A NOTE ON THE ASSAY OF HYOSCYAMUS.[1]

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The present method of the United States Pharmacopœia for the assay of hyoscyamus and its preparations has been subject to much criticism but, although the literature on the subject is extensive, no definite modifications have been suggested. The amount of alkaloid in the tincture, as well as in the crude drug, is so minute that it is difficult to obtain closely-agreeing results by the present method of analysis.

Caines (1) made a study of several methods for the assay of hyoscyamus and its extracts with the view of ascertaining whether the assay methods for belladonna were applicable to hyoscyamus. Markwell and Walker (2) noted that the method of the British Pharmacopœia for the assay of belladonna leaves is not identical with that of the extract and the tincture. In the former case no heat is used to drive off the chloroform before titration, while in the latter case the chloroformic extract is heated, thereby driving off the volatile alkaloids and causing low and inconsistent results. Exler (3), after a study of the stability of hyoscyamine under conditions experienced in assay procedures, advises the avoidance of assay procedures which will tend to hydrolyze the alkaloids. Reindollar (4) has shown that the U. S. P. X method for the assay of tincture of hyoscyamus is not sufficiently accurate to insure concordant results in the hands of different skilled analysts using special precautions as suggested by Mr. Reindollar. He prepared a specimen with great care and submitted portions to each of three expert analysts. The results were not in agreement, although each chemist checked his own results quite well. Stikarofsky (5) submitted specimens of tincture of hyoscyamus to four independent analysts to be assayed according to the U. S. P. X method. These results did not check and he concluded that the variations were due, at least in part, to prolonged heating of the alkaloidal extractions before titrating. The U. S. P. X in referring to the evaporation of solvents specifies that, due to the sensitivity of the alkaloids of hyoscyamus to heat, the solutions of these alkaloids should not be evaporated to dryness on a water-bath. It was suggested that the drug and the tincture be assayed by the U. S. P. X method with the slight modification that no heat be used in any of the evaporations.

The U. S. P. X type process B for drugs and type process D for galenicals were used, respectively, for the assay of the crude drug and the tincture. In order to hasten and facilitate evaporation of the alcohol from the tincture, and the solvent from the immiscible-solvent extractions, a vacuum desiccator was used. This was fitted with a two-hole rubber stopper through which were inserted two glass tubes, one of which was drawn out into a very fine capillary, which dipped just below the surface of the liquid undergoing evaporation. This solution can be placed in a deep crystallization dish of suitable diameter to fit into the desiccator. By applying suction to the other tube, a very fine stream of air bubbles can be drawn through the solution. By means of a screw-clamp and rubber tube attached to the glass tube drawn into a capillary the stream of air bubbles and the amount of vacuum

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can be regulated. The temperature of the laboratory in which the samples were analyzed varied from 18°–25° C. In the titration of the alkaloids, twentieth-normal acid was substituted for tenth-normal acid, and a dilution of methyl red, the indicator used, was kept nearby as a comparator for the end-points, all of which were run to a standard tint. In order to show the comparison between the U. S. P. X method and the same method without any heat being used in the evaporations, the crude drug and the tincture were assayed by both procedures and the results are shown in the following tables:

TABLE I.—ASSAY OF CRUDE DRUG.

Results expressed as % total alkaloids (as Hyoscyamine).

U. S. P. X Method.		U. S. P. X Method, Absence of Heat, Use of Vacuum Desiccator for Evaporation of Solvents.	
Sample 1	0.054	Sample 1	0.075
2	0.052	2	0.077
3	0.050	3	0.074
4	0.055	4	0.076
5	0.049	5	0.077
Average	0.052	Average	0.076

TABLE II.—ASSAY OF TINCTURE OF HYOSCYAMUS.

Results expressed as grams per 100 cc. of total alkaloids (as Hyoscyamine).

U. S. P. X Method.		U. S. P. X Method, Absence of Heat, Use of Vacuum Desiccator for Evaporation of Solvents.	
Sample 1	0.00514	Sample 1	0.00836
2	0.00448	2	0.00707
3	0.00321	3	0.00770
4	0.00386	4	0.00717
5	0.00257	5	0.00900
6	0.00323	6	0.00885
7	0.00295	7	0.00805
8	0.00350	8	0.00779
9	0.00250	9	0.00811
10	0.00523	10	0.00830
Average	0.00367	Average	0.00804

SUMMARY.

The U. S. P. X method for the assay of the tincture of hyoscyamus, as well as for the crude drug, appears to be satisfactory if proper precautions are taken to preserve the alkaloids against decomposition by heat during the assay procedure.

Higher yields can be obtained by avoiding heat during evaporation of the solvents. The increase in yield by the U. S. P. method, using no heat in the evaporations is probably due, in part, to ammonia soaps extracted along with the alkaloids.

The use of a vacuum desiccator is suggested in order to hasten and facilitate evaporation at room temperatures.

LITERATURE CITED.

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(2) Markwell and Walker, *Chemist and Druggist*, 109 (1928), 525.

(3) Exler, *Pharm. Weekblad*, 65 (1928), 1152.
(4) Reindollar, JOUR. A. PH. A., 14 (1925), 789.
(5) Stikarofsky, *Ibid.*, 16 (1927), 30.

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THE PHARMACOGNOSY, CHEMISTRY AND PHARMACOLOGY OF VIBURNUM. III. HISTORY, BOTANY AND PHARMACOGNOSY OF VIBURNUM OPULUS L. VAR. AMERICANUM (MILLER) AIT.*

BY HEBER W. YOUNGKEN.

INTRODUCTION.

The American variety of *Viburnum Opulus* has been the theme of many contradictory discussions and reports within the past half century alike by botanists, pharmacognosists and pharmacologists. The purpose of this investigation, at least so far as the botanical and pharmacognic phases are concerned, is an attempt to straighten out this tangle first through historical studies and then by new research work upon authentic plants, representative specimens of which, including separated barks, have been permanently deposited in the herbarium of the Massachusetts College of Pharmacy.

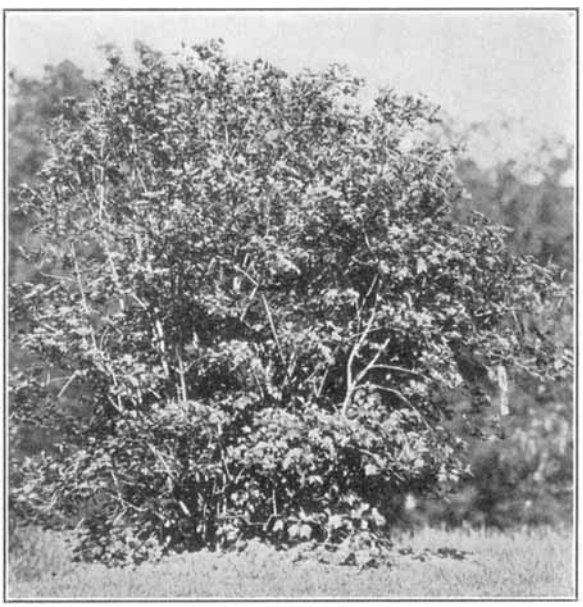

Fig. 1.—*Viburnum Opulus* Linné var. *americanum* (Miller) Aiton. Shrub growing in Arnold Arboretum.

Detailed reports upon the chemistry and pharmacodynamics of the botanically standardized bark of this species will be published later by the collaborators on these phases of the investigation who are Florin J. Armhein (on chemistry) and James C. Munch (on pharmacodynamics).

HISTORY.

The taxonomic history of this plant takes us back to less than a decade before the American Revolution.

As early as 1768 Philip Miller in his Gardener's Dictionary (1) briefly described it as a distinct species which he named *Viburnum Americanum* or American Guelder Rose. He took

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