of Xanthorrhiza, fails to separate much of the berberine. Sulphuric acid, however, readily breaks the combination, and a strong excess of sulphuric acid added to the cold alcoholic percolate is followed by a precipitation of considerable mono-berberine sulphate.

Yield of Berberine.—Mr. Perrins only obtained 0.107 per cent. of nitrate of berberine, which was partly owing to the fact that nitric acid will not completely separate the alkaloid. We have obtained an average of 320 parts of mono-berberine sulphate from 27,124 parts of Xanthorrhiza rhizome, or 1.1 per cent.

PHARMACOPŒIAL HISTORY.—Xanthorrhiza became officinal in the first issue of the Pharmacopœia, as "Xanthorrhiza, or Yellow Root," the officinal, part being "Radix, the Root." The New York edition of the Pharmacopœia also recognized it, and all subseqent editions of the U. S. P. gave it a position, until discarded in 1880. This plant having never been of any importance to the medical profession and scarcely even an article of commerce, it is surprising that it should have cumbered the pages of this publication for the period of half a century.

UNOFFICINAL PREPARATIONS.—Only an infusion has been recognized, and Dunglison gives the preparations as—Xanthorrhiza, one ounce; water, one pint; dose, one and a half to three fluid ounces.

* Mr. Merrell was endeavoring to show that the yellow coloring matter of hydrastis was not berberine, and he called it *hydrastia*. This view he afterward abandoned.

MEDICAL HISTORY AND PROPERTIES.—The first reference to this plant was in the Medical Repository,* in which Dr. Woodhouse gave a record of the uses to which he put the plant. All subsequent statements have been based upon these investigations.

Prof. B. S. Barton in his collections † gave it some attention and considered it a bitter that might replace columbo and other simple bitter tonics. The "New Dispensatory," by Thatcher, 1810, accepts Xanthorrhiza as "preferable to all our native bitters," and states that Mr. John Bartram used the plant with Prussian blue to color the plumage of birds green. In the first edition of the United States Dispensatory, 1833, we find that "Xanthorrhiza possesses properties closely analogous to those of columbo, quassia, and other simple tonic bitters; and may be used for the same purposes and in the same manner." To this, nothing has since been added, and although we thus find Xanthorrhiza most favorably introduced by the leaders of medicine of the early yart of this century, and although it has been officinal in the Pharmacopœia since its first issue (1820) until discarded in 1880, it has failed to obtain a foothold. It has never been a favorite with either Botanic or Eclectic physicians and it is hardly recognized by them. In this connection we must revert to the fact that although known to Eclectics, and possessing berberine in nearly as great proportion as hydrastis, they persistently refused to use it in place of that drug, asserting that its action was not at all similar. The investigations of Professors Bartholow, Sattler, Shoemaker, and others (see Hydrastis), now show that these conclusions were rational, as at least one of the very active principles of hydrastis is entirely absent from Xanthorrhiza.

The dose of powdered Xanthorrhiza rhizome, as given by Dr. Woodhouse, was from 20 to 40 grains, and an equivalent amount of the infusion or tincture. This is still accepted.

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ADDENDA

TO

DRUGS AND MEDICINES OF NORTH AMERICA.

By J. U. and C. G. Lloyd.

Vol. I., No. 3. March, 1885.

Cimicifuga Americana.—We are anxious to obtain the fresh rhizome of this species of Cimicifuga for the purpose of microscopic study in comparison with that of Cimicifuga racemosa. Will not some of our readers, who reside where this plant is found, favor us with a root? We presume the fruit pods remain on the plant all the year, as they do in the C. racemosa, in which case it will be an easy matter to identify the plant. All our efforts last summer to obtain a root failed. We wrote to every one whom we knew in the mountainous region of Pennsylvania, and although several thought at first that they could send us a specimen, no one succeeded. If this reaches the notice of any one who can obtain a rhizome, either now or next summer, we would be glad if they will drop us a postal card.

Illicium Floridanum.—Our attention has been called by Mr. Henry C. C. Maisch to an inaccuracy in the picture of this plant published in the last "Addenda." The gynæcium is represented as composed of eight pistils. An examination of the flowers of the plant in our herbarium convinces us that less than twelve would be an unusual number. Gray and Chapman both give the number as "*six* or more."

Mullein in Dysentery.—"In Dysentery I have found Mullein to be a specific, used as follows: Boil handful of dry leaves in one pint of milk, strain, and let the patient drink freely of it. Also useful in Diarrhœa and Summer Complaint of children. I have used it for a number of years. I use it in every case of Dysentery and never have any trouble in curing them. In addition, I often advise steaming with Mullein in boiling water."—Dr. A. J. Krehbiel.

Modiola Multifida.—"The negroes of the South use this plant, as they say, "to bring the women right"—that is, with dysmennorrhœa or obstructed menstruation. They call it here *Ground Mole*, because it lies close to the ground and runs over the surface."—Dr. Chas. C. Thornton.

The plant belongs to the natural order Malvaceæ, and is related to the Cotton plant. Reasoning from analogy, we should say that the negroes have some grounds for their faith. While Malvaceous plants are mostly mucilaginous, it is of interest to learn that this relative of *Gossypium herbaceum* has been used empirically for the diseases in which Gossypium is asserted to be of value. In this connection we call attention to the fact that both plants have been introduced by Southern negroes, who certainly could not have reasoned from their relationships.

Bigelow's Medical Botany.—We wish to acknowledge the receipt of a set of "Bigelow's Medical Botany," through the kindness of Mrs. E. G. Dalton. The work is a monument of labor, and although it was issued about sixty-five years ago, nothing in the line has ever appeared since to equal it in many particulars. In looking at the amount of expense that was necessary to execute the plates, it is strange that so early in the history of medicine it would have received sufficient support to have been finished. To this work and Barton's, that appeared about the same time, is due the credit of the popular introduction of most of medicinal agents now used. It is a fact that nine-tenths of the native drugs now in common use were illustrated and figured in that work.

ADDENDA

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PENTSTEMON PALMERII.—According to Dr. A. L. Siler, the leaves of this plant, which is a western species, have quite a reputation in intermittent fever.

THE WESTERN COPTIS.—We are indebted to Thomas Howell for an interesting account of the two western species of Coptis, that will appear in the June issue of the Quarterly.

TROLLIUS LAXUS.—We present on the opposite page an engraving of Trollius laxus. It will be inserted in the June number of "Drugs and Medicines of North America," but as many botanists receive this "Addenda" who are not subscribers to the former work, we present it here for their benefit. The plant is of rather rare occurrence, being found in swamps of Central New York to New Jersey and Delaware. It resembles a large flowered Ranunculus, but in structure of fruit it is allied to Caltha and is placed in the tribe Helleboræ. Little is known regarding its medical properties, but a full botanical description will accompany the plate in the "Quarterly." Many interesting facts regarding the habits and history of the plant have been furnished us through the kindness of Prof. Peck.

VERVAIN AS A CURE FOR RHEUMATISM.—The following notes from Cameron Mann, a well-known botanist of Kansas City, are worth recording:

"The following remedy for rheumatism was recently communicated to me by a respectable lady, who had found it quite successful in her own case, and also with several of her friends. It was given her by an old negress who claimed many years ago to have been told of it by an Indian. The medicine is made by boiling the root and part of the stalk of one of the blue Vervains in vinegar for twelve hours, and then rubbing the decoction upon the afflicted parts. Which of the species was used I could not tell from the specimens shown me, as these consisted simply of root and stalk, with, fortunately, one stalk bearing the withered flowers. This latter identified the plant as a Verbena, but there being no leaves I could not tell whether it was V. angustifolia, V. hastata, V. stricta or V. bracteosa, all four being natives here. But it was one of the four. The remedy certainly has some merit, whether due to the vinegar or the vervain. But it undoubtedly helped several people suffering from inflammatory rheumatism. Thinking it might find a place in your miscellaneous notes, I send this statement."

MORUS RUBRA IN URINARY DISEASES.—The following extracts are taken from a letter from a druggist in Piqua, O.:

"We send by express to-day the bark of Mulberry Root. One of our physicians has been using it for some time in Urinary or Bladder Diseases, such as scanty Urine, Catarrh of the Bladder, and Gravel. It came into use in this locality upon the suggestion of a person who had seen it used in the East, and several of our citizens that we know had suffered for a long time, seem to have been permanently cured. It seems to have no efficacy unless it be used while green, and has only been prepared in decoction. For that reason the Doctor wants a preparation of the green root. He thinks its virtue is due to some volatile principle which is lost when the root is dry. But in preparing the decoctions I know that they have boiled it some time, which, it seems to me, would dissipate a *volatile* principle."

It is not necessary that the loss of virtue by drying a plant is altogether by evaporation. For example, the fresh corm of the Indian turnip is very acrid, the dry is almost inert, and yet we doubt if the loss of this acrid principle is by volatilization. The acrid principle of the Ranunculaceæ, the pepper of Polygonum punctatum, etc., are not lost by evaporation alone. In making a decoction it is true a temperature of somewhat more than 212° F. is employed, but it may be that the medicinal constituent of black mulberry is rather stable under these circumstances, and yet will entirely perish when exposed to the action of the air during the drying of the plant.

FLORIDA PLANTS.—We have received from Edna Pearl Lisk, a little girl who lives in Florida, nice specimens of the following plants in flower January, 1885: Pinguicula pumila, Phoradendron flavescens, Indigofera Anil, and Chaptalia tomentosa.



TROLLIUS LAXUS.

OUR HERBARIUM.

We take, we trust, a pardonable pride in giving an account of our private collection of herbarium specimens. Six years ago we made, as our first, a small exchange with Wm. L. Canby. We have since corresponded and exchanged with many botanists of this and foreign countries, and the result is a collection of such proportions that a description will not be amiss. The collection consists of about twelve thousand plants, as nearly as we can estimate. It is contained in 90 volumes, which by count average over 125 specimens each, and we have perhaps a thousand plants in the process of mounting. We consider that we have only just made a fair start, and, as the writer is yet a young man and our main ambition lies in this direction, we expect some day to have a collection invaluable for reference and study.

The plants are mounted on sheets of paper, size ten by fifteen inches, and are bound in the "Emerson Binder," This binder permits the volumes to be taken apart at any time and additions made in their proper places. The plants are arranged by Countries, or Sections, or, in case of Western plants, by Individual Collectors, and each lot is arranged in the sequence of the Natural Orders, hence enabling us to refer to any particular plant as readily as to a word in the dictionary. The volumes are labeled on the back with the country, and the genus at which it begins. The collection has the appearance of a library and requires but two book-cases, and these take up a small amount of space, considering the number of plants they contain. The same number of specimens, put away in the usual way in drawers, would require a room specially for their accommodation.

The following is a synopsis of the collection:

United States.—Eastern Section. Seventeen volumes. This represents our first four years' work, as of late years our attention has been most specially directed to foreign exchanges. It would not be easy to name all the botanists who have contributed to it, but the list would embrace a majority of our active collectors. It has always been a rule with us never to propose an exchange with a botanist except on the recommendation of some one whom we knew, and the result has been that in but very few instances have we received indifferent specimens. We call to mind the following who are largely represented in the collection: Ezra Brainerd, J. Donnell Smith, C. G. Pringle, Lester F. Ward, C. A. Gross, C. D. Fretz, F. H. Hosford, H. M. Denslow, Walter S. Deane, Chas. Mohr, H. N. Patterson, Dr. A. Gattinger, J. W. Congdon, H. F. Jaeger, P. E. Pierson, F. Blanchard, Jos. Blake, M. E. Hyams, R. I. Cratty, Alice J. Heading, G. W. Hubbard, M. B. Flint, W. P. Conant, W. W. Bailey, Dr. Howe, Wm. Crabtree, C. F. Wheeler, L. H. Bailey, Dr. Haberer. *Western Section.*—Our exchanges in Western United States have been comparatively few. The specimens were mostly obtained by exchange with the Department of Agriculture at Washington, through the kindness of W. P. Conant. California is represented by three volumes of miscellaneous collectors and two collected by Mrs. R. F. Bingham; Arizona and New Mexico by two volumes, Colorado and Kansas by one volume. There are two lots of plants that we prize very highly among the Western plants. Both are beautifully preserved, and each is tolerably complete for its section. One of these is two volumes of Washington Territory plants, collected by W. N. Suksdorf; the other, two volumes of Texas plants from J. Reverchon.

England is represented by eight volumes. Botany in England has been reduced to a very exact science, and fine points of differences between varieties and species are noted, which in this country would be entirely overlooked. Thus it requires all the letters of the alphabet to indicate the different varieties of the common species of Rosa that are described and characterized. An English exchange is apt to be disappointing to an American. The plants have a general coarse, weedy appearance, and most of them are familiar, either as weeds in this country or common plants. We miss the delicate deep woods specimens, and the showy flowers of mountainous countries. If we may be permitted to judge by our experience, the botanists of England are, as a rule, poor collectors. In fifteen or twenty exchanges we obtained but two lots that we would call good specimens. These were from Chas. Bailey and Eyre de Crespigny.

The German Empire is about as fully represented in our collection as our home flora, having sixteen volumes. In addition to being careful students, the Germans are good collectors, and the specimens are well preserved. Many hybrids are collected and labeled, especially in certain families, as Salix, Verbascum, Rubus, Cirsium, etc. Do we not have hybrids in this country, or are they not detected?

Austria and *Switzerland* have fourteen volumes in the collection. These are all fine specimens,

the flora of the Swiss and Tyrolean mountains being very rich in showy plants.

France and *Italy* comprise eight volumes, mostly from France. It embraces a fine lot of plants from the "Société Dauphinoise," which we obtained by exchange with R. Neyra. The genus Hieracium is the largest and most difficult of France, as it is of most continental Europe. It stands in the position the Aster and Solidago do in this country, only far more numerous in number of species.

Norway and *Sweden* have three volumes in the collection. The plants present the stunted appearance of cold countries, without the showy alpine flowers. A recent exchange with a Swedish botanical club, the plants of which are not yet mounted, will more than double our representation from these countries.

New Zealand has four volumes. We value these plants very highly, and have the fullest set, to our knowledge, of New Zealand plants in this country. The specimens have a singular and odd appearance, entirely different from plants with which we are familiar. Veronica is a large genus in New Zealand and comprises many shrubs. Epilobium is also one of the largest of the genera. Shrubby Senecios with thick coriaceous leaves; climbing Lycopodiums, that grow to the tops of the tallest trees; Droseras with bipartite leaves; shrubby Fuchsias, ten to thirty feet high; Rutaceous plants with one-foliate, compound leaves, are a few that impress us as among the oddest. New Zealand is preëminently the land of Ferns. There are one-eighth as many species of Ferns described as of all Flowering Plants together. We are fortunate to have secured almost a complete set of these Ferns, nicely preserved and accurately named by Prof. Geo. M. Thomson, author of the recently published "Hand-book of New Zealand Ferns."

Australia has six volumes in the collection. Two of these, which are mostly from the Melbourne Botanical Gardens and communicated by W. R. Guilfoyle, are well preserved; the other four volumes are as poor excuses for specimens as we have ever seen offered. The late Baron Von Mueller was one of our Australian correspondents, and we have a large number of the difficult Eucalyptus genus named and labeled by him. We prize them highly on account of the authority, though it is greatly to be regretted that they are such indifferent specimens.

Since we began the publication of "The Drugs and Medicines of North America" our time has been so taken up that we have had no leisure to devote to botanical exchanges, but we now have the publication running smoothly and expect to engage actively again in our favorite pursuit. We have on hand a large stock of duplicates, numbering somewhere from five to ten thousand. These are all labeled with printed labels. We have recently printed a check list of the most common plants around Cincinnati, which will greatly aid us. We shall be glad to hear from any collector in any locality who desires exchange and who collects first-class specimens.

THE USE OF GINSENG IN CHINA.—The following letter from Mr. Kwong Ki Chin, a highly educated gentleman, and former professor of the Chinese Language in Yale College, is of special interest on account of its reliability. It was written to us in 1881, in reply to our inquiries on the subject:

"The Chinese physicians make frequent use of ginseng root, particularly in Canton province, but do not regard it as a panacea. The fact and occasions of its use are quite familiar to me from my having studied and practiced medicine for some time in China.

The Chinese ginseng grows in but few localities, is very scarce, and commands a high price—the best commanding a hundred times its weight in silver, and from that down to half its weight, according to the locality where it is grown. The native article has different and more tonic properties than the imported. We think it strengthens the breath, and sometimes saves life. The emperor and his friends consume nearly all the high-priced native product.

Doubtless the medicinal value of the plant is exaggerated, and the popular belief in its virtues heightened, by the example of the imperial family and wealthy persons in using it.

That imported from America is considered to have cooling properties and to be especially useful in yellow fever and inflammation of the bladder. It is also given for tenderness and enlargement of the liver, and whenever the urine is high colored. It is also considered to promote the discharge of urine. Sometimes persons who have taken liquor to excess, eat a little of it with benefit to relieve the tipsy feeling. We regard it as opposite in properties to ginger root and cinnamon.

It is not used for incense.

You are at liberty to mention my name in connection with the statement, if you desire."

THE PAMPHLET LITERATURE OF AMERICAN BOTANY.—The numerous lists that have been published from time to time of local or State catalogues of plants are a great aid to us in studying the distribution of plants that we desire to map in our "Quarterly." We are anxious to obtain as complete a set of these lists as possible, and we append a statement of those that we have, arranged by States. To any botanist who will mail us a list or catalogue not mentioned in our statement, we will make an *adequate return* by means of our "Quarterly." Local lists or published lists of plants offered for exchange will also be of value:

General.—Catalogue of Forest Trees of North America; Chas. S. Sargent, 1880.—Ferns of the United States; D. C. Eaton, 1880.—Catalogue of Plants of N. E. United States; A. H. Curtiss, 1873.—Forests and Trees of North America; J. G. Cooper, 1860.—Grasses of the United States; George Vasey, 1883.—North American Carices; L. H. Bailey, Jr., 1884.

Southern States.—Native and Naturalized Plants of South Carolina; H. W. Ravenel, 1883.—Catalogue of Plants of North Carolina; Rev. M. A. Curtis, 1867.—Flora of Wilmington, N. C.; M. A. Curtis, 1834.—Native Resources of Alabama, Forest Products; Chas. Mohr, 1883.—Plants of Alabama; Charles Mohr and Eugene A. Smith, (no date).—Flora of Georgia (author not known); from White's Statistics of Georgia, 1849.—Notes on the Flora of Tennessee; A. Gattinger, 1884.

Western States.—Plants of Southern California; S. B. and W. F. Parish, 1882.—Catalogue of Flora of Oregon, Washington and Idaho; Thomas Howell, (no date).—Flora of Southern and Lower California; S. R. Orcutt, 1885.—Medicinal Flora of Kansas; Robert J. Brown, 1881.—Catalogue of the Phænogamous Plants of Iowa; J. C. Arthur, 1876.—Flora of Jackson County, Mo., by Frank Bush, 1882; also first supplement to same, by Frank Bush and Cameron Mann, 1885.

Eastern States.—Portland Catalogue of Maine Plants; Portland Society of Natural History, 1868.—Flora of Vermont; George H. Perkins, 1882.—Plants of Malden and Medford, Mass., by Middlesex Scientific Field Club, 1881.—Catalogue of Plants near Yale College, by Berzelius Society, 1878;—Catalogue of Plants of New Jersey; O. R. Willis, 1877.—Catalogue of Plants of Buffalo; David F. Day, 1883.—Catalogue of Plants of New York; J. Torrey, (no date).—Catalogue of Plants of Dutchess Co., N. Y.; A. Winchell, 1851.—List of Plants of Fishkill, N. Y.; W. A. Stearns, 1880.—Catalogue of Plants of Elgin Botanic Garden; D Hosack, 1811.—Catalogue of Plants of New York; Jacob Green, 1814.—Flora of Lancaster County, Pa.; James Galen, 1884.—Plants Appearing in Flower at Philadelphia; James Darrach, 1853.—List of rare plants near Eaton, Pa.; L. De Schweinitz, 1824.—Guide to the Flora of Washington; Lester F. Ward, 1881.—Flora Columbiana; J. Brereton, 1831.

Central States.—Plants of Wisconsin, by G. D. Swezey, 1877.—Flora of Michigan; N. H. Winchell, 1860.—Catalogue of Plants of Michigan; Charles F. Wheeler and Erwin F. Smith, 1881.—Catalogue of Flowering Plants of Southern Peninsula of Michigan; N. Coleman, 1873.—Medicinal Plants of Michigan; A. B. Lyons, 1877.—Notes on the Native Trees of the Lower Wabash; Robert Ridgeway, 1882, with additions and corrections.—Flora of Jefferson County, Indiana; John M. Coulter, 1874.—Flora of Lower Wabash Valley; J. Schneck, M. D., 1875.—Plants of Indiana; C. R. Barnes, 1881.—Catalogue of Plants of Jefferson County, Ind.; Chas. R. Barnes, 1874.—Flora of Central Eastern Indiana; A. J. Phinney, 1882.—Catalogue of a collection of plants made in Illinois and Missouri by Charles A. Geyer; George Engelmann, 1844.—Flora of Miami Valley, Ohio; A. P. Morgan, 1878.—Catalogue of Flowering Plants of Cincinnati; Jos. F. James, 1879; additions and corrections to same, Davis L. James, 1881.—Report on a Belt of Kentucky Timbers; L. H. De Friese, 1879.—Report on the botany of Barren and Edmonson Counties, Ky.; John Hassy, 1875.

Canada.—Synopsis of the Flora of the Valley of St. Lawrence and the Great Lakes; John Macoun and John Gibson, 1877. (Note.—Our copy is incomplete, extending only to the Umbelliferæ. We would be glad of the remainder.) List of New Brunswick Plants; James Fowler, 1880. Additions to List of New Brunswick Plants; G. N. Hay, 1882, 1883 and 1884.—Botany of the Upper St. John, by G. N. Hay, 1883.—Flora Ottawaensis; James Fletcher, 1879-84.—Catalogue of Canadian Plants, Part 1, Polypetalæ; John Macoun, 1883.

From our friend, Walter Deane, of Cambridge, we learn that Prof. Sereno Watson is now spending a few months botanizing in Guatemala. Dr. Gray is in Southern California.

To Botanists.—In our "Quarterly" we prepare maps illustrating the geographical distribution of the plants under consideration. Thus far, maps of Anemone acutiloba, Anemone Hepatica, and Hydrastis canadensis, have been issued. These maps are acknowledged to be of great botanical interest, and to make them complete we would like the aid of every botanist in the country. A very large number have already favored us, but there are still many who have made no report. It will take but a moment's time to drop us a postal card and answer the following questions regarding the plants on which we are now at work, and it will be a kindness to us as well as a valuable record to the world. *Do the following plants grow in your locality, and how abundantly:*

1st. Coptis trifolia.
2d. Xanthorrhiza apiifolia.
3d. Aconitum uncinatum.
4th. Actæa alba.
5th. Actæa rubra var spicata.
6th. Cimicifuga Americana.
7th. Cimicifuga racemosa.

To every one who has replied in the past we mail a complete set of this "addenda" here with, and will send future numbers until Vol. I. of "Drugs and Medicines" is completed. We make the same offer to those who answer now. Please reply at once.

Southern Plants.—We present as a supplement a list of plants collected by A. W. Latimer near Lumpkin, in South-eastern Georgia. So little is recorded about the plants of the Southern States that this list, though the result of only two collecting trips, necessarily but a mere fragment, and is of botanical interest. We hope to be able to add to it from the result of this year's collection by Mr. Latimer. The plants are beautifully collected, and we have preserved them as a special volume in our herbarium.

Botanical Books.—Through the kindness of C. W. Merrill, Librarian of the Public Library, Cincinnati, and of Walter Deane, of Cambridge, and Prof. Chas. Rice, of New York, we have access to most works on American botany. We have a large library of our own and are desirous of adding to it, and will be glad to purchase any of the following books, or for any one of them we will exchange a two years' subscription to our "Quarterly." Before sending any book, however, drop us a postal card, and if we have not previously secured it we will advise you: Eaton's Manual, 1st edition; same, 2d ed.; same, 3d ed.; same, 7th ed.; Elliott's Sketch of South Corolina and Georgia; Gray's Manual, 2d ed.; same, 3d ed.; same, 4th ed.; Muhlenberg Catalogue, 1st ed.; same, 2d ed.; Rafinesque Florula ludoviciana; Rafinesque, Flora of Louisiana; Rafinesque, New Flora and Botany of N. A; Torrey & Gray, Flora, 1st vol.; same, 2d vol.; Torrey, Flora of Northern and Middle Sections of U. S.; Wood, Class-book, 2d ed.; same, 3d ed.; same, 4th ed.; Darlington, Flora Cestrica, 1st ed.; same, 2d ed.; Bigelow, Florula Bostoniensis, 2d ed.; same, 3d ed.; Barton, Flora virginica; Barton, Floræ Philadelphicæ; Barton, Compendium Flora Philadelphia, 2d ed.

Sô-Mokou-Zoussets.—This is the title of the most recent addition to our botanical library. It reached us with the regards of our friend, Dr. Charles Rice, of New York, who spent eighteen months in Japan. Hence, aside from the peculiar intrinsic value of this rare production, it is dear to us as a present from our talented friend, and we prize it above all other members of our library. It is a complete work (20 volumes) on the herbaceous plants of Japan, by a native writer, Iinouma Yokoussai; written in the Japanese characters and printed and bound after the peculiar manner of Japanese works. The paper and style of binding are a curiosity in themselves. Every plant is illustrated with a page drawing, and these are well executed and remarkably true to nature. Each plant is labeled with the Latin name, although without this aid many plants, common to Japan and America, would be recognized at once. In the Ranunculaceæ, for instance, are Aconitum uncinatum, Anemone Hepatica, Coptis trifolia, Trautvetteria palmata and Caltha palustris. The work was originally issued in 1856 by Iinouma Yokoussai, whose portrait adorns the front (or back, as we would call it) of the first volume of the work. The edition that we have was printed at Tokio in 1874, and is a revision by Tanaka Yosiwo. The Latin names are edited by Savatier, an authority and recent writer on Japan plants.

Back Numbers.—At the request of quite a number of subscribers to the "Addenda," we reprint the previous issues on paper uniform with that used in the "Drugs and Medicines of North America." To each subscriber we mail herewith a complete set to date. To those who are not subscribers we will send the back numbers and also the present year on receipt of 25 cents.

THIS ISSUE.—It will be noticed that this issue of the "Addenda" is almost wholly botanical. It will be sent to every botanist in the United States, and on this account was gotten up specially for the purpose. Our medical and pharmaceutical subscribers need not he alarmed, however; we will make up for it to them in future issues.

BOOKS SPECIALLY DESIRED.—A very complete set of book references to each plant is an important feature of the "Quarterly," and already commands special commendation from Europe and America. We need access to the following books, however, to make our chain complete. If any of our readers have either of the works, it will be a great favor indeed to us if they will inform us: Barton, Compendium Flora Philadelphia, 2d edition; Barton, Flora Virginica; Muhlenberg, Catalogue, 1st edition; Gray, Manual, 3d edition; Eaton, Manual, 1st edition; same, 7th edition.

OUR QUARTERLY.—We have made no effort to obtain subscribers to our "Quarterly" from the purely botanical readers for fear that, as it is primarily intended for physicians and pharmacists, there might be too much matter regarding the medical and chemical properties of plants that might necessarily be of little interest to the botanist. We are pleased to know, however, that we number a large number of prominent botanists on our subscription list, and we are more than pleased with the reception they give our articles. The following is the botanical portion of the work for 1884. Each article contains a full botanical history, geographical distribution, generic and specific description, botanical analysis, common names, allied species, etc., etc., also illustrations:

Clematis virginiana; full plate of the plant. Cut of Clematis crispa, figure of stem of Clematis virginiana, microscopic structure of stem.

Thalictrum dioicum; cut of leaf.

Thalictrum anemonoides; full plate of the plant, cut of tuberous roots, cut of fruit-head.

Anemone nemorosa; cut of plant, fruit-head of Anemone dichotoma, fruit-head of Anemone virginiana.

Anemone patens var Nuttalliana; full plate of plant, in flower and fruit, cut of achene.

Anemone acutiloba; full plate of plant, cut of flower, stamen petal and achene (magnified), cut of fruit, cut showing extreme form of leaves, cut of abnormally developed flower, map showing distribution of Anemone Hepatica and Anemone acutiloba, cut of leaf of Anemone acutiloba, cut of leaf of Anemone Hepatica, cut of leaf of Anemone Hepatica from Europe.

Ranunculus bulbosus; full plate of plant, cut of petal and section of leaf-stalk, cut of leaf of Ranunculus bulbosus, leaf of Ranunculus acris, leaf of Ranunculus repens, flower of Ranunculus sceleratus (magnified), cut of Ranunculus abortivus.

Caltha palustris; cut of flowering top of plant, cut of fruit.

Hydrastis canadensis; full plate of plant, cut of flower bud, cut of fruit and mature leaf, map showing geographical distribution, cut of dried rhizome, microscopic structure of rhizome.

The present year will probably complete the Ranunculaceæ, and will include the genera Coptis, Aquilegia, Delphinium, Trollius, Xanthorrhiza, Aconitum, Actæa and Cimicifuga.

ILLICIUM PARVIFLORUM.—Who can give us a habitat for this rare southern shrub? We have inquired by personal letter of every botanist in the South, who we think would be likely to have collected the plant, and can get no definite information. If any one can give us a habitat, either from a published record, herbarium specimen, or personal knowledge, we would be glad of the information.

ISANTHUS ("Flux Weed").—"In your 'Addenda' to the 'Drugs and Medicines of North America," you mention the fact that a large number of plants are called 'Flux weed.' I have observed the same thing, in the numerous letters enclosing plants for identification. The last instance was in a letter from a physician, Dr. Needham, of New Albany, Indiana, who enclosed a specimen of what proved to be *Isanthus cæruleus*, "False Pennyroyal," (Wood and Gray). In appearance it resembles Hedeoma, but differs in that it has no odor, and the leaves and stems are viscid.

Dr. N. writes me that it enjoys a wide reputation among the country people in the treatment of flux (dysentery). Owing to its successful use, several physicians adopted it and report good results. It is asserted to have cured some desperate cases. It is usually given in wineglassful doses of an infusion of indefinite strength. The plant has but little strength, and the tincture is dark greenish-black, and, but for the alcohol, nearly tasteless.

The name "Flux weed" is applied to Euphorbia hypericifolia, which certainly has curative powers in dysentery."—E. M. HALE, M. D.

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An exhaustive pamphlet on Bovine Virus, its production and preparation, with a comparison of the respective merits of Bovine and Humanized Lymph, containing, also, a description of our Vaccine Farm, will be sent by mail to those who desire it.

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Tongaline is a combination of Tonga with powerful salicylates, whereby the remedial properties of the Tonga are secured and increased. **Each fluid drachm of Tongaline represents: Tonga, 30 grains; Extractum Cimicifugæ Racemosæ, 2 grains; Sodium Salicylate, 10 grs.; Pilocarpin Salicylate, 1-100 grain; Colchicin Salicylate, 1-500 grain.**

It is taken internally and intended to reach the cause of the complaint, not merely to allay the symptoms. Contains no opium in any form whatsoever. Is attended with no injurious nor unpleasant reactionary effects.

DOSE: Teaspoonful. In acute cases every hour until pain ceases, then discontinue. In chronic forms, four to six times per day at regular intervals. To prevent recurrence, every two hours.

St. Paul, Minn., Nov. 16, 1883.
I am prescribing Tongaline with satisfactory results. For the indefinite aches and pains of nervous patients it is superior to any other anodyne. For nervous headache or muscular rheumatism it is almost a specific.
PARK RITCHIE, M.D.

Cleveland, Ohio, July 30, 1883.
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Plainfield, N. J., March 11, 1884.
Have used Tongaline constantly for some months both in private and hospital practice, and found it all I could have desired.
C. M. FIELD, M.D.

St. Louis, July 20, 1883.
I have found Tongaline a useful combination in rheumatic neuralgia.
C. H. HUGHES, M.D.

Louisville, Ky., June 12, 1883.
I have used Tongaline during the past few weeks in neuralgic affections, many of them in a severe form, with the most gratifying results, and these results have been quite uniform.
T. S. BELL, M.D.

Cincinnati, March 11, 1884.
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O. D. NORTON, M.D.

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Prof. ATFIELD, F.R.S., F.I.C., F.C.S., etc., Oct. 8, 1883.—"I now find that "Maltine" contains from three to five times as much diastase as any Extract of Malt in the market."

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It is also due the reader that an acquaintance should be made with the names of those upon whom we have called as specialists, and we shall pursue that course in the future.

Dr. Charles Rice, of New York City, has kindly read the entire proof of the work, and many valuable changes were made at his suggestion.

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The material from which the engravings were drawn was furnished, Hepatica by Davis L. James, and Ranunculus by A. B. Clute.

Prof. E. M. Hale contributed the paper on Homœopathic use of Hepatica.

Mrs. Louisa Reed Stowell described the microscopic structure of Hepatica.

Prof. Virgil Coblentz, Springfield, Ohio, verified one work on Anemonin.

For information regarding the Commercial History of the Drugs, we are indebted to the following foremost houses of America:

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All the plates of this number, and most of the figures, were specially drawn for this work by Mr. J. A. Knapp. Fig. 22 was taken from Baillon's History of Plants, and Fig. 13 from "The Lens."

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Figures 25 and 26 are taken from Gray's Genera of Plants of the United States. The rest are original.

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ACKNOWLEDGMENTS.

It will be observed that this number of our work is exclusively confined to the study of the products of Hydrastis canadensis. Anticipating the extent and importance of this section, many months ago, we associated with ourselves a number of scientists, who entered into special lines of work with an interest that we feel will be highly appreciated. To their zeal and energy may be ascribed the completeness of this section, for our own unaided efforts must have left many gaps that would have appeared conspicuous.

While we have aimed to credit each of these gentleman in the body of our work, we can not neglect to take this method of extending our thanks. Prof. Virgil Coblentz, Springfield, Ohio, went over several tedious analyses of berberine and its salts, most especially the phosphate of berberine.

Prof. J. F. Eykman, Tokio, Japan, is engaged upon the study of Hydrastine, and although his paper did not reach us in time for this publication, it will doubtless appear elsewhere, at some future day, to enrich our literature.

Dr. T. L. A. Greve was among the first in our country to study the alkaloids of Hydrastis, and produce them for commerce. We are indebted to him for many contributions to our knowledge of these commercial products, and we revert with pleasure to the conversations we have had on these subjects.

Mr. William J. Huck contributed the micro-drawings of berberine and its salts, that appear in this number, and they are most accurately made.

Prof. F. B. Power, of the University of Wisconsin, was interested in both berberine and hydrastine, but particularly the latter. His series of patient investigations, contributed both to the interest of the American Pharmaceutical Association, 1884, and our work, are highly appreciated, and it was through his instrumentality that the services of Mr. Huck were obtained.

Prof. A. B. Prescott, of the University of Michigan, devoted considerable attention to the third alkaloid of Hydrastis, and without the views of Prof. Prescott, our paper on this subject would have been quite imperfect. We are gratified to have been able to present a summing up of his review.

Prof. E. Schaffer, of Louisville, Ky., some years ago, carried on a series of investigations, to which we refer. It is to be hoped that they will yet be completed and published in full.

A number of prominent medical men are engaged in special investigations, and are preparing papers on the medical properties of Hydrastis and its alkaloids, for next number. Due acknowledgement will be given next issue.

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TO OUR SUBSCRIBERS.

With the present issue we complete the first year of our Quarterly. That the work has met with success far beyond our most sanguine expectations we can only attribute to the liberality and intelligence of the great Pharmaceutical, Medical and Botanical professions. To each subscriber who has aided us by his patronage, and to the many who are constantly encouraging us with words of approval and endorsement, we return our sincere thanks.

For the coming year we can promise no more than we have done in the past: we shall spare no expense to make the work complete in illustrations and contents as it proceeds.

We have requests from a number of subscribers to issue it more frequently with an increased subscription price. It would be very gratifying to us if we were enabled to progress more rapidly, but we fear that should we make the attempt it would be at the expense of quality or completeness of the work, and we are unwilling to do it. Should we be able to accumulate copy, we will increase the number of pages, as we have done in the present number, without extra charge.

FOR THE PHARMACIST.—All the departments of the work relating to this profession will be kept at its present standard. The large number of pharmacists who have subscribed to the work is a sufficient guarantee that it is appreciated. We invite your attention to the list (published on the 4th page of this pamphlet) of the members of the American Pharmaceutical Association who have subscribed. That the work meets with favor from such a representative part of the profession is a matter of especial pride to us.

TO THE PHYSICIAN.—We can promise even more next year than we have given in the past. It was unfortunate that the plants we have, by their botanical relationship, been compelled to consider thus far were mostly unimportant from a therapeutical point of view, and little could be said regarding their medical properties. The plants to be considered next year will comprise some of the most important of the materia medica, and the therapeutical properties will be written by the leading authorities and specialists in each school of medicine. In the next issue, Hydrastis will be as exhaustively considered from a medical standpoint as it has been in the present from a chemical and therapeutical point of view. Special papers have been prepared on the subject by eminent authors.

TO THE BOTANIST.—And we are gratified to know we have among our readers a large number who have subscribed merely for the botanical features of the work, we promise that this department shall not suffer by comparison with the publication during the past year.

1885 will complete Volume I. With the last issue we shall send a complete index, and make arrangements whereby our subscribers can have the volume bound, cheaply and elegantly.

The first number of 1885 will be dated January and issued early in the year. Please forward us your renewal at once, so there will be no delay in receiving the first issue; but before renewing read what we have to say on the following pages, as very likely it will be to your advantage.

Respectfully, J. U. & C. G. LLOYD.

SECURE NEW SUBSCRIBERS TO THE WORK.

We aim to make it to the interest of our patrons in renewing to send one or more new subscribers to the work. You are acquainted with the merits of the publication, and we trust can freely recommend it to your professional friends. A word from you as a reader will have more effect toward inducing others to subscribe than any representation that we can make. A druggist in Cincinnati has brought the work to the attention of the physicians who patronize his store, and the result has been a dozen subscriptions. Others have done as well, and most persons can obtain one or more subscribers.

Considerable expense last year was necessitated by the introduction of the work to our patrons. If our subscribers will save us this expense by each securing one or more *new* subscribers, we promise something handsome in return in the size of the work.

As a further inducement, we make following proposition: We expect each new subscriber will desire the back numbers for 1884, as his work would otherwise be incomplete. We will renew your subscription for 1885 and send the work to a *new* subscriber for 1884 and 1885 for **$2.25,** the regular subscription price for both being **$3.00.** This makes your subscription for 1885 cost you only TWENTY-FIVE CENTS.

For every additional subscription for the two years, 1884 and 1885, we will furnish to you at $1.50 net. You can either reap the benefits (as they are really due you), or can give the subscriber a part, as you may see proper. The journals we mail to new subscribers will not contain this proposition, as we wish to recognize the assistance of those who encouraged us at the beginning.

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Volume I.] MARCH, 1885. [No. 5.

DRUGS AND MEDICINES OF NORTH AMERICA

A QUARTERLY

Devoted to the Historical and Scientific Discussion of the Botany, Pharmacy, Chemistry and Therapeutics

OF THE

MEDICINAL PLANTS OF NORTH AMERICA

THEIR CONSTITUENTS, PRODUCTS AND SOPHISTICATIONS

J. U. LLOYD,
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ACKNOWLEDGMENTS.

The specimens of powdered hydrastis examined and recorded on pages 146 and 147, were kindly furnished by Prof. J. B. Bond, Little Rock, Ark.; Mr. J. W. Colcord, Lynn, Mass.; Prof. Lewis C. Diehl, Louisville, Ky.; Mr. E. Eliel, North Bend, Ind.; Mr. R. M. Hatton, Zanesville, O.; Mr. Geo. W. Kennedy, Potteville, Pa.; Mr. John Nippgen, Chillicothe, O.; Mr. Alonzo Robbins, Philadelphia, Pa., and Mr. Geo. W. Sloan, Indianapolis, Ind. We thank these gentlemen for their courtesy, whereby we were enabled to present so fair an average of the hydrastis of commerce.

To Mr Leslie Soule, Mr. E. S. Ely and Mr. W. M. Schmitt we acknowledge our indebtedness for assistance in the examination of hydrastis in our laboratory, as recorded in the following pages.

The papers from the representatives of the various bodies of practitioners will particularly interest physicians, and we highly appreciate the honor extended this publication by the authors. The subjects are as follows:

Page.

"The Physiological Effects and Therapeutical Uses of Hydrastis," by Prof. Roberts Bartholow, M. D., LL. D., - - - - - - - - - - - - - - - - 156

"The Homœopathic Uses of Hydrastis," by Prof. E. M. Hale, M. D., - - - - - 161

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ACKNOWLEDGMENTS.

Our thanks are extended to the following gentlemen for special contributions on the uses of hydrastine and berberine in medicine.

Dr. John V. Shoemaker, Hydrastis and Hydrastine in Diseases of the Skin, pp. 177-180

Dr. F. W. Langdon, Action of Hydrastine Hydrochlorate on the Genito-Urinary Mucous Membranes, pp. 180-181

Dr. J. A. Jeancon, The Physiological Action and Therapeutic Uses of Berberine, pp. 207-209

To Mrs. Louisa Reed Stowell we are indebted for the elaborate Microscopic Examination of Coptis and the Micro-Illustrations, pp. 198-204

We are indebted to the following botanists for aid in the botanical section, in addition to many botanists who have been previously acknowledged as having helped us with information regarding the distribution of plants:

Walter Deane has supplied us with many missing references to Hydrastis and other information.

Dr. Joseph V. Haberer furnished the specimen from which the drawing of Trillium laxus was made.

Chas. H. Peck read the botanical portion of the articles on Trillium and Coptis, and made many valuable additions to the text.

Dr. Chas. Rice has given us some notes on the derivation of French words (see note p. 188).

The Rev. Thos. Morong, Prof. J. Macoun, Thomas Howell and A. O. Ingalls supplied the specimens and material from which our cuts of the western species of Coptis were made.

R. L. Hunkerson sent us fresh Coptis trifolia for our drawing, and also the fresh rhizomes from which Mrs. Stowell prepared her excellent article on the microscopic structure.

A. O. Ingalls, who has devoted much study to the distribution of western plants, furnished the synopsis of the western distribution of Coptis species (see p. 97).

Mr. A. O. Ingalls and Thomas Howell have each given us an exhaustive account of the habits, etc., of the western species of Coptis based on personal observations.

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ACKNOWLEDGMENTS.

For aid and specimens in preparing this number, our thanks are extended to the following gentlemen:

Wm. O. Cusick has given us some interesting notes on the Western Delphinium.

A. L. Siler furnished the fresh root of Aconitum Fischeri, and Thos. Howell and W. N. Suksdorf the specimens of flowering plant from which our drawings were made.

Dr. Chas. Rice has helped us out with our Etymological inquiries.

Chas. Bailey, F. L. S., has given us some most valuable information regarding the original specimens of Aconite in the European Herbariums, which we regret was received too late to be included in the work.

The clinical investigation of Aconitum uncinatum was performed by Dr. W. E. Hallowell, of Randal's Island Hospital, N. Y.

The interesting lines of physiological investigation with Aconitum uncinatum and Aconitum Fischeri, were made by Prof. Roberts Bartholow, of the University of Pennsylvania.

To Prof. F. B. Power, of the University of Wisconsin, and Prof. Virgil Coblentz, of the Cincinnati College of Pharmacy, is due the chemical investigation of Aconitum uncinatum and Aconitum Fischeri.

Walter Dean has favored us with the fresh pedicels of the Actæas, and Mrs. L. R. Stowell has furnished the result of her investigation of their microscopic structures.

A few of the small figures were copied from Prof. Gray's "Genera" and Baillon's "History of Plants," but the most of the small cuts and all the full-page engravings are original.

NOTICE REGARDING DELAY.

The plan of the work, making it necessary to complete each subject as the work proceeds, has caused some delay in the issue of this number, waiting the result of the physiological action of Aconitum uncinatum and Aconitum Fischeri. There will be no delay with next issue.

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ACKNOWLEDGMENTS.

For the exhaustive botanical paper on Cimicifuga in this issue we are largely indebted to the active co-operation of several botanists.

The specimen from which the illustration is drawn was furnished by Davis L. James.

Walter Deane favors us with many notes from the library of Harvard University.

Mr. Albert Commons sent us an interesting form of the plant described on page 250.

The many botanists who have contributed the geographical information have been previously mentioned.

To J. Donnell Smith we are obliged for authentic rhizomes of Cimicifuga americana, an interesting and very rare plant.

Kate F. Kurtz sent us a supply of the rhizomes of a very robust form of Cimicifuga racemosa, found in the mountains of Pennsylvania.

We acknowledge our thanks for the following special articles written for the work:

The Microscopical Structure of Cimicifuga Racemosa, by Louisa Reid Stowell; page 258.

The Alleged "Crystallizable Neutral Principle" of Cimicifuga Racemosa, by Prof. Robt. R. Warder; page 264.

Examination of Cimicifugin for the Detection of a Crystalline Substance, by Prof. Virgil Coblentz; page 269.

NOTICE REGARDING BINDING.

We find that we were not able to complete the Ranunculaceæ, or Volume I., of the work with the present issue, but it will be finished with the next issue. In order that all who have subscribed to the work for 1884 and 1885 may have Volume I. complete, we shall mail No. 9 to all. It will be dated March, 1886, but will be issued as soon as possible—some time in January.

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ACKNOWLEDGMENTS.

The present number consists of several articles on the medical action of Cimicifuga racemosa, and a consideration of the plant Xanthorrhiza apiifolia.

For the exhaustive papers on Cimicifuga we are indebted to the following gentlemen:

Prof. Eric E. Sattler M. D., of the Miami Medical College of Cincinnati, representing the Regular School of Medicine.

Prof. E. M. Hale M. D., of the Chicago Homœopathic College, representing the Homœopathic School of Medicine.

Prof. John King M. D., of the Eclectic Medical Institute of Cincinnati, representing the Eclectic School of Medicine.

For a full account of the habits and growth of Xanthorrhiza apiifolia, we desire to acknowledge our obligations to Thos. M. Peters, of Moulton, Ala., and for a flowering top of the same plant to Dr. I. J. M. Goss. Thanks are due to Mr. Z. Z. Schultz, who spent considerable time in our laboratory searching for a white alkaloid in the rhizome of this plant.

NOTICE.

The present issue, No. 9, Vol. I., while not due till March, is issued now in order to complete the volume. The next issue, No. 1, Vol. II., will not be mailed until the regular time.

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The present issue completes Vol. I. of the work. We send herewith index, preface and new title-page, to replace the one printed with No. 1 of the work.

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