The Alkaloid of *Banisteriopsis inebrians* Morton*

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The stems of *Banisteriopsis inebrians* were found to contain 0.15 per cent of the alkaloid harmine, but the other alkaloids that accompany harmine in *peganum harmala* could not be detected. The leaves were found to contain an alkaloid which was partly identified as harmine.

BANISTERIOPSIS INEBRIANS (*Malpighiaceae*) was first described by Morton in 1931 as a tall liane, climbing more than 300 meters. The branches are terete and smooth, with thorns up to 4 millimeters in diameter, and bearing numerous, brown, glabrous lenticels. The leaves are broadly elliptical, olive-green in color, and glabrous except for a few persistent hairs (1).

In some South American countries the natives use in certain ceremonial rites an indefinite mixture of plants that they call "yage." According to Holmes, Bayon extracted from one of these mixtures an alkaloid that he named telepathine because of the physiological action of yage (2). Later, Villalba examined a plant called yage and separated from it two alkaloids that he named yageine and yagenine (3).

In 1924 Rusby identified a plant called yage in the Amazon Basin as *Banisteria caapi* Spruce (4), since then renamed by Morton as of the genus *Banisteriopsis* (5). Seil and Putt extracted from Rusby's samples three alkaloids, but did not investigate their properties (6). In 1928 Merck isolated the principal alkaloid and named it banisterine (7), but subsequent investigators have identified it as harmine (8, 9), previously obtained from the seeds of *Peganum harmala* L. (10). It has not been definitely established that *B. caapi* contains more than one alkaloid, nor that yageine and telepathine were from this plant, although both of the last names, as well as banisterine, are commonly given as synonyms of harmine. Yagenine has not been confirmed, nor have the second and third alkaloids of Seil and Putt.

EXPERIMENTAL

The material used in this study was received by Heber W. Youngken of the Massachusetts College of Pharmacy from Columbia, South America. It consisted of the stems and the leaves of *Banisteriopsis inebrians* Morton, as identified by him and confirmed by R. E. Schultes of the Bureau of Plant Industry, Washington, D. C.

The total amount of alkaloids was estimated in the coarsely ground stems, using the method described for belladonna leaf U. S. P. XIV. The value found was 0.145%, calculated as harmine $C_{13}H_{12}N_2O$.

Isolation of Alkaloids.—Approximately 700 Gm. of the coarsely ground stems was moistened with a mixture of 1 part of stronger ammonia water, 1.25 parts of alcohol, and 2.5 parts of ether. The moistened material was packed into a large Soxhlet apparatus and allowed to macerate for twelve hours, after which time it was exhausted by percolation with chloroform. The chloroformic solution was completely extracted with normal sulfuric acid. After filtration, the acid solution was heated to boiling and rendered alkaline with stronger ammonia water, giving a fine brown precipitate. This precipitate was filtered, dried, redissolved in chloroform, again extracted with acid, and precipitated with ammonia water. After heating the mixture, the precipitate assumed the form of conglomerates of brown, needle-shaped crystals, which were removed by filtration and dried.

Purification.—The dried precipitate was dissolved in a minimum amount of hot methanol, mixed with activated charcoal, and heated for several minutes on a water bath. The hot mixture was filtered, and the filtrate upon standing deposited white, shiny crystals which were filtered, washed, and dried at room temperature. The melting point of 260° (corr.) with some decomposition was not altered by recrystallization. The compound was soluble in alcohol, methanol, chloroform, or acids, but was only slightly soluble in water or alkalies.

The Hydrochloride.—A portion of the alkaloid was dissolved in alcohol, and to this solution was added ether acidified with hydrochloric acid. The hydrochloride precipitated from the mixture in the form of white crystals. It gave a blue fluorescence under ultraviolet light and melted at 261° with decomposition. In the anhydrous state it melted at 319° and contained about 12.5% of chlorine.

Identification.—The identity of the alkaloid as harmine was determined by comparison with a carefully purified sample from the seeds of *Peganum harmala* L. Both gave the same spectrogram, with minimum absorption at 272 mμ and maximum absorption at 300 mμ. Both melted at about 260° with decomposition, and a 50% mixture of the two melted at the same temperature. The hydrochlorides were both colorless but gave a blue fluorescence under ultraviolet light.

Other Alkaloids.—No evidence could be obtained for the presence of any other alkaloid. Harmaline, which can be detected by Amelink's acetaldehyde test (11) in the crude product from *Peganum harmala*, was not present in the precipitated alkaloids

* Received July 14, 1953, from the Massachusetts College of Pharmacy, Boston, Mass.
Presented to the Scientific Section, A. PH. A., Salt Lake City meeting, August, 1953.
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of *B. inebrians*. Harmalol is easily demonstrated in harmala by the green fluorescence under ultraviolet light of an aqueous solution, but no such evidence could be found for its occurrence in *B. inebrians*.

The Leaves.—The leaves were extracted in a manner similar to the one used for the stems. A solution of the resulting product in hydrochloric acid gave a precipitate with Mayer's reagent and a blue fluorescence under ultraviolet light. In view of these facts, it may be assumed that harmine is also present in the leaves.

REFERENCES

(1) Morton, L., *J. Wash. Acad. Sci.*, **21**, 486(1931).
(2) Holmes, E., *Pharm. J.*, **119**, 111(1927).
(3) Villalba, B., *J. Soc. Chem. Ind. (London)*, **44**, 205T (1925).
(4) Rusby, H., THIS JOURNAL, **13**, 98(1924).
(5) Morton, L., *Proc. Biol. Soc. Wash.*, **43**, 157(1930).
(6) Seil, H., and Putt, E., THIS JOURNAL, **13**, 99(1924).
(7) Merck, E., *J. Soc. Chem. Ind. (London)*, **47**, 542 (1928).
(8) Dalmer, O., *Deut. med. Wochschr.*, **55**, 1592(1929).
(9) Brückl, K., *Z. Krist.*, **74**, 202(1930).
(10) Göbel, F., *Ann.*, **38**, 363(1841)
(11) Amelink, J., *Pharm. Weekblad.*, **68**, 221(1931).

Notes

A Note on the Use of Amberlite IR-45 in the Ion Exchange of Sympathomimetic Amines*

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WORK IN THIS laboratory[1] on the determination of sympathomimetic amines by means of ion exchange has shown that the various methods reported in the literature for amines (1-3) were not satisfactory with all of our compounds. A number of ion exchange resins were used experimentally by the authors. Amberlite IR-45 was found to be suitable for the quantitative separation of a large group of sympathomimetic amines including several which have phenolic groups and could not be satisfactorily separated with other ion exchange resins.

EXPERIMENTAL

Procedure.—Eight grams of the anion exchange resin, Amberlite IR-45, were soaked in 25 ml. of distilled water for twenty-four hours. With the aid of additional distilled water the mixture was poured into a chromatographic column, 2 cm. x 20 cm., in which a small piece of glass wool had previously been placed. Another small piece of glass wool was placed on the top of the column. The resin was regenerated before each determination by passing 50 ml. of 4% sodium carbonate solution through the column. The column was washed free of sodium carbonate with 200 ml. of previously boiled and cooled distilled water.

Twenty-five to 50 mg. of amine salt was dissolved in 25 ml. of 50% ethyl alcohol, the solution was passed through the column, and the filtrate was collected and saved. The column was then rinsed with an appropriate amount of 75% ethyl alcohol to remove the amine base, and the rinsings were added to the filtrate. The combined solution was titrated with 0.1 *N* hydrochloric acid using a *p*H meter or 2 drops of methyl red T. S. as indicator. The results are recorded in Table I.

TABLE I.—RECOVERY OF SYMPATHOMIMETIC AMINES

Amine Salt	75% EtOH Required to Remove Free Amine from Column, Ml.	Recovery, %
1-Ephedrine sulfate	200	100.05, 98.85, 98.55, 98.26
Racephedrine sulfate	200	99.93, 99.61, 97.45
Propadrine hydrochloride	100	98.94, 98.16
Paredrine hydrobromide	200	98.43, 98.23
Aramine hydrogen tartrate	200	99.14, 98.67, 98.24, 97.20
Orthoxine hydrochloride	200	99.99, 99.94, 98.95
Privine hydrochloride	200	99.85, 99.60, 99.60
Vonedrine hydrochloride	200	100.06, 99.03, 98.27
dl-Methamphetamine hydrochloride	200	99.81, 99.75, 99.00
d-Methamphetamine hydrochloride	200	100.56, 99.62, 99.36
Tuamine sulfate	200	98.47, 97.20

Details of this and further work in the ion exchange and separation of sympathomimetic amines will be published at a later date.

REFERENCES

(1) Baggesgaard-Rasmussen, H., Fuchs, D., and Lundberg, L., *J. Pharm. Pharmacol.*, **4**, 566(1952).
(2) Jindra, A., and Rentz, J., *ibid.*, **4**, 645(1952).
(3) Jindra, A., and Rentz, J., *Ceskoslov. farm.*, **1**, 625 (1952); through *Chem. Abstr.*, **47**, 5071(1953).

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