Chinese Journal of Physiology, 1932, Vol. VI, No. 3, pp. 265—270.

THE ALKALOIDS OF CHINESE DRUG PEI-MU, FRITILLARIA ROYLEI

PART I. PEIMINE AND PEIMININE

T. Q. CHOU

Note on their physiological properties by

K. K. CHEN

(From the Department of Pharmacology, Peiping Union Medical College, Peiping)

Received for publication March 30, 1932

The Chinese drug Pei-Mu 貝母, identified as *Fritillaria Roylei* (1) or as *Fritillaria Verticillata*, Willd. var. Thumbergii, Baker. (2) is one of the most popular drugs used in China. The corms of this plant are prescribed in fevers, coughs, dysuria, hemorrhages, deficiency of milk, threatened mammary abscess, rheumatism and diseases of the eye. It is much cultivated in Chekiang and also in Szechuan, the latter variety being regarded as much superior to any other and commanding a higher price. The corms are easily crushed by the teeth to a white starchy and almost tasteless powder. The alkaloidal constituents of this drug have been investigated by Yuan (3) who isolated from Pei-Mu an impure hydrochloride melting at 268°C and more recently by Fukuda (4) who isolated from *Fritillaria Verticillata*, Willd. var. Thumbergii, Baker., two crystalline alkaloids, Verticin $C_{18}H_{33}NO_2$ or $C_{19}H_{35}NO_2$ and Verticillin, $C_{19}H_{33}NO_2$ and an amorphous one, Fritillarin $C_{19}H_{33}NO_2$.

The present work consists of the chemical investigation of Pei-Mu from Chekiang and has resulted in the isolation of two crystalline alkaloids, for which the names Peimine and Peiminine are suggested by the writer, differing from Verticin and Verticillin of Fukuda in both their molecular formulæ and properties. Peimine has a molecular formula $C_{19}H_{30}NO_2$ a melting point 223°C and is optically inactive and Peiminine has a molecular formula $C_{18}H_{28}NO_2$, a melting point 135°C and a specific rotation—62.5°. Both Peimine and

Peiminine formed well defined crystalline salts and possessed similar physiological properties as reported by Dr. K. K. Chen, to whom the writer is indebted for the note appended to this paper.

The investigations made with Pei-Mu of the Szechuan variety will be reported later on.

EXPERIMENTAL

Five kilograms of the Chinese drug Pei-Mu from Chekiang, in the form of starchy corms, were finely powdered and percolated with 95 per cent alcohol at room temperature for a few days. The alcoholic extract was separated and evaporated at low temperature to a syrup. The residue was taken up with a sufficient quantity of 2 per cent aqueous hydrochloric acid and filtered from the insoluble matter. The material, obtained on rendering the acid solution alkaline with sodium carbonate, was extracted several times with ether. The ethereal solution was dried and distilled, leaving behind an impure basic residue, from which the alkaloids Peimine and Peiminine were isolated after a long and tedious study.

1. *Peimine* $C_{19}H_{30}NO_2$.

It has been isolated from the crude basic product by means of its hydrobromide. When crystallised pure, it separated out from alcohol in small prisms (see fig. 1), melting at 223° to a clear liquid. It was easily soluble in most organic solvents and insoluble in petroleum ether and water. A 0.4 per cent solution in alcohol in 1 dm tube gave a specific rotation of 0°, whence $[\alpha]$ 24/D=0°. It had the molecular formula $C_{19}H_{30}NO_2$ according to the following analysis. The substance used was dried at 110°C until constant in weight.

1. 0.1184 gm substance gave 0.3259 gm CO_2 and 0.1084 gm H_2O C=75.06; H=10.13.
2. 0.1194 gm substance gave 0.3287 gm CO_2 and 0.1088 gm H_2O C=75.07; H=10.12.
3. 0.1209 gm substance gave 5.1 cc moist nitrogen at 22°C and 776 m.m. pressure N=4.85.

Calculated for the formula $C_{19}H_{30}NO_2$, C=75.0; H=9.86; N=4.60.

Its hydrobromide crystallised from alcohol in prisms, m.p. 288°C and its hydrochloride in needles, melting at 295°C.

2. *Peiminine* $C_{18}H_{28}NO_2$.

It has also been isolated by means of its hydrobromide which was more soluble in alcohol than that of Peimine. It crystallised out from a mixture of alcohol and petroleum ether in prismatic needles (see fig. 2.) melting at 135° to a clear liquid. It was readily soluble in alcohol, acetone and chloroform less so in ether, and benzene and insoluble in petroleum ether and water. A 0.4 per cent solution in alcohol in 1 dm tube gave a specific rotation −0.25°, whence $[\alpha]_{D}^{24} = -62.5°$

Fig. 1.
Peimine $C_{19}H_{30}NO_2$
M. P. 223°C
S. R. =0°

Fig. 2.
Peiminine $C_{18}H_{28}NO_2$
M. P. 135°C
S. R. = − 62.5°

It had the molecular formula $C_{18}H_{28}NO_2$ according to the following analysis:—

1. 0.1187 gm substance gave 0.3244 gm CO_2 and 0.1053 gm H_2O C = 74.53; H = 9.85.
2. 0.1170 gm substance gave 0.3193 gm CO_2 and 0.1004 gm H_2O C = 74.42; H = 9.53.
3. 0.1333 gm substance gave 5.4 cc moist nitrogen at 22°C and 768 m.m. pressure N = 4.61.

$C_{18}H_{28}O_2$ required C = 74.48; H = 9.65; N = 4.82.

It formed a hydrobromide, prisms, m. p. 292°C and a hydrochloride, prisms, m. p. 295°C.

The following table gives the comparison of Peimine and Peiminine with Verticin and Verticillin of Fukuda.

TABLE 1.

A comparison of Peimine and Peiminine with Verticin and Verticillin

	Peimine	Verticin	Peiminine	Verticillin
Molecular formula	$C_{19}H_{30}NO_2$	$C_{18}H_{33}NO_2$ or $C_{19}H_{35}NO_2$	$C_{18}H_{28}NO_2$	$C_{19}H_{33}NO_2$
Melting point	223°	224-224.5°	135°	Sinters at 130° Melts at 148-150° Resolidifies at 157-159° Decomposes at 212-213°
Specific rotation	0°	—10.66°	—62.5°	——

There is some resemblance between the m. p. of Peimine with that of Verticin; whether Fukuda worked with the same drug or with other species of this liliaceous plant cultivated in Japan, is not known to the writer.

Physiological tests (By Dr. K. K. Chen.)—Since Pei-Mu has been recommended very widely in China as a cough remedy, we ran several experiments in dogs for anti-spasmodic and depressive action, but could not yet prove the justification of such a belief. Both Peimine and Peiminine are very similar in their physiological action, and have an M. L. D. of 0.9 mg per kg in white mice by intravenous injection and an interesting action on the frogs' heart by perfusion into the inferior vena cava. They produce slight increase in tone, block and periodicity. In large doses, they have a slight depressor action on the blood pressure.

SUMMARY

From the corms of the Chinese drug Pei-Mu 貝母 two crystalline alkaloids have been isolated, Peimine and Peiminine. Peimine has a molecular formula $C_{19}H_{30}NO_2$, m. p. 223° and is optically inactive. It forms well crystallised salts; hydrobromide, prisms, m. p. 288°, hydrochloride, needles, m. p. 295°. Peiminine has a molecular formula of $C_{18}H_{28}NO_2$, m. p. 135° and a specific rotation -62.5°.

Both Peimine and Peiminine are similar in their physiological action and have a M. L. D. of 0.9 mg per kg in white mice by intravenous injection.

LITERATURE

1. Stuart, G. A. — Chinese materia medica, 1911, 178.
2. Read, B. E. and Liu, J. C. — Plantae medicinalis sinensis, 1927, p. A. I. **51**, No. 620.
3. Yuan, S. W. — Allgem. med. Ztschr. d. Chineschen Reich, 1923, **1.5**, 12.
4. Fukuda, M. — Science reports, Tohoku, Japan, 1929, (1) **18**, 323 (Cf. Chem. Ztralbl., 1930, **1**, 988).

中國貝母之有機鹼質

其一. 貝母素甲及貝母素乙

趙承嘏

關於貝母素甲與乙之生理性質之略記

陳克恢

私立北平協和醫學院藥理學系，北平.

貝母爲吾國最風行藥物之一，分浙貝母與川貝母兩種，今作者從浙貝母中取出二有機鹼質，命名曰貝母素甲(Peimine)及貝母素乙(Peiminine)，貝母素甲之分子式爲$C_{19}H_{30}NO_2$，熔點爲223°C.，旋轉度等於零，貝母素乙之分子式爲$C_{18}H_{28}NO_2$，熔點爲 135°C.， 旋轉度爲-62.5° 貝母素甲與乙之藥性甚毒；兔之體重每公斤，如注射貝母素甲與乙 0.9 公絲時即能致死。其詳細之生理性質，已由陳克恢君作一專篇報告不久將在本雜誌登載。