does not grant a certificate to any product which does not meet this standard (58). Patee and Nelson (28) expressed a belief that this value constitutes a suitable potency for Fluidextract of Ergot from the standpoint of the clinician as well as the manufacturer. Bourne and Burn (59) found that the effective hypodermic dose of ergotamine or ergotoxine in obstetrics is between 0.5 and 1.0 mg. Since oral doses usually must be somewhat larger because of the absorption factor it is believed that at least 1.0 mg. of alkaloid should be contained in a dose of fluidextract. A 0.05 per cent alkaloid content corresponds to 0.5 mg. per cc. Therefore, this value provides for an alkaloid content of 1.0 mg. in the U. S. P. dose of Fluidextract of Ergot.

As a result of a thorough review of ergot literature and because of the results obtained in this investigation, the author agrees that an alkaloid content of 0.05 per cent, in terms of either ergotamine or ergotoxine base, in Fluidextract of Ergot provides for a therapeutically active preparation which will be satisfactory to the physician. Because of his experience in biologically testing practically all lots of crude ergot imported during the past two years and in testing fluidextracts marketed by practically every manufacturer in this country, the author is confident that Fluidextract of Ergot of this potency can be satisfactorily prepared from the crude ergot now available.

(*To be continued*)

A PHARMACEUTICAL STUDY OF HYDRASTIS CANADENSIS.

BY RUBY HIROSE AND H. A. LANGENHAN.

(*Continued from p. 353, April Issue.*)

ASSAY AND PURITY RUBRIC.

The 1900 U. S. Pharmacopœia (1) was the first to introduce either a purity rubric or an assay. The rubric read, "not less than 2.5 per cent of Hydrastine." The 1910 revision (2) introduced a limit of leaves, stems and foreign matter and changed the alkaloidal requirement to, "not less than 2.5 per cent of ether-soluble alkaloids." The revision of 1920 (3) added to this, "and not more than 3 per cent of acid-insoluble ash."

The assay method introduced into the revision of 1900 (4) consisted of macerating 15 Gm. of Hydrastis No. 60 powder with 150 cc. of ether and 5 cc. of ammonia water for one-half hour; then adding 15 cc. of water to cause the drug to agglutinate, and decanting 100 cc. of the supernatant liquid. The ethereal liquid is extracted with several portions of aqueous sulphuric acid solution; the combined acid solutions made alkaline with ammonia water and extracted with ether. The combined ether extractions evaporated to a constant weight at 100° C. The revision of 1910 followed the same procedure except that the quantity of drug used is 10 Gm., instead of 15 Gm.; and 100 cc. of ether is added; then decanting 50 cc. This procedure is also included in the 1920 revision of the U. S. P.

With no distinct change in the assay process as given in the revisions of 1900 and 1910, it may be assumed that the results obtained were "ether-soluble alkaloids" and not Hydrastine as specified by the 1900 revision.

Methods for assaying Hydrastis appeared sometime previous to 1900. One of the first methods is found in the Eclectic Dispensatory (5) (1862).

The Hydrastis root was extracted with alcohol, the tincture evaporated and the residue mixed with water. The whole was filtered and a quantity of hydrochloric acid added to the mixture. On evaporation, a crystalline precipitate was obtained, which on drying turned yellow. Microscopic examination showed their prismatic shape. This was assumed to be pure Hydrastin. The alkaline nature of the substance was confirmed by the Varrentrapp method for nitrogen determination.

Lercher (6) (1878) extracted the alkaloids by simply preparing a cold water solution of the drug, strongly acidulating with hydrochloric acid to precipitate out the berberine. Then alkalinizing the mother liquor with ammonia. Hydrastine was precipitated out and recrystallized from alcohol.

Moerk (7) (1894) extracted the powdered Hydrastis with ammoniacal ether and purified the alkaloid by washing out with dilute hydrochloric acid, with subsequent extraction of the alkaloid with ammoniacal ether and alcohol mixture. The ether present in small amount facilitated the crystallization.

Eberhardt (8) (1889) moistened the drug first with dilute hydrochloric acid, extracted with water, then alkalinized with dilute ammonia solution, filtered and the precipitated alkaloid, was dissolved in the smallest amount of hot chloroform. This solution was filtered through glass wool and mixed with excess of cold alcohol. Hydrastine crystallized out on stirring or shaking the mixture.

Thompson (9) (1893) determined both the Hydrastine and the berberine content. He percolated the crude drug with hot alcohol for about two to three hours. The alcoholic solution was diluted to 100 cc. with the same menstruum. To an aliquot portion, a mixture of hydrochloric acid, sulphuric acid and ether were added. This was allowed to stand twenty-four hours in a cool place. The resulting crystals were transferred to a counterpoised filter-paper. The berberine alkaloid washed with ether and alcohol mixture and dried. The weight multiplied by 0.9017 gave the berberine content, and when multiplied by forty gave the percentage. For Hydrastine, the neutral filtrate is mixed with "treated" sawdust, this is dried, placed in a flask and Modified Prolliu's Mixture was added (25 cc. of ether, 100 cc. chloroform, 25 cc. alcohol, 10 cc. of stronger ammonia water). After shaking for several hours, 50 cc. of the ethereal liquid was evaporated to dryness, then redissolved in $N/100$ sulphuric acid. The excess acid was determined with $N/100$ ammonia water. Each cc. of $N/100$ sulphuric acid represent 0.00383 Gm. of Hydrastine. This multiplied by forty equals the per cent in the drug.

Keller (10) (1894) extracted the crude alkaloids by using a mixture of 4 cc. of ether and 8 cc. alcohol and 20 cc. water. After heating for twenty-four hours Hydrastine crystallized out. Berberine was precipitated from the mother liquor as the tri-iodide or a nitrate.

The British Pharmacopœia (11) (1901) offered a standard assay of Hydrastis consisting of percolating the drug forty-eight hours with acid alcohol containing a little glycerin. The percolate concentrated in vacuo, then diluted with water containing two per cent sulphuric acid and five per cent potassium iodide. An aliquot portion filtered and alkalinized, the alkaloid extracted with ether chloroform mixture (three to one), and evaporated. A few drops of chloroform were added with $N/40$ acid; the chloroform removed by blowing air through it, and the excess acid titrated with a standard alkali.

Gordin and Prescott (12) (1899) favored the determination of Hydrastine by the periodide method. The drug is macerated over night with ammoniacal ether containing a little alcohol. Current of air is passed through to remove the ammonia. The drug is subjected to Soxhlet extraction using absolute ether, until completely extracted. The ether is evaporated spontaneously. The residue is dissolved in acidulated water to make 100 cc., 20 cc. of the filtered solution is accurately measured (2 Gm.) into a flask containing 20 to 30 cc. of standard iodine solution. From the amount of iodine consumed the amount of Hydrastine can be determined by using the factor of the hexiodide, that is 0.60403 of Hydrastine for every cc. of iodine solution used. The berberine is precipitated with acetone as the insoluble berberine acetone, this in turn is decomposed with $N/20$ potassium iodide. The solution is filtered and the excess determined with standard silver nitrate solution; residual titration with $N/40$ ammonium sulphocyanate

using ferric alum indicator. One cc. of $N/20$ KI used is equivalent to 0.016725 of berberine.

Schreiber (13) (1901) utilized the Soxhlet for extracting with ether. Best samples yielded 4.16% and the poor samples yielded 2.185% of Hydrastine by this method.

Hankey (14) (1906) in commenting on the U. S. P. assay doubts the advisability of using aliquot parts of ether solution. He also states that the alkaloid Hydrastine was never isolated white, as the yellow alkaloid was always present in sufficient amounts to give the yellow color.

Lyons (15) (1920) states that Hydrastine can be determined by saponification with hydriodic acid (sp. gr. 1.71) in a Benedik apparatus. One gram of Hydrastine is equivalent to 1.248 Gm. of silver iodide.

Herron (16) (1918) concludes that leaves and tops are most valuable since they contain less berberine than Hydrastine. Both ether and benzol are recommended for solvents in extraction by percolation.

Schmidt (17) (1920) exhausted the root by percolation with ammoniated benzol for twenty-four hours and re-crystallizing the alkaloid from alcohol.

Fromme (18) (1903) exhausted Hydrastis root with a mixture of ether, petroleum ether and ammonia as a means of obtaining the hydrastine.

Davis (19) (1915) concludes from his examination of Hydrastis, that the results obtained by the German assay are the best; the Belgian method is fairly good; the Hungarian not so good and that the Dutch, French and Swiss, also the U. S. P. IX are not practical. However, U. S. P. equals the German in accuracy if alcohol is evaporated before shaking out with ether to prevent taking up too much plant extractives. Belgian and German methods are accurate for determining Hydrastine in rootstocks.

Wattiez (20) (1920) used silicotungstic acid for isolating Hydrastine from the powdered rhizome by first refluxing with alcohol at 70°, precipitating the berberine with hydrochloric acid after one hour's standing. For Hydrastine, 5% solution of silicotungstic acid is added and the mixture is boiled. After standing twenty-four hours, the crystals are washed and calcined to constant weight. The resulting weight multiplied by 28.57 gives the weight of Hydrastine in 100 Gm. of the original powder.

An International assay of Hydrastis (21) (1921) dissolves the dried aqueous extract in $N/10$ hydrochloric acid and measuring the excess acid with $N/10$ sodium hydroxide, using methyl orange as an indicator. Each cc. of hydrochloric acid is equivalent to 0.0383 Gm. of Hydrastine.

Mackie and Cleary (22) (1923) comment on the separation of Hydrastis alkaloid by the difference in the solubilities of the hydriodides. Precipitation of berberine iodide is a time reaction and is not complete. The dilution given by the British Pharmacopœia for difference in solubilities of the iodides is an optimum. Therefore, the official assay is not based on their solubilities as believed before, but in the difference of solvents. Hydrastine is precipitated by ammonium hydroxide, but soluble in excess, and berberine is insoluble in ether. After the Hydrastine has been removed from the alkaline solution, berberine is extracted with strong hydrochloric acid or precipitate as the insoluble acetone salt.

Wasichy and Joachimowitz (23) (1919) assayed berberine in the drug grown in Austria. The powdered drug is macerated for forty-eight hours with 95% alcohol. To an aliquot portion of the extract an excess of the Mayer's Reagent is added and the whole filtered. The precipitate is washed with water containing a little Mayer's Reagent, and then transferred into a separatory funnel. Sodium chloride and ether are added and the mixture is shaken for thirty minutes. To 100 cc. of the clear berberine chloride solution an excess of ether solution of picrolonic acid is added. The precipitate of berberine picrolonate is collected in a Gooch crucible and dried to constant weight at 100° C. Relation of berberine picrolonate to berberine is as 600.25 is to 353.26.

Davis (24) (1915) precipitated out the berberine with ethyl acetate, liberating the berberine with 10% sodium hydroxide and finally shaking it out with ether-chloroform mixture.

The assay of Hydrastis has not been limited to the drug itself, but also applied to the fluidextract and the tincture. The U. S. P. (1910) assay for fluidextract directs the use of 10 cc. of the fluidextract mixed with 85 cc. of distilled water containing 2 Gm. of KI., water added to make 100 cc., and the mixture shaken several minutes; 50 cc. of the mixture are placed in the separatory funnel, alkalinized with ammonia water and the alkaloid shaken out with ether. When

dried and weighed, the residue should weigh 0.2 Gm. equivalent to 2 Gm. of ether-soluble alkaloid in 100 cc. of the fluidextract.

Simon (25) (1885) determined Hydrastine in the fluidextract by adding ether and ammonium hydroxide to the extract which had been previously warmed to remove the excess alcohol. To the tincture, he added water to separate the oil and the resin before isolating the alkaloid. Eberhardt (25) (1885) found difficulty in isolating the alkaloid from the fluidextract by the addition of ammonium hydroxide due to the accompanying brown flocculent precipitate. This precipitate was first removed by filtering through a pledget of cotton.

Rusting (26) (1899) concentrated the fluidextract mixed with water to certain weight and filtered the mixture through talc or infusorial earth. Tragacanth was used to facilitate the separation of the ethereal layer, and petroleum ether to remove the canadine.

Eldred and Pence (27) (1908) offer a comparison of four methods with the U. S. P. method. Puckner (28) (1908) just prior to this, called to the attention an error introduced by the 1900 U. S. P. assay. The error attributed to the berberine hydriodide precipitate carrying down the Hydrastine, hence 50 cc. taken for examination did not fully represent 5 cc. of the fluidextract.

The following tables give the comparative results:

1. *Puckner Method.*—Similar except that the fourth alkaline ether extraction was made and weighed separately. Results are given per 100 cc. of fluidextract:

Three extractions	1.96 Gm.	1.968 Gm.
Fourth extraction	0.044 Gm.	0.042 Gm.
Total	2.004 Gm.	2.010 Gm.

The alkaloidal residue softens at 110° C. and melts at 127° C. Results show that iodine precipitation retains Hydrastine when washed according to Puckner Method.

2. *Ether Extraction Method.*—Five cc. of the fluidextract placed in a separator with 10 cc. of 2% sulphuric acid and 30 cc. of water. The alkaloid extracted with ether after alkalinization.

Three extractions	2.15 Gm.	2.174 Gm. per 100 cc.
Fourth extraction	0.027 Gm.	0.018 Gm. per 100 cc.
Total	2.177 Gm.	2.192 Gm. per 100 cc.

The alkaloidal residue softens at 111° C. and melts at 130° C.

3. *U. S. P. Method.*

Three extractions	1.902 Gm.	1.892 Gm.
Fourth extraction	0.03 Gm.	0.046 Gm.
Total	1.932 Gm.	1.938 Gm.

The residue softens at 118° C. and melts at 128° C.

4. *U. S. P. Method,* acidulated with sulphuric acid and washed four times with ether, then made alkaline and extracted with four portions of ether.

Hydrastine	1.776 Gm.	2.756 Gm.

The alkaloid melts at 130° C. without previous softening. Non-alcoholic fluidextract of Hydrastis was assayed by method "2" before adding glycerin, then adjusted to 1.25 Gm. per 100 cc. by the addition of glycerin. This gave 1.244 Gm. per 100 cc. Same preparation by Puckner process gave 1.186 Gm., indicating the presence of glycerin.

These experiments eliminated the aliquot part method and indicated that the high temperature at which the residue is dried practically removed the glycerin.

Jones (29) (1915) made a comparative assay of Hydrastis and its fluidextract according to U. S. P. methods.

Process.	Drug assayed by U. S. P. VIII.	Fluidextract assayed by U. S. P. VIII.	Fluidextract assayed by U. S. P. IX.
1. U. S. P. VIII	4.15	3.52	4.22
			4.2
2. U. S. P. VIII	3.12	2.56	3.14
3. U. S. P. plus 20% glycerin	3.83	2.61	3.21
			3.26
4. Purchased product		2.00	2.26

Products 1 and 2 are made strictly according to the U. S. P. VIII formula. Product 3 is made by the same process except that it contains 20% of glycerin instead of the official 10%. From the above data, the results obtained are higher in the U. S. P. IX assay than in the U. S. P. VIII method as compared to the drug. In Process 3, 10% glycerin proved more efficient in the extraction than the 20%. The high results of U. S. P. IX is not incorrect. The amount of ether used in maceration is too small to prevent a crystallization of Hydrastine. This was corroborated by Dichgan (*Apoth. Ztg.*, 45 (1914), 498–450), who used two and a half times as much ether in proportion by the Swiss method.

The Proposed Dutch assay (30) (1925) is a gravimetric process. Tragacanth is used to aid the separation of the ethereal layer and petroleum ether to remove the alkaloid, canadine. By this procedure 0.040 Gm. of Hydrastine should be isolated from 3 Gm. of the rhizome and 0.039–0.041 Gm. from 55 cc. of the fluidextract.

REFERENCES.

(1) U. S. P., 1900.
(2) *Ibid.*, 1910.
(3) *Ibid.*, 1920.
(4) PROC. A. PH. A., 42 (1894), 188.
(5) *A. J. P.*, 34 (1862), 141.
(6) *Ibid.*, 50 (1878), 470.
(7) *Ibid.*, 66 (1894), 201.
(8) PROC. A. PH. A., 37 (1889), 709.
(9) *Ibid.*, 41 (1899), 257.
(10) "Yearbook, British" (1894), 136.
(11) *A. J. P.*, 73 (1901), 211.
(12) *Ibid.*, 71 (1899), 257.
(13) PROC. A. PH. A., 50 (1902), 854.
(14) *Am. Druggist*, 49 (1906), 361.
(15) A. B. Lyons, "Chemical Assay of Organics and Galenicals" (1920), 149.
(16) YEAR BOOK, A. PH. A., 7 (1918), 257.
(17) *Ibid.*, 9 (1920), 620.
(18) "Yearbook, British" (1903), 91.
(19) *Ibid.*, (1916), 15; also 4 (1915), 125.
(20) YEAR BOOK, A. PH. A. 9 (1920), 289.
(21) "Yearbook, British" (1921), 247.
(22) *Ibid.* (1925), 430.
(23) YEAR BOOK, A. PH. A., 8 (1919), 235.
(24) "Yearbook, British" (1916), 15.
(25) *Am. Druggist* (1885), 84.
(26) *A. J. P.*, 71 (1899), 344.
(27) PROC. A. PH. A., 56 (1908), 836–838.
(28) *Ph. Review*, 26 (1908), 132.
(29) JOUR. A. PH. A., 4 (1915), 106–108.
(30) "Yearbook, British" (1925), 303.

The following table offers a summary of the results obtained by various assayers. The data was obtained through the Digest of Comments and Yearbook:

ETHER-SOLUBLE ALKALOIDS.

Reporters.	No. of samples.*	Minn.	Max.	References.
Roberts, J. H.		2.75		JOUR. A. PH. A., 11 (1922), 636.
Ewe, G.	60	3.29–	4.20	Penn. Ph. Assn., 9 (1920), 310.
Dohme, R. L.	4	2.53	5.5	"Proc. N. W. D. A." (1917), 85.
Sayre, *et al.*	5	2.42	2.99	"Rep. Kans. Bd. Health," 113 (1917), 112 and 263.

* This represents the number of lots assayed.

Reporters.	No. of samples.*	Minn.	Max.	References.
Scoville, W. L.		2.23–	3.7–5.5	JOUR. A. PH. A., 6 (1917), 410.
Anon.	10	2.15	5.59	PROC. A. PH. A., 5 (1916), 119.
Patch, E. L.	3	3.2	4.2	JOUR. A. PH. A., 5 (1916), 539.
Roberts, J. G.	13	2.51	3.45	"Proc. Pa. Ph. A.," 5 (1916), 113.
Scoville, W. L.	1		2.7	JOUR. A. PH. A., 5 (1916), 539.
Swift, E. G.	6	2.23	5.5	*O. P. D. R.*, No. 10 (1916), 46.
Vanderkleed, C.	5	3.16	5.39	JOUR. A. PH. A., 5 (1916), 539.
Caesar & Loretz	10	2.25	4.21	*Jahres-Bericht* (1907), 50.
Jensen, H. P.	15	2.6	3.6	*Evans Anyl. Notes* (1914), 37.
Linke, H.	3	2.57	3.03	*Apoth. Ztg.*, 29 (1914), 637–639.
Mann, E. W.	9	1.96	3.44	*Ann. Rep.*, Southall Bros., (1914), 15.
Vanderkleed, C.	2	3.22	3.42	PROC. A. PH. A. (1914), 160.
Dohme & Engelhart			3.0	*O. P. D. R.*, 83 (1913), 55.
Brown, L. A.	5	0.79	2.5	"Proc. Ky. Ph. A." (1913), 55.
Caesar & Loretz	14	2.81	4.64	*Jahres-Bericht* (1913) 107.
Engelhart,	9	1.5	3.5 (8)	JOUR. A. PH. A., 2 (1913), 164.
Gane, E. H.	2	3.13	3.6	*Ibid.*, 2 (1913), 680.
Kebler, L. F.	1		3.01	*Ibid.*, 2 (1913), 1095.
Patch, E. L.	3	1.6	3.44–0.48	JOUR. A. PH. A., 2 (1913), 1095.
Roberts, J. G.	2		2.45	PROC. A. PH. A. (1913), 96.
Mulford Laboratory	6	2.9	4.09	JOUR. A. PH. A., 2 (1913), 978.
Caesar & Loretz		2.66	3.62	*Jahres-Bericht* (1912), 81.
Gane, E. H.	7	2.72	3.5 (4)	JOUR. A. PH. A., 1 (1912), 500.
Jensen, H. P.	19	2.3	3.5	*Evans Anyl. Notes*, 7 (1912), 38.
Mann, E. W.	3	2.31	2.55	*Ann. Rep.*, Southall Bros. (1912–1913), 13.
North, H.	43	2.55	4.12	*Rep. Lehn & Fink, Analyt. Dept.* (1910–1913), 47.
Patch, E. L.	3	3.02	3.2	JOUR. A. PH. A., 1 (1912), 500.
Scoville, W. L.	34	2.5	3.5	*Ibid.*, 1 (1912), 1341.
Noyes, C. R.	5	2.7	3.0	"Proc. Minn. Ph. A." (1911), 75.
Ferguson, G. A.	12	2.51	3.21	"Proc. N. Y. Ph. A." (1911), 152.
Vanderkleed, C.	11	2.88	4.85	*Ibid.* (1911), 132.
Smith & Cline	3	2.65	3.4	*Analyt. Rep.* (1911), 25.
Evans	10	2.77	3.46	*Ibid.* (1911–1912), 36.
Caesar & Loretz		2.6	4.44	*Jahres-Bericht* (1911), 56–57.
Clark, A. H.	30	2.5	4.5	BULL. A. PH. A., 5 (1910), 124.
Eldred, Frank,	19	2.8	3.8	PROC. A. PH. A., 58 (1910), 892.
Gane, E. H.	2	2.7	3.1	*Ibid.*, 58 (1910), 743.
Ladd, E. F.	17	1.7	5.8	*Bull. Agri. Exp. Sta. N. D.*, 1 (1910), 254.
Vanderkleed, C.	12	2.6	5.33	"Proceedings Pa. Ph. A." (1910), 147.
Caesar & Loretz		2.63	4.06	*Jahres-Bericht* (1910), 50.
Gane & Webster	13	2.13	3.33	*Drug Topics*, 23 (1908), 325.
Vanderkleed, C.	8	2.8	4.03	"Proceedings Pa. Ph. A." (1908), 88.
Smith & Kline	3	3.0	4.00	*Analyt. Rep.* (1908), 23.
Roder, P.	5	2.43	2.71	*Jahres-Bericht* (1908), 117.
Carr & Reynolds		1.14	3.17	*London J. Ph.*, 26 (1908), 543.
Caesar & Loretz	9	3.59	4.22	*Geschaft-Bericht* (1908), 51.
Clark, A.	15		2.5	PROC. A. PH. A., 56 (1908), 836.
Carr & Reynolds		1.14	3.17	*Lon. J. Ph.*, 26 (1908), 543.
Hankey		2.75		"Proc. Pa. Ph. A. (1907), 70.
Vanderkleed, C.	11	2.5	4.4	*Ibid.*, 89.

Reporters.	No. of samples.*	Minn.	Max.	References.
Caesar & Loretz	2	2.68	4.64	*Geschaft-Bericht* (1907), 50.
Roder, P.	11	2.16	2.86	*Jahresb. Wein* (1907), 104.
Roder, P.	15	0.08	3.14	*Pharm. Post.*, 39 (1906), 284.
Smith & Kline	2	2.2	2.85	*Lab. Reports* (1906), 17.
Sayre, L. E.	18	1.55	2.95	Bull. Kans. Bd. Health (1907), 44.
Vanderkleed, C.	7	2.5	3.55 (2)	"Proc. Pa. Ph. A." (1906), 223.
Jones, H. M.	14	2.26	4.22	JOUR. A. PH. A., 4 (1915), 106-108.
Slothmer, G. A.		1.03	1.23	"Pa. Ph. A." (June 21, 1927).
Schmidt, Elsa		1.2	2.69	*A. J. P.*, 71 (1899), 86.

EXPERIMENTAL.

The Hydrastis was obtained from the Skagit Valley Golden Seal Company of Mt. Vernon in the fall of 1927. The farm contains twenty-two acres of Golden Seal, all under artificial slat shade. It is equipped with an efficient irrigation system, also with washing machine and a drying kiln. No restrictions were offered as to the time of collection, quantity, dug, or location of experimental plots. Markers were placed so that the work could be carried on during succeeding years. During the winter, both dried and fresh drug was delivered at the laboratory upon request. An expression of appreciation is hereby implied for the generous cooperation of Mr. J. A. Boyce, president of the Skagit Valley Goldenseal Company.

To further the investigation in Hydrastis and other drug plants, the company has established the Skagit Valley Goldenseal Farm Fellowship, in the University of Washington, College of Pharmacy.[1]

TABLE I.

Stock no.	Yrs. age.	No. of plants.	No. of buds.	Total weight Gm.	Rhizome, Gm.	Root, Gm.	% Wt. rhizome.	% Wt. root.	% Crop compared to No. 3.
7	12	..	..	212	112	100	52.78	47.22	....
3	6	9	76	455	145	310	31.87	68.13	100
4	6	8	74	330	75	255	22.7	77.3	72.5
22	6	..	..	360	100	260	27.8	72.2	....
2	5	12	83	225	65	190	25.5	74.5	56.0
6	4	6	56	132	22	110	16.7	83.3	29.0
1	3	6	54	172	32	140	18.6	81.4	37.8
5	3	5	25	148	33	115	22.3	77.7	32.5

Remarks.—Numbers 3, 4, 2, 6, 1 and 5 were harvested the latter part of September 1927. Four square feet were dug, each from the corner of a bed. Number 7 represents the yield of a circle about 20 inches in diameter; the roots were so intermeshed as to form a solid network about 6 inches thick. Number 5 represented plants propagated from cuttings of 6-year old plants, the age represents the time since the cuttings were planted. This lot was characterized by having root clusters 18 inches long. The samples were washed, air-dried and then placed in the drying kiln having an average temperature of 120° Fahrenheit. Number 22 represents a sample taken from the drying kiln at the Skagit Valley Goldenseal Farm. After the samples were dried a rough count of plants and buds was made, and the sample weighed. The rhizomes and roots were separated by hand, each weighed separately and then ground. All ground samples were preserved in tightly closed glass containers for further investigation.

It is of interest to note that the average ratio of buds to plants is about 9 to 1, No. 5 being the exception. The total weight decreases appreciably with the decrease in years. In

[1] NOTE: A report of the investigation for 1928 and 1929 will be given before the Scientific Section, A. PH. A., at Baltimore, in May 1930.

fact, Nos. 3 and 4 show a decided difference. (Number 22 taken from kiln.) This difference was noticeable even in the farm tract. Number 4 representing a "poor stand" attributed, by the foreman of the farm, to the soil conditions. It may also be assumed, based only on the above table, that the older plants, not only yield a higher total weight, but also a greater percentage yield of rhizome.

NOTE: No definite conclusions may be drawn from only one year's results. This work will be continued with the hope of obtaining information not only of scientific interest but of commercial value also.

This comment applies to all of the experimental data submitted.

TABLE II.

Stock no.	Age.	Alkaloidal Content. Plant.	Rhizome.	Root.	
7	12	3.08	3.44	3.00	
3	6	3.12	3.8	2.8	
4	6	3.00	4.03	2.7	
10	6	2.43			From drying kiln at farm
22	6	2.71	3.1	2.5	From drying kiln at farm
2	5	2.91	3.4	2.77	
6	4	3.00	3.86	2.75	
1	3	3.27	3.30	2.56	
5	3	2.73	3.5	2.6	
8	2	3.00			Regular sowing
9	2	2.20			Thick cluster, spilled seed
12	6				2.30 "nuggets"
13	6			2.70	Rhizomes transplanted, small number
11	6				1.42 fibre from washing
15	6				1.46 fibre from washing (1926 crop)
17	6			1.93	1926 crop, broken off roots
23	2			2.23	Roots cut from plants reset 1927
14					0.88 dried whole leaf from stock
18					2.20 leaf tissue only (see No. 16)
16					0.45 stems only from No. 18
20					1.73 leaf tissue-leaves killed by fungus
19					0.07 stems from No. 20

Remarks.—From the above table it becomes apparent that the total alkaloidal content of the plant does not vary to any great extent irrespective of the age. Numbers 10 and 22 show a lower alkaloidal content than Nos. 3 and 4. All being of the same age. The first two were washed and dried in the farm plant; the second two (3 and 4) in the laboratory. (See Table No. 1—Remarks.) From the information available relative to the process used at the farm, it is assumed that the fault lies in the curing. Experiments are being conducted in an attempt to ascertain this.

As has been reported, the alkaloidal content of the rhizome is greater than that of the roots. The ratio between the two is variable. This difference in alkaloidal content is equalized by the variation in ratio of weight of rhizome to roots.[1] (See Table No. 1.) During the process of washing some of the roots and rootlets are broken off. These are collected, dried and listed as fibre. Numbers 11, 15, 17 represent this by-product. It varies in quality from very fine rootlet to moderately sized root. (No. 17.) Plants taken from the seed bed for resetting, are trimmed before transplating. Number 23 represents these "trimmings." The leaves taken from numbers 1 to 10 were dried in the laboratory, the stems separated from the leaf tissue, by hand, and each assayed separately. Among the leaves were some that were black in color and dry when picked that had been killed by a fungus growth (Nos. 19, 20). Number 14 represents a sample of whole leaf taken from the kiln at the farm. Before harvesting the drug plant, the leaves are removed by pulling. The procedure often removes buds and portions or rhizomes.

[1] NOTE: The results of the 1928 and 1929 investigations seem to indicate that this condition is not constant. The results of these two years do not comply as do the results of 1927.

These "nuggets" are broken off and dried separately. Number 12 represents the dormant leaf bud with a portion of the rhizome (nuggets) obtained from six-year old plants.

The U. S. P. X method of assay was used. The results given being the average of two or more assays. The column indicating the total alkaloidal content is computed, based upon the relative yield weights, and alkaloidal content of the rhizome and roots.

TABLE III.

		% Total Ash.			% Acid Insoluble Ash.			% Acid-Soluble Ash.		
No.	Age.	Plant.	Rhizome.	Root.	Plant.	Rhizome.	Root.	Plant.	Rhizome.	Root.
7	12	5.41	3.55	7.5	1.46	0.66	2.37	3.95	2.89	3.13
3	6	6.67	3.60	8.12	3.15	0.80	4.24	3.52	2.80	3.88
4	6	7.85	3.2	9.18	3.36	0.76	4.28	4.49	2.44	4.90
13	6			5.09			0.99			4.10
10	6	5.08			2.11			2.97		2.97
22	6	4.60	3.26	5.1	0.583	0.47	0.66	4.017	2.99	4.63
2	5	5.5	3.28	6.35	1.92	0.85	2.33	3.58	2.43	4.02
6	4	5.28	3.03	6.65	1.32	0.15	1.56	3.96	2.88	5.09
1	3	5.85	3.29	6.45	1.49	0.74	1.67	4.36	2.55	4.78
5	3	3.02	2.9	3.06	0.677	0.15	0.83	2.34	2.75	2.23
8	2	5.28			0.54			4.74		
9	2	7.58			2.53			5.05		
12			3.48			0.34			3.14	
15				9.47			2.72			6.75
17				7.03			0.75			6.28
11				12.95			4.63			8.32
		Whole Leaf	Tissue	Stems	Whole Leaf	Tissue	Stems	Whole Leaf	Tissue	Stems
14		6.08			1.06			5.02		
16				8.66			1.22			7.44
18			6.55			2.12			4.43	

Remarks.—Considerable variation exists in the amount of acid-insoluble ash found. This is due to the care exercised in washing the samples. Numbers 10 and 22 were washed and dried at the farm plant. These show evidence of a more careful washing than those washed by hand in the laboratory. Numbers 15, 17 and 11 represent samples of small roots and rootlets broken off during the washing process at the farm plant. They are listed as fibre and considered as a by-product. Number 11 was quite fine and dusty. The results given in the columns "plant" were computed, based upon the relative weights of rhizome and roots and their respective ash contents. (See Table No. 1.) The per cent of acid-soluble ash represents the difference between the total and acid-insoluble ash. The U. S. P. X method for ash determination was used.

TABLE IV.

			Ash.			
No.	Age.	% Alkaloid.	Total.	Ac. ins.	H_2O.	Absolute alkaloid.
7	12	3.08	5.41	1.46	4.47	3.27
3	6	3.12	6.67	3.15	2.954	3.32
4	6	3.00	7.85	3.36	2.68	3.19
10	6	2.43	5.08	2.11	5.0	2.61
22	6	2.71	4.60	0.583	4.28	2.85
2	5	2.91	5.50	1.92	3.0 (Rt)	3.06
6	4	3.00	5.28	1.32	4.0 (Rt)	3.13
1	3	3.27	5.85	1.49	3.0 (Rt)	3.41
5	3	2.73	3.02	0.677	5.0 (Rt)	2.89
8	2	3.00	5.28	0.54	4.07	3.15
9	2	2.20	7.58	2.53	3.47	2.34

Remarks.—Table No. 4 offers a summary of the analysis of the whole drug. The absolute alkaloidal content was computed, and represents the drug with no moisture present and no

acid-insoluble ash. The average for the above is 3.02 per cent; with the plants varying in age from 2 to 12 years. Various deductions may be made. However, this is considered as preliminary work, and the results of future years' investigation are necessary before conclusions may be offered.

APPENDIX.

Attention has been called to the difference in alkaloidal content of several lots taken from the tract containing 6-year old plants. (See Table No. 2—compare Nos. 3 and 4 with Nos. 10 and 22.) On the assumption that, apparent loss of alkaloids in the farm plant cured drug was due to the curing process used, several preliminary, but crude tests were carried out in an attempt to ascertain if exposing the freshly washed drug to a high degree of heat, would affect the alkaloidal content.

Ten-gram samples of the powdered Hydrastis were thoroughly wetted with water. These samples were dried in a hot air oven using different temperatures. The length of time to dry the samples approximated about forty-eight hours.

The samples were assayed according to the U. S. P. X method. The following table represents the results obtained from the experiment:

No.	Part.	Temperature.	% Alkaloid.	% Alkaloid before wetting.	% Loss.
4	Root	120–127° C.	1.495	2.67	43.8
3	Root	120–127° C.	1.70	2.83	39.4
12	Fibre	100° C. 6 hrs. 35° 24 hrs.	2.07	2.35	29.0
4	Root	100° C. 6 hrs. 35° 24 hrs.	2.088	2.67	21.8
5	Root	35° C.	2.35	2.62	10.5
2	Root	35° C.	2.234	2.77	19.3

The results would seem to indicate that the maximum temperature for drying the drug is considerably below 35° C. Material has been obtained for carrying on the investigation on fresh plants.

Hydrastine is hydrolyzed into hydrastinine and opianic acid when high heat is applied, or in the presence of oxidizing agents and water as follows:

$$\underset{\text{Hydrastine}}{C_{21}H_{21}O_6N} + HCH \qquad \underset{\text{Opianic acid}}{C_{10}H_{10}O_5} + \underset{\text{Hydrastinine}}{C_{11}H_{13}O_2N}$$

M. W. 383.28 M. W. 207.112

Complete oxidation of the Hydrastine would yield 54.036 per cent of its weight as hydrastinine.

UNIVERSITY OF WASHINGTON,
COLLEGE OF PHARMACY,
SEATTLE.

THE EFFECT OF CERTAIN HYPOGLYCEMIC DRUGS UPON THE GROWTH OF THE SEEDLINGS OF LUPINUS ALBUS.

BY JOHN C. KRANTZ, JR.

Introduction.—In 1923 Ellis and Eyster (1) studied the effect of insulin and glucokinin upon the growth of maize seedlings. They observed that either of these drugs in concentrations less than 0.005 per cent promoted the growth of these seedlings whereas in concentrations greater than this value a definite retardation of