163. *A New Alkaloid from the Bark of* Holarrhena Antidysenterica.

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The bark of *Holarrhena antidysenterica* is used in Burma as a remedy for dysentery and as a febrifuge under the name of lettôk. An examination of the bark derived from local sources has shown the existence of another alkaloid in addition to those already described by other workers. The alkaloid content of the bark varied between 1·36 and 1·2%. The alkaloids were extracted by three methods : (1) cold dilute hydrochloric acid, (2) cold alcohol, (3) hot alcohol. A second extraction with alcoholic ammonia (Siddiqui and Pillay, *J. Indian Chem. Soc.*, 1933, **10**, 673) yielded an extra 0·1—0·2% of alkaloids. The crude alkaloids were isolated from the solutions in the usual way and an alkaloid giving a hydrochloride soluble in water but sparingly soluble in hydrochloric acid was found. This base, $C_{17}H_{25}O_2N$, was purified through the *hydriodide*, m.p. 256° (decomp.), and obtained as a light brown powder, m. p. 350—352°. It does not appear to be identical with any of the alkaloids previously described as present in the bark of *Holarrhena antidysenterica* (conessine, $C_{24}H_{40}N_2$, m. p. 125°, Haines, *Pharm. J.*, 1865, ii, **6**, 432; conessimine, $C_{20}H_{38}N_2$, m. p. 100°; holarrhine, $C_{20}H_{38}O_3N_2$, m. p. 240°; holarrhimine, $C_{21}H_{36}ON_2$, m. p. 183°, Siddiqui and Pillay, *J. Indian Chem. Soc.*, 1932, **9**, 553; *iso*conessimine, $C_{23}H_{38}N_2$, m. p. 92°; conimine, $C_{22}H_{36}N_2$, m. p. 130°, *idem*, *ibid.*, 1934, **11**, 283; holarrhemine, $C_{24}H_{38}ON_2$, m. p. 197°, Pyman, J., 1919, **115**, 63; kurchine, $C_{23}H_{38}N_2$, m. p. 75°; kurchicine, $C_{20}H_{36}ON_2$, m. p. 175°, Ghosh and Ghosh, *J. Indian Chem. Soc.*, 1928, **5**, 477; norconessine, $C_{23}H_{38}N_2$, b. p. 240°/0·7 mm., R. D. Haworth, J., 1932, 631; conessidine, $C_{21}H_{32}N_2$, m. p. 123°; conkurchine, $C_{22}H_{32}N_2$, m. p. 153°; kurchenine, $C_{21}H_{32}O_2N_2$, m. p. 335—336°, Bertho, Schuckmann, and Schönberger, *Ber.*, 1933, **66**, 786) and the name *lettocine* is suggested for it. It appears to be a tertiary base and to contain no hydroxyl groups. The amount present in the bark is less than 0·1% and we are accumulating a sufficient quantity for further examination. The aqueous mother-liquor after the extraction of alkaloids by chloroform was tested for quaternary ammonium bases, but none were found.

No alkaloids were found in the latex of the tree. Alcoholic extraction yielded two colourless crystalline solids of the resinol type which are under investigation.

Experimental.

1580 G. of the powdered bark were extracted with 7 l. of 1% hydrochloric acid and the solution was made faintly acid to Congo-red with 10% aqueous ammonia and extracted with chloroform. The aqueous solution was basified with aqueous ammonia and the precipitated alkaloids were extracted in chloroform, dried, and recovered (14·5 g.). Alternatively, 4200 g. of the bark were extracted with 6 l. of rectified spirit, the solution distilled under reduced pressure, the residue treated with 1% hydrochloric acid, and the alkaloids isolated as before (35 g.). The crude bases (49·5 g.) were treated with 700 c.c. of 5% hydrochloric acid; the insoluble hydrochloride was collected and dissolved in water (300 c.c.), and the solution made alkaline with 10% aqueous ammonia and extracted four times with chloroform. The chloroform extract was shaken with 5% hydrochloric acid, and the aqueous solution added to the above solution of hydrochlorides, but the precipitated hydrochloride was filtered off and dissolved in water. This solution was basified with ammonia and extracted with chloroform, and the alkaloid recovered (5·7 g.) was dissolved in rectified spirit (20 c.c.), and 10% hydriodic acid added until the solution was acid to Congo-red. The dark brown *hydriodide* (5·9 g.) was crystallised twice from hot rectified spirit and obtained as a yellowish-brown, microcrystalline powder, m.p. 256° (decomp.) [Found : I, 31·9 (Carius), 32·8, 32·6. $C_{17}H_{25}O_2N$,HI requires I, 31·5%].

The hydriodide, triturated with aqueous ammonia, gave *lettocine*. This separated from chloroform–light petroleum as a light brown, microcrystalline powder, m.p. 350—352° [Found : C, 74·4, 74·9; H, 8·9, 8·9; N, 5·1, 5·2; *M* (ebullioscopic in chloroform), 298, 313, 292, 284, 295. $C_{17}H_{25}O_2N$ requires C, 74·2; H, 9·1; N, 5·1; *M*, 275]. The base is soluble in alcohol and chloroform, sparingly soluble in ether and light petroleum. The picrate, crystallised from hot absolute alcohol, had m. p. 198°. The oxalate was soluble in water and sparingly soluble in ethyl alcohol. The base was recovered unchanged after some hours' boiling with acetic anhydride.

The base was (1) dissolved in aqueous oxalic acid and extracted four times with ether, and (2) made into a paste with lead hydroxide and extracted with alcohol; in both cases it was recovered unchanged in m. p. Crystallisation from ethyl alcohol–acetone also left the m. p. unchanged.

The Methiodide.—The base (0·3 g.) was boiled for 3 hours with methyl alcohol (5 c.c.) and methyl iodide (1 c.c.). The solvent was distilled, and the dark brown residue crystallised from hot methyl alcohol; m. p. 235° (Found : I, 30·5. $C_{18}H_{28}O_2NI$ requires I, 30·6%).

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