

V.—*Hydroxycodine: a New Alkaloid from Opium.*

By JAMES JOHNSTON DOBBIE and ALEXANDER LAUDER.

THE new opium alkaloid, which forms the subject of this communication, was discovered by Messrs. T. and H. Smith, of Edinburgh, who were good enough to place a small quantity of the hydrobromide in our hands for investigation. The alkaloid is found in very small quantity in the last mother liquors obtained in the working up of the opium alkaloids, after all the other alkaloids have been eliminated.

The alkaloid is readily soluble in water, alcohol, ether, chloroform, benzene, or amyl alcohol, but, so far, has not been obtained in a crystalline condition. From all these solvents it separates in the form of a varnish. The alkaloid has no definite melting point; on heating, it begins to soften about 40° , and is completely melted at 51° .

Of the common salts, the *hydrobromide* and the *hydrochloride* both crystallise well; the hydrobromide is, however, much less soluble than the hydrochloride, and it was therefore selected for analysis. It readily crystallises from water in large, hard, prismatic crystals, which contain no water of crystallisation. The crystals were dried at 100° , and gave the following results on analysis:

0.3344 gave 0.6678 CO_2 and 0.1808 H_2O . $\text{C}=54.46$; $\text{H}=6.00$.

0.3318 „ 0.6614 CO_2 „ 0.1680 H_2O . $\text{C}=54.36$; $\text{H}=5.62$.

0.4502 „ 14 c.c. N_2 (moist) at 17° and 742 mm. $\text{N}=3.52$.

0.2988 „ 9 c.c. N_2 (moist) „ 14.4° and 754 mm. $\text{N}=3.50$.

0.6056 „ 0.284 AgBr . $\text{Br}=19.95$.

0.5210 „ 0.244 AgBr . $\text{Br}=19.92$.

Mean, $\text{C}=54.41$; $\text{H}=5.81$; $\text{N}=3.51$; $\text{Br}=19.94$.

$\text{C}_{18}\text{H}_{21}\text{O}_4\text{N}\cdot\text{HBr}$ requires 54.54 ; $\text{H}=5.55$; $\text{N}=3.53$;

$\text{Br}=20.20$ per cent.

Platinichloride.—The alkaloid was dissolved in dilute hydrochloric acid, and precipitated with excess of platinum chloride; the precipitate was well washed, and dried at 100° for analysis:

0.3258 gave 0.4942 CO_2 and 0.1296 H_2O . $\text{C}=41.36$; $\text{H}=4.42$.

0.2452 „ 0.3725 CO_2 „ 0.0975 H_2O . $\text{C}=41.43$; $\text{H}=4.44$.

0.2744 „ 7 c.c. N_2 (moist) at 14° and 755 mm. $\text{N}=2.98$.

0.1768 „ 0.0328 Pt . $\text{Pt}=18.55$.

0.2764 „ 0.2280 AgCl . $\text{Cl}=20.39$.

$(\text{C}_{18}\text{H}_{21}\text{O}_4\text{N})_2\text{H}_2\text{PtCl}_6$ requires $\text{C}=41.54$; $\text{H}=4.23$; $\text{N}=2.69$;

$\text{Pt}=18.75$; $\text{Cl}=20.48$ per cent.

Determination of Methoxyl Groups.—The number of methoxy-groups was determined by Zeisel's method:

0.4052 gave 0.2408 AgI. OMe=7.82.

0.3426 „ 0.2064 AgI. OMe=7.93.

OMe·C₁₇H₁₈O₃N·HBr requires OMe=7.83 per cent.

Methiodide.—The methiodide was prepared by dissolving a small quantity of the alkaloid in a mixture of methyl iodide and methyl alcohol. The methiodide separated in colourless plates. It was recrystallised from methyl alcohol, and dried over sulphuric acid:

0.2076 gave 0.1098 AgI. I=28.57.

C₁₉H₂₄O₄NI requires I=27.79 per cent.

This result is sufficient to show that the alkaloid is a tertiary base.

Specific Rotation.—An aqueous solution of the hydrobromide is slightly dextrorotatory:

I. 5.1884, in 100 of water, gave, in a 1-dcm. tube at 20°, α + 0.9°; D_D²⁰ 1.0158; whence [α]_D²⁰ + 17.07°.

II. 5.0741, in 100 of water, gave, in a 1-dcm. tube at 20°, α + 0.9°; D_D²⁰ 1.0154; whence [α]_D²⁰ + 17.4°.

Colour Reactions.—With Fröhde's reagent, the new alkaloid gives a yellowish-green colour, which gradually changes to blue; and with Mandelin's reagent a yellowish-green, also changing to blue on keeping. These reactions are practically identical with those given by codeine with the same reagents.

Absorption Spectra.—The absorption spectra of an aqueous solution of the hydrobromide were photographed. The spectra show a well-marked absorption band at 1/λ 3500. The position of this band is identical with that of codeine (Hartley, *Phil. Trans.*, 1885, Part II, 471; Dobbie and Lauder, *Trans.*, 1903, **83**, 605), but the codeine band is very slightly more persistent.

The discoverers propose the name *neopine* for the new alkaloid. Although, owing to the small quantity of material at our disposal, the chemical evidence is still incomplete, the alkaloid is almost certainly a hydroxycodine, but it is not identical with the hydroxycodine prepared by Ach and Knorr (*Ber.*, 1903, **36**, 3067) by the oxidation of codeine. Its formula differs from that of codeine only in the possession of an additional atom of oxygen, which, owing to the solubility, is probably present in an hydroxyl group. Like codeine, it contains only one methoxyl group. Further evidence of the close relation between the two alkaloids is afforded by the practical identity of their absorption spectra.

The physiological action of the new alkaloid has been investigated by Professor Stockman, of Glasgow University.

THE GOVERNMENT
LABORATORIES, LONDON.

EDINBURGH AND EAST OF SCOTLAND COLLEGE
OF AGRICULTURE, EDINBURGH.