SINOMENINE AND DISINOMENINE. PART IX. ON ACUTUMINE AND SINACTINE.

By Kakuji GOTO and Hideo SUDZUKI.

Received September 21, 1929. Published October 28, 1929.

Two new alkaloids were isolated from the root of *Sinomenium acutum Rehd et Wills*, so that the plant contains at least five well characterised alkaloids as the following.

1. Sinomenine $C_{19}H_{23}NO_4$
2. Diversine
3. Disinomenine $(C_{19}H_{22}NO_4)_2$
4. Acutumine
5. Sinactine

the latter three being first isolated by one of the authors (K.G.).

I.

Acutumine has the molecular formula $C_{20}H_{27}NO_8$ or $C_{21}H_{27}NO_8$ and its absorption spectra resembles rather that of narceine. It accumulated in chloroform solution, as free base, when weakly acidic diversine part of the extract of the drug was subjected to purification. The cystallisation was acceralated by addition of methyl alcohol. It forms pale yellow needles of m.p. 240° and very scarcely soluble in ordinary organic solvents. Its content in the root amounts to ca. 1/100 of the sinomenine.

No salt of acutumine has hitherto been obtained in crystalline form. The gold double salt is also amorphous and melts rather sharply at 199~200°. The specific rotatory power of the hydrochloride is $[\alpha]_D = +60.20°$.

The analytical date are the following. After Pregl. C=56.98, 56.89, 56.81, 57.46, 57.15; H=6.82, 5.81, 5.93, 6.51, 6.62%.
After Liebig C=56.88, 58.19, 58.20, 57.91; H=5.88, 6.42, 7.29, 6.34%.
After Dumas N=3.36, 3.38%.

From these results, the molecular formula $C_{20}H_{27}NO_8$ can be most plausibly assigned to it. Yet calculated as an alkaloid of narceine group, $C_{21}H_{27}NO_8$ may be preferred. The decision must be made only when the decomposing experiments were carried out, for which the materials is not sufficient at present.

Molecular weight. From the calcination of gold salt: 406. After Rast (this method is rather doubtful for some of the alkaloids): 381, 445, 393.

Functional groups.

1. Acutumine does not give ferric chloride reaction, potassium ferricyanide reaction and diazo-reaction. The existence of phenol hydroxyl is therefore excluded.

2. Methoxyls. Acutumine contains three methoxyl group, as are revealed by the Zeisel's method:

CH_3O=22.48, 22.70, 22.77, 22.80, 23.41%. Calc. for $3CH_3O$ in $C_{20}H_{27}NO_4$ (=409): 22.79%.

3. N-Methyl. After Herzig-Meyer's, found: N=4.34%. Calc: 3.66%.

4. Methylendioxy-group is not present in acutumine. (Controll: narcotine, narceine, berberine etc.).

5. Ketone group. One ketone group is existent in acutumine, since it forms a semicarbazone, which crystallises in beautiful, long needles. It does not melt even at 290°. (Found: N=11.66%. Calc. as monosemicarbazone: 12.06%).

6. Carboxyl group. Existence of a carboxyl group is suspected, since acutumine is very weakly basic, being precipitated from its hydro-chloride solution by sodium acetate (when its concentration reaches to ca. 5%.) Yet no definite proof has yet been given.

Constitution of acutumine. From what has been said above, the molecular formula of acutumine may be represented in the following way.

$$C_{14}H_{10} \text{ or } C_{15}H_{10} \begin{cases} 3\ CH_3O \\ >CO \\ -\ COOH \\ N-\ CH_3 \\ 2\ H_2O \text{ (Crystall water?)} \end{cases}$$

Assuming that acutumine has a skeleton of narcotine group, $C_{14}H_{10}$ are not sufficient for the construction of a protopapaverine skeleton and the molecular formula $C_{21}H_{27}NO_8$ is suspected to be better fitted for the alkaloid. The question will be decided by degradation, when we isolated a large quantity of the substance.

II.

Sinactine hydrochloride accumulates in chloroform, when the latter is repeatedly used in the extraction of the alkaloids without evaporation, but the base is removed by means of hydrochloric acid from it. Since this hydrochloride is very scarcely soluble in water (0.74%), it can be easily purified from sinomenine.

The free base is precipitated in needles from the solution of its hydrochloride by means of ammonia. It can be recrystallised from methyl alcohol. m.p. 174°.

The hydrochloride is yellow and decomposes at 272°.

The gold double salt is amorphous.

The platinum double salt is beautiful crystals and melts at 245~247°, darkening at 240°.

The specific rotation of free base in chloroform (C=ca. 1%) is $[\alpha]_D = -312°$.

Analysis. Found: C=71.03, 70.30, 70.52, 70.96; H=6.41, 6.68, 6.30, 6.41; N=3.87%. Calc. for $C_{19}H_{21}NO_4$(=327): C=69.73; H=6.40; N=4.28%.

Mol. Weight. Found: 309.2 (by the calcination of the platinichloride)

Functional groups.

1. Sinactine has no free phenol group, since it does not give the three reactions of phenol as were given with acutumine.

2. Sinactine has a methylendioxy group, as it gives much precipitates with phloroglucine-sulphuric acid.

3. Sinactine has two methoxyl groups. (Found: 18.87%. Calc. for $2CH_3O-$ in $C_{19}H_{21}NO_4$: 18.99%).

4. Sinactine has no N-methyl group. Heating for 2 hours at 300° or thereabout with $IH+INH_4$, it gave no precipitate with silver nitrate.

Constitution of Sinactine. The absorption spectra of sinactine almost coincide with that of laudanosine, and there can be no doubt that sinactine is an alkaloid belonging to tetrahydropapaverine group.

The molecular formula $C_{19}H_{21}NO_4$, in which two methoxyl, one (presumably) methylendioxy and no N—methyl groups are traced, makes sinactine an isomeride of veratryl-nor-hydro hydrastine, which W.H. Perkin jun. synthetised in 1924.[1]

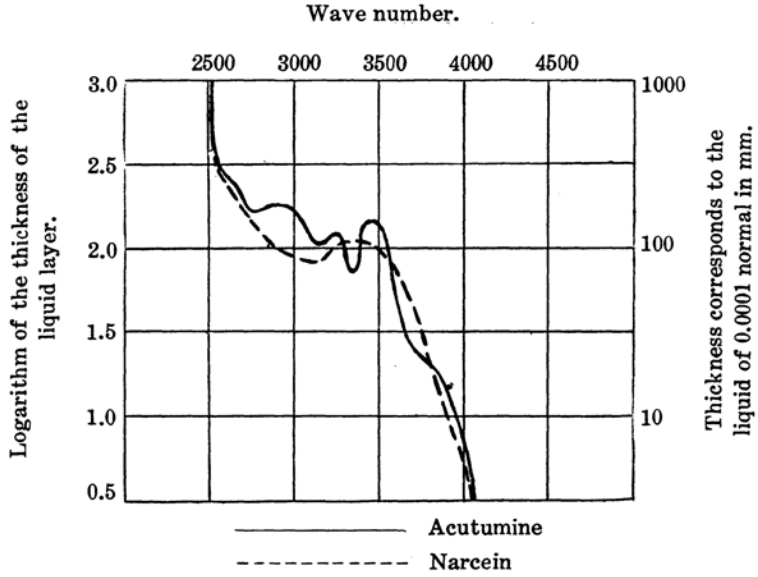

Fig. 1.

(1) *J. Chem. Soc.*, **1924**, 1677 & 1696.

But there is a remarkable difference between sinactine, veratryl-norhydro-hydrastine and the epi-form of the latter in the melting points. The latter two melt at 84° and 96° respectively whilst sinactine melts at

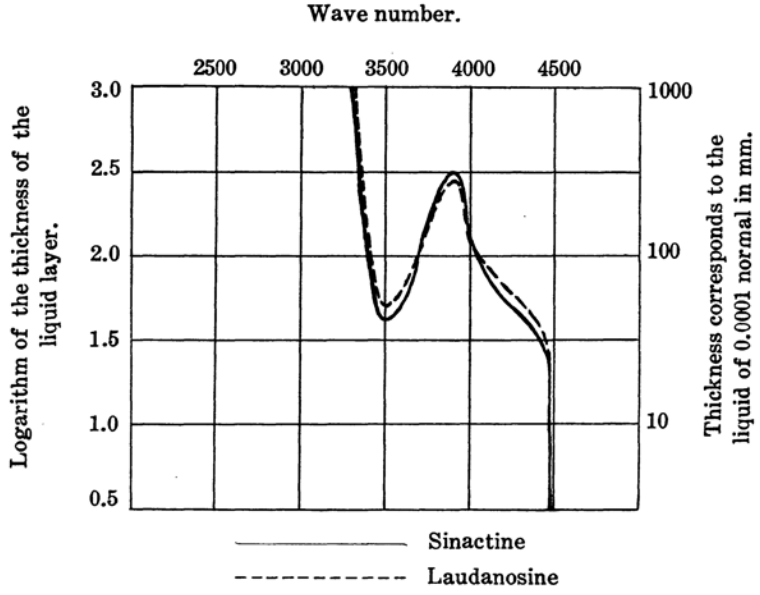

Fig. 2.

174°, almost 100° degrees higher than they do. This difference we should like to explain by suspecting that the methoxyls and methylen-dioxy group are attached to the different positions from those in the synthesised alkaloids.

The Department of Chemotherapy,
Kitasato Institute, Tokyo.