[CONTRIBUTION FROM THE SCHOOL OF PHARMACY OF THE UNIVERSITY OF THE PHILIPPINES]

THE ALKALOIDS OF ARGEMONE MEXICANA

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Many years ago Schlotterbeck[1] has shown that *Argemone mexicana*,[2] which is more familiarly known as mexican or prickly poppy, does not contain morphine. He isolated two alkaloids from this plant and on the basis of precipitation and color reactions he concluded that one of them was berberine. He identified the other alkaloid as protopine because of its melting point (204°) and color reactions.

Since then many alkaloids of the berberine type have been reported in the literature. According to Feist[3] palmatine gives also an acetone compound and responds to other reactions which Gordin[4] used for the identification of berberine. It appears, therefore, that the identification of berberine can no longer be done by precipitation and color reactions alone. In view of the foregoing reasons and of the fact that Schlotterbeck did not analyze his alkaloids, the present authors deemed it necessary to reinvestigate this plant.

By a method of isolation described in the experimental part, two alkaloids have been isolated from *Argemone mexicana*. One is a quaternary and the other is a tertiary base. The former was converted by reduction into a colorless tertiary base melting at 173–174° which by analysis and mixed melting point proved to be identical with tetrahydroberberine. The second base crystallized from a mixture of chloroform and methanol in nice monoclinic prisms melting at 207°. It responded to all the color reactions of protopine and on the basis of elementary analysis and mixed melting point with authentic material kindly furnished by E. Merck, Darmstadt, it was recognized as protopine.

Therefore, the assumption of Schlotterbeck that *Argemone mexicana* contains berberine and protopine proved to be correct.

Experimental

The material used consisted of whole plants collected at San Juan, La Union, and carefully deprived of the seeds; 568 g. of the air-dried powdered material was extracted until free from alkaloids with alcohol acidified with acetic acid. The alcohol was recovered from the alcoholic extract, the residue taken up with acidified water and filtered. The filtrate was first shaken out with ether in acid solution to remove neutral and indifferent substances, then rendered alkaline with potassium hydroxide and

[1] Schlotterbeck, THIS JOURNAL, **24**, 238 (1902).

[2] A native of tropical America. Introduced into the Philippines and known locally as *diluariu*, *kachumba* and *kasubang-aso*.

[3] Feist, *Arch. Pharm.*, **245**, 596 (1907).

[4] Gordin, *ibid.*, **240**, 146 (1902).

shaken out again with ether. The aqueous portion (A) was acidified with hydrochloric acid and set aside. On spontaneous evaporation of the ether a partly crystalline and sirupy residue remained. It was dissolved in diluted hydrochloric acid; rendered alkaline with potassium hydroxide and shaken out again with ether, this process being repeated many times until a white residue was left. This was dissolved in a little chloroform and an equal amount of methanol added. After three weeks' standing clusters of nice monoclinic prisms melting at 207°[5] separated. The melting point of a mixture of an equal amount of these crystals and protopine (m. p. 207°) furnished by E. Merck, Darmstadt, was 207°. The crystals gave the following color reactions: (1) with sulfuric acid, deep blue-violet; (2) with Froehde's reagent, violet-green changing to deep blue and finally becoming green; (3) with Mandelin's reagent, violet, then bluish-green, and finally blue; (4) with concentrated nitric acid, colorless in the cold, turning yellow on heating. The microanalysis gave values agreeing fairly with the values calculated for protopine.

Anal. Subs., 2.371 mg.: CO_2, 5.893 mg.; H_2O, 1.261 mg. Calcd. for $C_{20}H_{19}O_5N$: C, 67.95; H, 5.48. Found: C, 67.78; H, 5.95.

Tetrahydroberberine.—The yellow aqueous acid solution (A) that had been set aside in the isolation of protopine was reduced with zinc dust and sulfuric acid until the solution became almost colorless and filtered. The filtrate was cooled rapidly, treated with ammonia water until the precipitated zinc hydroxide redissolved and shaken out with ether. The ethereal solution was repeatedly shaken with dilute potassium hydroxide, washed with a little water and dried. On concentrating the ether crystals melting at 173–174°[6] separated. The melting point of a mixture of these crystals with tetrahydroberberine (m. p. 173–174°) was 173–174°.

Microanalysis. Subs., 2.720 mg.: CO_2, 7.089 mg.; H_2O, 1.509 mg. Subs., 2.609 mg.: AgI, 3.558 (Zeisel–Pregl–Friedrich). Calcd. for $C_{20}H_{21}O_4N$: C, 70.74; H, 6.24; OCH_3, 18.29. Found: C, 71.08; H, 6.21; OCH_3, 18.01.

Summary

The alkaloids of *Argemone mexicana* have been correctly identified as berberine and protopine.

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[5] The melting point of pure protopine is reported at 207° by W. H. Perkin, Jr., *J. Chem. Soc.*, **109**, 1023 (1916), and by P. W. Danckwortt, *Arch. Pharm.*, **250**, 615 (1912).

[6] Späth and Polgar, *Monatsh.*, **52**, 117 (1929), reported that pure tetrahydroberberine melts at 173–174°.