5. The physiologic activity of fresh, standing and decomposed infusions is independent of their $p_H$.

6. The true acidity of tinctures of digitalis is rather high, being nearly equivalent to that of a $n/10{,}000$ hydrochloric acid.

REFERENCES.

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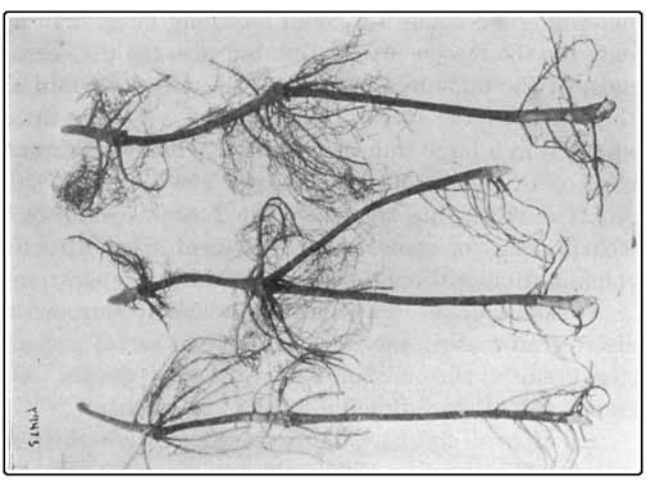
## PHYTOCHEMICAL NOTES.*[1]

### 95. A CHEMICAL STUDY OF THE RHIZOME AND ROOTS OF PODOPHYLLUM PELTATUM L.

BY H. L. KUESTER.

*Collection and Drying.*—The rhizome and roots used in the experiments subsequently recorded were collected in the vicinity of Madison between the dates of October 1 and November 12, 1924. Part of the drug was harvested in the Pharmaceutical Garden where two rows of the plant have been cultivated under natural shade since 1920 or 1921. Part of the material was from wild plants that had not been transplanted previously. In harvesting the material in the Garden, the buds were separated and replanted. So far as the wild material is concerned, the same course was followed in order to insure against extermination of the plant.



Rhizomes and Roots of Podophyllum Peltatum.

RHIZOMES AND ROOTS OF PODOPHYLLUM PELTATUM.

The rhizomes show the striking difference in growth during the season of 1923 as compared with that during the season of 1924. The bud end of the new growth of rhizome, together with the roots near the bud were cut off for replanting. The remaining portion of the rhizome, together with the roots attached thereto, was dried to drug and used in the investigation here reported.

The soil was carefully removed from rhizome and roots by washing. The imperfectly drained material weighed 18,290 grams. Air dried, it weighed (November 21st) 5950 grams. The loss of 12,340 grams represents 67.4 per cent of the original weight. This is probably somewhat too high because of the imperfect

* From the laboratory of Edward Kremers.

[1] Presented to Scientific Section, A. PH. A., Des Moines meeting, 1925.

removal of water from the washed material. Moisture determinations made separately for both rhizome and roots in connection with smaller amounts of fresh material gave the following results:

| | Wt. before drying, Gm. | Wt. after drying, Gm. | Loss, per cent. |
|---|---|---|---|
| | Oven dried (at 65°). | | |
| Rhizome | 77.26 | 28.49 | 63.1 |
| Roots | 50.37 | 24.18 | 52.0 |
| | Air dried (at room temp.). | | |
| Rhizome | 64.6 | 29.65 | 52.6 |
| Roots | 65.4 | 34.59 | 47.1 |

It becomes apparent that the roots contain less moisture than the rhizomes.

*Separation into Rhizome and Roots.*—While during digging no thought was had as to the complete removal of the roots from the soil, it seemed desirable, for reasons that will become apparent from work reported later, to separate roots from rhizome and to determine the approximate percentage of each. That this determination could not claim anything more than approximation is evident, not only for the reason just stated, but also for the reason, previously indicated, that most of the buds had been removed with a certain amount of rhizome and roots to perpetuate the species by replanting. The air-dried material was coarsely comminuted in a large iron mortar after which separation into rhizome and roots was effected by means of a very coarse sieve. The 5950.0 grams of drug previously reported, when thus treated, yielded 3990.0 grams or 67.5 per cent of rhizome and 1920.0 grams of roots, or 32.5 per cent after deducting a loss of 15 grams during comminution and one of 25 grams during separation.

*Comminution.*—The coarsely broken up rhizomes and roots were powdered in a disintegrator using the finer of the two sieves accompanying the machine. The 3990 grams of rhizome suffered a loss of 30 grams. Owing to an accident the 1920 grams of rootlets suffered a loss of 224 grams.

*Analytical Sifting.*—These powders were then sifted in a set of analytical sieves. That portion which did not pass through the No. 20 sieve is referred to as No. 0. The sifting of the rhizome powder was carried out in two lots by way of control.

| Time of shaking. | Degree of fineness. | Lot I. Weight in grams. | Lot I. Percentage. | Lot II. Weight in grams. | Lot II. Percentage. |
|---|---|---|---|---|---|
| 3 min. | No. 0 | 1.3 | 0.27 | 1.5 | 0.32 |
| 10 min. | No. 20 | 43.7 | 8.89 | 43.5 | 8.79 |
| 30 min. | No. 40 | 120.5 | 24.49 | 117.0 | 23.61 |
| 45 min. | No. 60 | 157.5 | 32.01 | 161.0 | 32.49 |
| 50 min. | No. 80 | 126.5 | 25.71 | 131.0 | 26.54 |
| 50 min. | No. 100 | 42.5 | 8.64 | 41.0 | 8.27 |
| | | 492.0 | | 495.5 | |
| Loss during sifting | | 8.0 Gm. = 1.6 per cent | | 4.5 Gm. = 0.9 per cent | |

During the process of sifting particularly of the No. 80 and No. 100 powders part of the drug escaped in the form of a fine dust, amounting to as high as 1.8 per cent, which caused severe irritation of the eyes. The operator used a respirator covering nose and mouth but had failed to protect the eyes.

In the sifting process of the root powder the totals only are recorded.

| Degree of fineness. | Weight in grams. | Percentage. |
|---|---|---|
| No. 0 | 10.5 | 0.6 |
| No. 20 | 480.5 | 28.7 |
| No. 40 | 370.5 | 22.1 |
| No. 60 | 377.0 | 22.5 |
| No. 80 | 357.0 | 21.3 |
| No. 100 | 80.5 | 4.8 |
| | 1676.0 | |
| Loss during sifting | 30.0 | 1.8 |

*Assay of Rhizome.*—Duplicate assays of each grade of powder were made according to the U. S. P. In place of the ordinary percolator, Soxhlet extractors with paper thimbles were used. In each case from 160 to 180 cc. of percolate were collected and the tincture evaporated to 20 cc. on a water-bath. Upon cooling and further spontaneous evaporation in a capsule numerous small crystals formed. These were separated (in several instances imperfectly) washed with a little alcohol and weighed. They were but very slightly soluble in cold alcohol, but soluble in cold water and cold 1 per cent hydrochloric acid. Their melting point, 184.5° to 186° does not correspond with that of any recorded constituent of Podophyllum. Because of their solubility in water, they cannot be regarded as a constituent of Resin of Podophyllum. Hence the weights of the crystals and of the "resin" are recorded separately.

| Fineness of powd. | | Weight of resin, Gm. | Percentage. | Weight of crystals, Gm. | Percentage. |
|---|---|---|---|---|---|
| No. 20 | A | 0.3555 | 3.55 | 0.4702 | 4.70 |
| | B | 0.3362 | 3.36 | 0.2576 | 2.57 |
| No. 40 | A | 0.4017 | 4.01 | 0.2523 | 2.52 |
| | B | 0.4190 | 4.19 | 0.1314 | 1.31 |
| No. 60 | A | 0.4152 | 4.15 | 0.1949 | 1.94 |
| | B | 0.4047 | 4.04 | 0.1604 | 1.60 |
| No. 80 | A | 0.3871 | 3.87 | 0.1545 | 1.54 |
| | B | 0.3739 | 3.73 | 0.1003 | 1.00 |
| No. 100 | A | 0.3937 | 3.93 | 0.1357 | 1.35 |
| | B | 0.4087 | 4.08 | 0.0989 | 0.98 |
| Total | | 3.8957 | Av. 3.89 | 1.9562 | Av. 1.96 |

The irregularities in the amounts of resin obtained by assay do not admit of drawing any very definite conclusions, with possibly one exception, *viz.*, that the No. 20 powder contains least resin, average 3.4 per cent as opposed to an average of about 4.0 per cent for Nos. 40, 60 and 100 powders, whereas that of No. 80 powder is about half way between, *viz.*, 3.8 per cent.

The percentage of crystals, however, is greatest in the coarsest powder and diminishes with fair regularity as the powders become finer. Because of the difficulty in separating the small crystals from a syrupy mother liquid the duplicates do not correspond as well as in the resin assay.

### ASSAY OF ROOTS.

These also were made in duplicate for each grade of powder. In this case no attempt was made to separate crystals.

| Fineness of powder. | Wt. of Resin, Gm. | Percentage. |
|---|---|---|
| No. 20 A | 0.4234 | 4.23 |
| 20 B | 0.4286 | 4.28 |
| No. 40 A | 0.5746 | 5.74 |
| 40 B | 0.5583 | 5.58 |
| No. 60 A | 0.5156 | 5.15 |
| 60 B | 0.5370 | 5.37 |
| No. 80 A | 0.5384 | 5.38 |
| 80 B | 0.5117 | 5.11 |
| No. 100 A | 0.5393 | 5.39 |
| 100 B | 0.5371 | 5.37 |
| Total | 5.1580 | Average percentage 5.16 |

The average percentage 5.16 per cent is somewhat higher than that of the rhizome, about 4 per cent. Again the No. 20 powder appears to contain somewhat less resin, *viz.*, 4.25 per cent than the finer powders. Yet it should be observed that the very next powder, *viz.*, No. 40, apparently has the highest resin content, *viz.*, 5.6 per cent.

*Preparation of Resin of Podophyllum.*—The U. S. P. 1910 directions were followed in every particular. Hence the percolation, so far as the preparation of the resin was concerned, was stopped when the alcoholic percolate ceased to be rendered turpid by water. The precipitated resin, was allowed to dry at room temperature in a dark place for four weeks. At the end of the period it was possible to powder the resin from the rhizome, but not that from the roots. The finished product from the rhizome was greenish brown in color and weighed 31.5 grams, hence the yield amounted to 3.15 per cent. Owing to an accident, part of the concentrate from the root was lost, hence the yield of 22.5 (= 2.25 per cent) is of no significance.

*Ash Determination of Resin.*—The results are herewith tabulated:

| | Rhizome. | | Roots. | |
|---|---|---|---|---|
| | I. | II. | I. | II. |
| Wt. of resin | 0.5028 Gm. | 0.4989 Gm. | 0.5016 Gm. | 0.5008 Gm. |
| Wt. of ash | 0.0032 Gm. | 0.0027 Gm. | 0.0022 Gm. | 0.0018 Gm. |
| Percentage of ash | 0.594 per cent | 0.541 per cent | 0.438 per cent | 0.359 per cent |

Hence the ash content of the resin from the roots is somewhat lower than that of the rhizomes. However, both are well within the pharmacopœial limits of 1.5 per cent.

*Sugar.*—Whereas for the preparation of the official Resin, alcoholic percolation was discontinued at the point indicated by the pharmacopœial directions, it was resumed with the same menstruum because of the crystals that had been observed as previously mentioned.

The handsome crystals were observed in connection with almost every assay. Having proven their organic nature, the practical absence of inorganic matter was revealed by ash determinations which yielded 0.115 and 0.117 per cent, respectively.

Quite accidentally their sweetish taste was discovered. However, they did not reduce Fehling's solution until after hydrolysis. With phenyl hydrazine the hydrolyzed solution yielded an osazone which melted (not recrystallized) at 188°.

*Collection of Drug in the Spring of 1925.*—The first lot was dug April 17th on Mendota Drive near the Black Hawk Country Club grounds on the north slope of the hill. The soil was a sandy loam and there had been no recent rains. The plants were hardly above ground. The moisture determinations by the xylene method yielded 65.0 per cent for the roots and 64.5 per cent for the rhizomes.

A second lot was collected May 2nd near the Illinois Central right of way west of the Cemetery. The plants were from six to twelve inches high. Recent rains had left the soil rather moist. Moisture determinations yielded 74.0 per cent for the roots and 74.1 per cent for the rhizomes.

A third lot was collected May 19th from the same locality. Moisture determinations yielded 73.2 per cent for the roots and 73.4 per cent for the rhizomes.

P. S. The sucrose, reported above, when recrystallized by A. H. Uhl, melted at 181–182°; $[\alpha]_D = +59°$; after hydrolysis $[\alpha]_D = -11°$. For sucrose $[\alpha]_D = 66.5°$; for inverted sucrose $[\alpha]_D = -32°$. Possibly the irregularities in melting point and angle of rotation are attributable to the presence of inorganic substances as indicated by the ash content. The amount of material was not sufficient to admit of purification by repeated crystallization.

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## THE VOLATILE OIL OF LEDUM GRŒNLANDICUM.*

BY E. V. LYNN, ARNOLD LEHMAN AND RUSSELL CAIN.

The plants of the genus *Ledum* are small, evergreen, ericaceous shrubs, growing in swamps, bogs and other wet places in the northern part of Europe, Asia and America. The species, *grœnlandicum*, is a native of North America, where it is called Labrador Tea and used, especially by the natives as a pectoral and tonic. It differs from others of the same genus by the rusty and hairy character of the lower side of the leaf. The whole plant, and particularly the leaf, has an aromatic odor and taste which is very pleasing. The agreeable odor of *Ledum grœnlandicum* suggested the possibility of valuable volatile constituents and an attempt was made to separate them.

The plant itself, commonly known as Labrador, Continental, or James Tea, presents a shrub-like growth, the stems being very stout and branching, occasionally reaching a height of five or six feet. The shrub is an evergreen, bearing snowy white flowers in a convex cluster. The leaves are alternate and sessile, ranging in length from one to three inches. They are oval shaped, narrow and entire, with upper surface smooth and the lower composed of densely matted, red-brown hairs.

As far as could be learned, no investigational work has ever been reported on this plant, although Ledum palustre has been examined repeatedly (see references). The latter gives by steam distillation from 0.3 to 2.0 per cent of a volatile oil, the yield apparently depending upon age of plants, season, habitat, portions used, etc. The oil is a greenish or reddish viscid liquid of a penetrating narcotic odor and a pungent, unpleasant and persistent taste, and consists of a stearoptene and a liquid portion in approximately equal proportions. The latter has a boiling point of 180° to 250° C., $d_{15}$ 0.93 to 0.96. It frequently does not separate

* Scientific Section, A. PH. A., Des Moines meeting, 1925.