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THE ALKALOIDS OF CORYDALIS AMBIGUA, CHAM ET SCH. (YEN-HU-SO) PART II. CORYDALIS F, G AND H.

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In a previous communication on Chinese Corydalis (Yen-hu-so) (1), the writer reported the isolation of five alkaloids from a non-phenolic fraction "2". They are provisionally named Corydalis A, Corydalis B, Corydalis C, Corydalis D, and Corydalis E, respectively. Corydalis A is identical with Corydaline in all respects and the other four are new. A preliminary examination of the physiological effects of Corydalis B by H.P. Chu (1) showed that it has narcotic and local anaesthetic properties and a cardiac augmentor action. The Corydalis B, used in Chu's experiments, was in the form of the hydrochloride which is only slightly soluble in cold water and causes some inconvenience in its administration. The preparation of other salts of Corydalis B was therefore attempted. It is now found that its neutral sulphate, crystallizing out from alcohol in six-sided prisms, is easily soluble in water, giving rise to a neutral solution, and consequently is more suitable for therapeutic use. The alkaloids, present in the other three fractions 1,3 and 4, have now been studied and 3 of them isolated in their pure state. Fraction 1, which is obtained by simply extracting the crude drug with benzene, consists of Corydalis A (Corydaline) and Corydalis D as its chief constituents. Fraction 3 which is phenolic and soluble in caustic alkalies, gives rise to two new phenolic bases, Corydalis F and Corydalis G, both of them having the same melting point but differing from each other in their optical activity, crystalline form and colour reactions. Corydalis F crystallises out from a mixture of chloroform and alcohol in the form of rhomboid crystals, melting at 237°C and has a specific rotation −250°.

Its molecular formula corresponds to $C_{20}H_{23}O_4N$ or $C_{20}H_{24}O_4N$. Corydalis G melts also at 237°, but crystallises out in the form of prisms and has a specific rotation of +300°. On account of the small amount of Corydalis G in hand, its molecular formula has not yet been determined. In 1923, Späth, Mosettig and Tröthandl (2) isolated from Corydalis tuberosa, corypalmine, a phenolic base, having a melting point 235–236°, a molecular formula $C_{20}H_{23}O_4N$ and a specific rotation (α) 16/D=+280°. It is consequently identical with Corydalis F in its melting point and molecular formula, but differs from it in its optical activity; whether it is identical with Corydalis G or not has to be further investigated. From fraction 4, a base in the form of its hydrobromide has been isolated and named Corydalis H. It is probably a quarternary base, as its hydrobromide is not decomposed by alkaline carbonates. When treated with barium hydroxide and extracted with chloroform, it gives rise to the formation of a new base which differs from Corydalis H by not giving the same hydrobromide. The other alkaloids present in Chinese Corydalis (Yen-hu-so) are still large in number and can only be fully investigated by working on a large quantity of raw material.

EXPERIMENTAL

(1) Sulphates of Corydalis B.

When Corydalis B was dissolved in a sufficient quantity of hot dilute sulphuric acid, on cooling its acid sulphate crystallised out as needles, m.p. 238°C. It was soluble with difficulty in cold water and strongly acid to litmus. Its neutral sulphate was obtained by treating Corydalis B with a calculated quantity of sulphuric acid in aqueous solution and evaporating the whole to dryness over a water bath. The residue was taken up with a little hot alcohol and set aside. The neutral sulphate crystallised out in the form of six-sided prisms, melting at 220°C. It was easily soluble in cold water, giving rise to a neutral solution.

(2) Corydalis F, $C_{20}H_{23}O_4N$ or $C_{20}H_{24}O_4N$.

It consists of the main constituent of fraction 3 which was separated from fraction 2 by means of a dilute solution of caustic soda. The phenolic bases were liberated from the sodium hydroxide solution by treating it with ammonium chloride and extracting with chloroform. The chloroform solution, when dried and distilled, left behind a crude phenolic basic residue. The whole was converted into its hydrobromide

in aqueous solution. When crystallised pure, the hydrobromide was worked up for Corydalis F by dissolving in water, making alkaline with potassium carbonate and extracting with chloroform. The crude Corydalis F so obtained was further purified by repeatedly recrystallising from chloroform with the addition of alochol until a constant melting point was obtained. Corydalis F forms colourless rhomboid crystals (see fig. 1) m.p. 237°C. It was sparingly soluble in organic solvents except chloroform, in which it was easily soluble on warming. Its chloroform solution and also its crystals became coloured on keeping. It dissolved in a dilute solution of caustic alkali forming a colourless solution. A 0.4 per cent solution in chloroform gave a specific rotation -1°, in 1 dm tube, (α) 25/D = -250°. Its molecular formula has been found to be $C_{20}H_{23}O$ N or $C_{20}H_{24}O_4N$ according to the following analysis:—

(i) 0.1180 gm substance gave 0.3036 gm CO_2 and 0.0757 gm H_2O, C=70.16; H=7.12.

(ii) 0.1180 gm substance gave 0.3034 gm CO_2 and 0.0735 gm H_2O. C=70.12; H=6.92.

(iii) 0.1194 gm substance gave 4.40 cc moist nitrogen at 25°C and 755 mm pressure, N=4.06.

Calculated for the formula	$C_{20}H_{23}O_4N$	or $C_{20}H_{24}O_4N$
	C=70.38	C=70.17
	H = 6.74	H = 7.01
	H = 4.10	N = 4.09

This substance may therefore have one of the above two formulae.

It showed the following colour reactions; concentrated sulphuric acid, colourless; Erdmann's reagent, yellowish orange; Froehde's reagent, violet and then blue. Its hydrobromide and hydrochloride were prepared.

(a) *Hydrobromide.* Prepared by dissolving pure Corydalis F in a slight excess of hot dilute hydrobromic acid. It separated out as a jelly at first, but was crystallised by warming the liquid. It formed prismatic needles (see fig. 2), melting at 222°C to a reddish liquid. It was soluble in water and alcohol.

(b) *Hydrochloride.* Obtained by dissolving Corydalis F in an excess of dilute hydrochloric acid. In pure water and alcohol, it was very soluble. It formed fine needles and contained some water of crystallisa-

tion. When air-dried, it melted below 100°C to a clear colourless liquid, then solidified gradually as the temperature rose and finally melted at 234°C.

(3) Corydalis G.

During the process of purifying Corydalis F by means of its hydrobromide, there was found a hard crust sticking to the bottom of the flask. It was separated, purified by recrystallising in water and converted into its free base as usual. The phenolic base so obtained, after being recrystallised several times from a mixture of chloroform and alcohol, formed prisms, (see fig. 3) melting constantly at 237°C, readily soluble in hot chloroform, but not in other organic solvents in which it was only sparingly soluble. Unlike Corydalis F it was dextro-rotatory; a 0.4 per cent solution in chloroform gave a specific rotation +1.20° in 1 dm tube, (α) 25/D = +300°. It showed the following colour reactions; concentrated sulphuric acid, colourless; Erdmann's reagent, yellowish orange; Froehde's reagent, violet, green and then blue. The last colour reaction differentiates Corydalis G from Corydalis F. Its hydrobromide crystallised out from water as prisms (see fig. 4), m.p. 247°C. On account of the small quantity of Corydalis G isolated in a pure state, the molecular formula has not been determined. An intimate mixture of Corydalis F and Corydalis G melted at 214°C.

(4) Corydalis H.

The fraction 4, an alcoholic extract as described in a previous communication (1) was concentrated in vacuo at low temperature. The aqueous residue which contained very little alcohol was first extracted with benzene to remove impurities, (and also some basic substances escaped from previous benzene extractions) and then with chloroform. The chloroform extract, when dried and distilled, left behind a dark resinous residue which was taken up with a little alcohol and allowed to crystallise. After standing in a cool place for several months, no crystals could be isolated. Acidified with hydrobromic acid, well formed prisms were obtained. When crystallised pure from alcohol, it formed yellowish long prisms (see fig. 5), m.p. 235°. It was found to be a hydrobromide and named Corydalis H. It was soluble in water, alcohol and chloroform. Its aqueous solution was optically inactive (α) 20/D=0°. A further quantity of the same hydrobromide was obtained from the above aqueous residue by acidifying with hydrobromic acid and extracting with chloroform. When dissolved in water, made alkaline with

potassium carbonate and extracted with chloroform, only unchanged hydrobromide was recovered. With excess of potassium carbonate until saturation, the substance partially resinifies. When treated with barium hydroxide and extracted with chloroform, a new base was obtained. It crystallised out from alcohol in the form of groups of plates (see fig. 6), melting at 153°C. It was insoluble in water, and soluble in alcohol and chloroform. Its hydrobromide salt melted at 228° instead of 235°, the melting point of the hydrobromide of Corydalis H.

SUMMARY

1. From the tubers of Chinese Corydalis (Yen-hu-so), Corydalis Ambigua, Cham et Sch. in addition to the five alkaloids already described in the last communication (1) three more new alkaloids have now been isolated and named Corydalis F, Corydalis G and Corydalis H. The first two are phenolic and the third is quarternary.

(a) Corydalis F.

$C_{20}H_{23}O_4N$ or $C_{20}H_{24}O_4N$ rhomboid crystals, m.p. 237°; (α) 25/D = -250°.

Hydrobromide; prismatic needles, m.p. 222°.

Hydrochloride, fine needles, melts in its water of crystallisation below 100°C, then solidifies and finally melts at 234°C.

(b) Corydalis G, prisms, m.p. 237°; (α) 25/D = +300°; hydrobromide prisms, m.p. 247°.

(c) Corydalis H, obtained only in the form of its hydrobromide, m.p. 235°C; (α) D = 0°. When treated with barium hydroxide and chloroform, a new base was derived, melting at 153°C.

2. Two sulphates of Corydalis B have been prepared, one acid and the other neutral, the latter is easily soluble in cold water and suitable for therapeutic use.

LITERATURE

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EXPLANATION OF PLATE III

Fig. 1. Corydalis F, m.p. 237°; (α) 25/D = −250°.
Fig. 2. Corydalis F, hydrobromide, m.p. 222°C.
Fig. 3. Corydalis G, m.p. 237°; (α) 25/D = +300°.
Fig. 4. Corydalis G, hydrobromide, m.p. 247°C.
Fig. 5. Corydalis H, hydrobromide, m.p. 235°; (α) D =0°.
Fig. 6. Base derived from Corydalis H, m.p. 153°C.

中國延胡索之研究

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在中國之延胡索中,作者曾提出五種鹼性物質,并定名爲延胡索素甲,延胡索素乙,延胡索素丙,延胡索素丁及延胡索素戊(參觀本報第二卷第二期二百零三至二百十八頁)。今又得有三種新鹼性物質,定名爲延胡索素己,延胡索素庚及延胡索素辛。三者皆係結晶物(參觀圖一,三,五)。關于三物之提取方法,化學性質及物理性質等請閱西文原文。