# COPTIS OCCIDENTALIS SALISBURY (FAM. RANUNCULACEÆ) WESTERN COPTIS. WESTERN GOLDTHREAD.[1]

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## INTRODUCTION.

Since large quantities of *Coptis occidentalis* are found growing in the mountains of northwestern Montana and northeastern Idaho, this investigation was made to determine the comparative medicinal value of this with that of the official *Coptis trifolia* found chiefly in eastern United States.

## REVIEW OF LITERATURE.

The first description of the plant, which was later to bear the genus name *Coptis*, was by Halenius (probably a student of Linnæus), who placed it with the Hellebores and named it *Hellebore* or *Helleborus Trifolius* (4). It was so-called by subsequent botanists until it was separated from the Hellebore family by Salisbury, who described the plant in 1807 and created the genus *Coptis* and named it *Coptis trifolia* (4).

The species name, according to Latin nomenclature, should have been *trifoliata*, but according to present accepted procedures, the first name stands as the species name. However, in some cases as in "Flora of the Rocky Mountains and Adjacent Plains" (3) the species name *trifoliata* is still used.

The genus name *Coptis* is taken from the Greek word *Kopo*, which means "to cut," from the cut or laciniated leaves of the hardy perennial plants of the Northern Hemisphere (1). According to the Index Kewensis, in the northern hemisphere this genus at present is composed of at least ten different species. Foreign species given in "Index Kewensis" are: *anemonæfolia*, *brachypetalæ*, *orientalis*, *quinquefolia*, *japonica* and *trifoliata* (19): C. *quinquefolia* **var.** *trifoliata*, *teeta* of the *Himalayas*, *chinensis* of China, *ospriocarpa* of India, and *marii* of Formosa.

Of the North American species, Index Kewensis had, up to 1925, recognized only *trifolia*, *occidentalis*, *venosa* and *asplenifolia*.

Following the description of trifolia in 1807, by Salisbury, a new species (*C. occidentalis*) was described by Nuttall in 1838, which for some time represented the plants found growing in the northwest.

Nuttall also split the genus *Coptis*, into Coptis and *Chrysocoptis*, on the basis of one flowered and ternately divided leaves for *C. trifolia* and 2–4 flowered and pinnately divided leaves for *C. occidentalis*, as representing the new genus *Chrysocoptis*. This latter genus has not been accepted by Index Kewensis as such, but is accepted as a synonym for *Coptis occidentalis*.

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AUTHOR'S NOTE: More work is being done upon the plants growing in Montana and gathered in various locations and at various altitudes as well as at different times of the year, the results to be published later in an additional paper.

Nuttall further divided the species of the west into *C. occidentalis* and *C. laciniata*, on the basis of the size of the leaflets, their lobes and incisions as described by Charles V. Piper in "Flora of Washington," 1906, page 276.

The species *Coptis trifolia* is the only one which has ever been official in either the United States Pharmacopœia or the National Formulary, and is at present official in the National Formulary V under the name Coptis; Synonym, Goldthread; Botanical name, *Coptis trifolia;* Family, *Ranunculaceæ* (13). The entire plant is official (and consists usually of a nearly equal mixture of rhizomes and pressed leaves) (6).

The habit, range and habitat of *C. trifolia* is given as follows: A low perennial, growing in moist woods and swamps of northeastern United States and Canada, extending westward to Alaska (6), woods and swamps of northeastern North America, south to Maryland; mountains of North Carolina and Tennessee, and northeast Iowa (5); Northern United States and Canada, in dark shady, moist woods (8); in morasses of Canada and Siberia, Lapland and Kamchatka (4); damp mossy woods and bogs, Newfoundland to Minnesota, British Columbia and to the Alleghanies in North Carolina (7); woods and bogs of Greenland, Maryland, Minnesota, British Columbia, Alaska and Eurasia (3).

Fig. 1.—*Coptis occidentalis.* Flowering plant. Note three flowers. Collected at Noxon, Montana, May 1931.

BOTANICAL DESCRIPTION AND HABITAT.

Descriptions and ranges of *Coptis* species, said to be growing in the Northwest, are as follows (12):

Herbs perennials, low, glabrous; root stalks creeping. Leaves ternately compound. Flowers white, solitary or few, on naked scapes. Sepals 5–7, petal-like, deciduous, white or greenish. Petals 5–6, small, linear, cucullate. Stamens 10–25; follicles, 3–12. (Gk., *Kopto* to cut; from the divided leaves.)

A. Leaflets obscurely 3-lobed; sepals oval or oblong; obtuse petals enlarged at the summit. West of the Cascade Mountains and east of the Cascade Mountains.

AA. Leaflets rather deeply lobed or segmented; sepals linear or ligulate, attenuate; petals enlarged near the middle.

B. Leaves ternate.

C. All three leaflets long, petioluled leaf divisions obtuse, obtusely dentate; seed oblong. In the Cascades. East of the Cascades. (See Fig. 1. *Coptis occidentalis.*)

CC. Middle leaflet long-petioled, lateral short, petioluled leaf divisions acute, acutely dentate; seed oval. West of the Cascades. In the Cascades.—*C. laciniata.*

BB. Leaves pinnately 5-foliate. West of Cascades.—*C. asplenifolia.*

There is some doubt as to the range of *C. trifolia* (3) (12), but no disagreement as to the range of *C. occidentalis* growing only in northwestern United States.

The plants, from which the rhizomes and rootlets were used in this investigation, were found growing in damp mossy and boggy woods of western Montana. They are usually found in damp ravines and swampy woods, where the Arbor Vitæ (*Thuja plicata*) thrives. Their range extends from the Bitter Root Mountains where the woods are not so moist, to the moist woods of the northwest ridges along the Continental Divide, which pass over the boundary into Canada. *C. occidentalis* is much smaller, with thin, paper-like leaves, in its southern range in the Bitter Root Mountains, than it is on the extreme northern border extending into Canada, where it is large and coarse. The plants reach their largest size in the high, moist ravines, west of the Continental Divide, extending into Idaho.

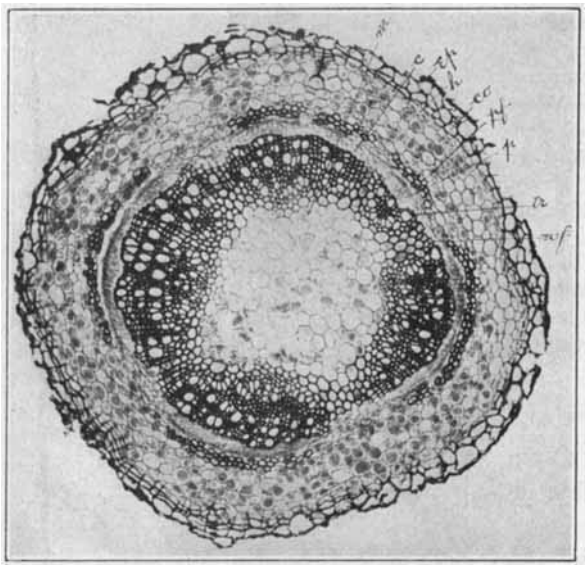

Fig. 2.—*Coptis occidentalis.* Transverse section of rhizome × 60.—*Ep*, epidermis; *h*, hypodermis; *co*, cortex; *pf*, pericyclic fibres; *p*, phloem; *c*, cambium; *tr*, tracheæ; *wf*, wood fibres in xylem; *m*, pith.

The official plant is collected while in flower, in May or June (5). Plants growing in Montana flower in April and May, putting up their pale, yellowish white flower while the ground is usually still frozen and covered with snow; this, and the pale, yellowish white color of the flowers, have given it the local name of "Snow Flowers." It is the first flower to appear in the springtime (near Noxon), in the mountains of western Montana, where the roots under investigation were obtained. Climatic conditions in Montana make it impossible to gather the rhizomes and rootlets while in flower, as it blossoms while the ground is usually frozen and covered with snow. It is not necessary to gather the entire plant of the western species as the rhizomes are twice as large as those of trifolia of the northeastern United States. Using only the rhizomes and rootlets raises the medicinal quality of the drug, as the over-ground portion of the plant contains less of the alkaloids than the rhizomes and rootlets.

This plant found growing in northwestern Montana, and northeastern Idaho, corresponds with the description of *Coptis occidentalis* (Nuttall) (3), (13); and of *Chrysocoptis occidentalis* (Nuttall) (10).

## EXPERIMENTAL PROCEDURE.

*Pharmacognosy.*—The rhizomes and rootlets were gathered in the fall, washed free from soil and leaf mold and dried. The sample was reduced to a No. 20 powder by first grinding the easily reduced portion to the required fineness in a Wyley mill and the remaining woody portion finished to the desired degree of fineness in a chaser mill, and the whole mixed thoroughly.

A portion of the powdered drug, after being irrigated with alcohol, exhibited under the

microscope, characteristics similar to those found in *Coptis trifolia*, but the cells were larger and their walls were thicker and the starch grains larger and more numerous (5*b*), (6), (13), (16).

Scrapings from the rhizomes of *Coptis occidentalis* in water mounts under the microscope (5*a*), revealed starch grains, simple or occasionally 2–3 compound, the single grains 16$\mu$ in diameter and varying from spheroidal, ovoid, oblong, spindle-shaped, sub-reniform concavo convex to irregular in form with a central to occasional excentric hilum, the latter frequently 2 to several cleft to crescent shaped, the lamellæ being distinct in some of the larger grains.

Most of the individual starch grains were up to 8$\mu$ in diameter.

The dried rhizomes were fixed by the usual method (5*a*), imbedded in celloidin and sections made.

Transverse sections through the internode of the rhizome showed the following histological structures:

1. A prominent large-celled epidermis with thick suberized outer walls.

2. A hypodermis of clear cells which undergo tangential division in the older rhizomes forming a cork cambium which begins to lay down subepidermal cork on its outer face.

3. A region of from 5 to 7 layers of starch and alkaloid containing cortical parenchyma cells with thin walls. The innermost layer of this region or endodermis did not differ in appearance from the other layers.

4. A pericycle of several layers containing an interrupted circle of lignified pericyclic fibre groups which alternate with starch and alkaloid containing parenchyma.

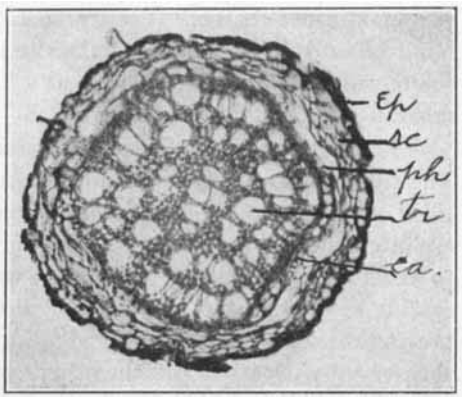


Fig. 3.—*Coptis occidentalis*. Transverse section of rootlet × 68.—*Ep*, epidermis; *sc*, secondary cortex; *ph*, phloem; *ca*, cambium, *tr*, tracheæ of xylem.

5. A circle of up to about 15 to 17 open collateral fibrovascular bundles which are separated from each other by narrow medullary rays with lignified walls. The phloem of these bundles is composed largely of sieve tubes and the xylem largely of tracheæ and wood fibres.

6. A large central pith composed of thin-walled parenchyma containing starch.

Berberine was most abundant in the parenchyma cells (5).

Longitudinal radial sections showed the tracheæ to be mostly bordered pored with circular to elliptical bordered pits. Some spiral tracheæ were evident in the protoxylem. The bordered pored tracheæ measured were up to 32 microns in diameter. Their end walls were oblique and porous.

The wood fibres and pericyclic fibres possess lignified walls with porous slits and pointed ends, the lumen being broader than the walls.

Both the cortical and pith parenchyma cells are elongated longitudinally. The chief differences noted between the sections studied of the rhizomes of this species and *C. trifolia* were:

1. The more extensive and less spongy pith in *C. occidentalis* than in *C. trifolia*.

2. The presence of a cork cambium and beginning deposition of cork tissue in *C. occidentalis* and its absence in *C. trifolia*.

3. The absence of a distinct endodermis in this species and its presence in *C. trifolia*.

4. The presence of sclerenchyma fibres in the pericycle of *C. occidentalis* and their absence of in the pericycle of *C. trifolia*.

5. The more extensive development of the xylem in *C. occidentalis* than in *C. trifolia*.

6. A larger number of root systems emanate from the rhizome of *C. occidentalis* than in *C. trifolia*.

A small sample of the drug was first extracted with ether and then with alcohol. Each of these extracts contained alkaloids according to U. S. P. X alkaloidal precipitation tests.

The marcs from the above extracts were further extracted with dilute alcohol and this extract tested for alkaloids with negative results. (The residue from the ether extraction was of a light yellow color, that from the alcohol was copious and of a dark red color.)

These preliminary tests suggested a method of analysis as follows: A sample of the powder was weighed out and placed in a Soxhlet extraction apparatus, macerated for several hours and extracted with anhydrous ether until exhausted: the extract removed and evaporated spontaneously, cooled and dried to a constant weight in a desiccator. (See Table I.) The marc from the ether extraction was removed and dried and then exhausted with absolute alcohol. The alcoholic percolate was evaporated to dryness at a low temperature on a water-bath, cooled and dried in a desiccator to constant weight. (See Table I.)

The residue from the ether extraction was of a pale greenish yellow color. The residue was dissolved in hot alcohol, thrown into ten times its volume of distilled water, acidulated with dilute hydrochloric acid and the oily resinous precipitate collected on a filter. The precipitate gave an oily stain and was resinous to the touch, completely soluble in warm sodium hydroxide solution and partly soluble in 80% alcohol, showing oil and resin. The filtrate from the oily resinous precipitate was made slightly alkaline with ammonia water and the precipitate shaken out with ether and the ether evaporated spontaneously, which left colorless crystalline plates, which gave a purplish color when first heated with sulphuric acid (5). This indicated the precipitate was probably Coptine. Further tests confirmed this and percentage yield was found to be as shown in Table I.

The residue from the alcohol extraction was dissolved in a small amount of hot water and strongly acidulated with hydrochloric acid, filtered and set aside over night. A copious deposit of bright yellow needle-shaped crystals formed. These were filtered, the mother liquor concentrated and more hydrochloric acid added and the solution heated to the boiling point and again set aside over night. The resultant crystals were added to those previously collected, the whole recrystallized from hot water and collected upon counter-balanced filters, interposed, dried in a desiccator and weighed. The crystals were found to be insoluble in ether, soluble in water and alcohol, and were of a bright yellow color and needle shaped, corresponding to Berberine hydrochloride (11). For percentage yield see Table I.

Samples of the powdered drug were placed in crucibles and incinerated according to the methods of the U. S. P. X. The ash was further treated by U. S. P. X method to determine the acid-insoluble ash. Results given in Table I.

The larger portion of the insoluble ash was found to be silica (16). The soluble portion subjected to qualitative analyses gave tests for iron, aluminum, calcium, magnesium and potassium. An aqueous extract of the powder also showed the presence of gallic and tannic acids, sugar, albumin and coloring matter.

*Coptis trifolia* yields 3.75 to 5.25% total ash, of which about one-tenth is silica, with iron, aluminum, calcium, magnesium and potassium present (6). (See Table I.)

Tests on the aqueous extract of *Coptis trifolia* showed the presence of tannic acid, gallic acid, starch, sugar, oil and resin, albumin and coloring matter.

TABLE I.—SHOWING COMPARATIVE ANALYSES OF *C. occidentalis* AND *C. trifolia.*

| | *Coptis occidentalis.* | *Coptis trifolia.* |
|---|---|---|
| Ether extractive | 2.65 % | 2.275% |
| Alcohol extractive | 19.2 % | 26.27 % |
| Total ash | 4.39 % | 4.35 % |
| Acid-insoluble ash | 0.490% | 0.39 % |
| Coptine | 0.31 % | 0.3 % |
| Berberine | 4.6 % | 3.0 % |

*Therapeutics.*—The various species of *Coptis* are said to contain from 4% to 8% of Berberine (19), to which its principal action is said to be due. It is said by recent authorities to be a simple bitter tonic, although it was formerly extensively used to heal aphthous sores in the mouth, as well as for various eye inflammations.

A 100% glycerite, made by preparing the fluidextract in the usual way, evaporating off the alcohol and making up to the original volume with glycerin, has given good results, when applied to aphthous and other scores in the mouth.

Since *C. occidentalis* contains the same constituents and about the same percentage of such constituents as *C. trifolia,* it appears logical that the medicinal effects of *C. occidentalis* should be equal and similar to those of *C. trifolia.* For this reason and because of the abundance of *C. occidentalis* in Montana and Idaho, it is suggested that *C. occidentalis* be included with *C. trifolia* in N. F. VI.

## CONCLUSIONS.

1. Analysis indicates that *C. occidentalis* contains the same active constituents in about the same amounts as *C. trifolia.*

2. For this reason and because of the abundance of *C. occidentalis* in Montana and Idaho, it is suggested that *C. occidentalis* be included with *C. trifolia* in N. F. VI.

3. *C. occidentalis,* because of its abundance and convenient collection, is suggested as a commercial source of the alkaloids Coptine and Berberine in preference to *C. trifolia.*

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## THE ASSAY OF HYOSCYAMUS.*

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Hyoscyamus has been official in the past four revisions of the U. S. Pharmacopœia, and an assay process has been described in the last three. The changes occurring in this assay have been primarily in that part of it dealing with the extraction of the alkaloids from the crude drug. In the U. S. P. VIII (first official process) the drug was macerated for 10 minutes with a mixture of 1 part of chloroform and 3 parts of ether; then ammonia water was added and the contents agitated during 1 hour. The final extraction was made from a basic mixture by the use of chloroform.

In the U. S. P. IX, the process of extraction was changed as follows: the drug was agitated during 2 hours with 300 cc. of a mixture of 1 volume of chloroform and 3 volumes of ether to which ammonia water had been added. An aliquot part of the immiscible solvent was then decanted and the assay completed as indicated in the first process. The U. S. P. X changed this to a percolation process, the same solvent being used.

Various workers encountered many difficulties in the assay of this drug with the result that a number of processes have been presented for consideration during the past decade.

Watkins and Palkin (1), workers in the Drug Control Laboratory, Bureau of Chemistry, U. S. Department of Agriculture, described a method for the assay of Hyoscyamus "which gave a yield of from two to three times as much alkaloid as that obtained by the U. S. P. IX and X methods."

In order to check the various processes for the assay of Hyoscyamus, C. B. Jordan, Dean of School of Pharmacy, Purdue University, Chairman of Subcommittee No. 6, U. S. P. Revision Committee, submitted samples from the same lot of drug in No. 60 powder to a number of experienced chemists for collaborative work. He requested that three processes be used as follows: Process No. 1 (2), the U. S. P. X process; process No. 2, which was the same except that the drug was allowed to macerate over night; process No. 3 (3), recommended by J. J. Durrett, who was, at that time, Chief, Drug Control, the U. S. Food and Drug Administration. The last was a hot extraction process very much like that used by Watkins and Palkin (1) in their work with this drug. This process required a special apparatus.

* An abstract based upon a thesis by H. G. DeKay submitted to the Faculty of Purdue University in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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