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THE CONSTITUENTS OF EUROPEAN *DATURA STRAMMONIUM* CULTIVATED IN CHINA

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The solanaceous plants, *Hyoscyamus niger, Atropa belladonna, Datura strammonium, Datura fastuosa,* and *Scopolia Japonica* are recognised in the various national pharmacopoeias. Amongst various alkaloids isolated from these plants, atropine, hyoscyamine and hyoscine are used to a considerable extent in medicine. At the suggestion of Dr. W.S. Sung and Mr. D. Barat of the Faculty of Pharmacy of the Université Franco-Chinoise, the seeds of *Datura strammonium,* kindly supplied by Dr. B. Augustin, of the Royal Institute for the Cultivation of Plants, Budapest, were cultivated in China, in the neighbourhood of Shanghai with a view to its possible commercial utilisation.

Work done previously on datura species by Dunstan and Brown [1901], Schmidt [1905, 1906, 1910], Kircher, [1905, 1906] Feldhaus, [1905] Andrews, [1911] and many others, showed that the alkaloids present in these plants were either hyoscyamine or hyoscine or both in varying proportions, occasionally with a small amount of atropine; the percentage of the total alkaloid present varying from 0.2 to 0.5 per cent. As differences in climate and soil are known to produce considerable alteration in the constituents of plants, the *Datura strammonium* cultivated in China, was chemically investigated, resulting in the isolation of hyoscyamine and hyoscine, in almost equal proportions, together with a small quantity of atropine. The total alkaloidal substance isolated amounted, however, only to 0.16 per cent, and the crystalline alkaloids, less than 0.1 per cent. On the other hand, 2 well crystallised neutral principles, amounting to about 0.3 per cent of the air-dried plant and appearing to be new compounds, have also been isolated, to which the names Datugen and Datugenin are provisionally assigned. Datugen has

a molecular formula $C_{13}H_{20}O_2$, a melting point 295°C and a specific rotation of + 41.6°, and Datugenin has a molecular formula $C_{16}H_{22}O_5$ a melting point 265°C and a specific rotation of +75°. Both of these do not show any glucosidal nature differing significantly from the glucosides scopolin of Eykman [1884] and hyoscypicrin of Höhn [1870] isolated from *Scopolia Japonica* and *Hyoscyamus niger*. L. respectively.

EXPERIMENTAL

Twelve kilogrammes of *Datura strammonium* in the form of stems and leaves, were finely powdered and percolated with 95 per cent alcohol at room temperature for about a week. The alcoholic extract was separated and concentrated at low temperature to a syrup. The residue was taken up with a sufficient quantity of 2 per cent hydrochloric acid and filtered from the insoluble resinous matter. The material obtained on rendering the acid solution alkaline with sodium carbonate, was extracted with chloroform. The chloroform solution was dried and distilled and the residue worked up for solanaceous alkaloids as following. The resinous matter insoluble in acid solution, was extracted with hot benzene. The benzene solution, when concentrated to a small volume and allowed to stand for a few days, deposited the neutral principles Datugen and Datugenin as a crop of crystals.

Isolation of hyoscine, hyoscyamine and atropine.
Hyoscine $C_{17}H_{21}O_4N$.

The crude basic residue obtained as above was taken up with a little alcohol and neutralised with an alcoholic solution of hydrobromic acid when hyoscine hydrobromide crystallised out rapidly on standing. Crystallised pure from alcohol, if formed colourless rhombic prisms; its melting point was, however, found to be indefinite after being previously dried at 100° C instead of 194° C, the melting point of hyoscine hydrobromide. Starting with the hydrobromide thus obtained, other salts were prepared with properties identical in all respects to those of hyoscine. The sulphate separated from alcohol on addition of acetone in six-sided prisms, m.p. 197°. The aurichloride crystallised from boiling water acidified with hydrochloric acid in orthorhombic plates, melting at 205°. The picrate formed yellow prismatic needles from water, m.p. 189°. When mixed respectively with the sulphate, aurichloride and picrate of hyoscine of E. Merck, their melting points remained

unchanged. The nitrogen content of the picrate was determined according to Kjeldahl's method with the following results:—
0.0819 g substance gave 0.01050 g NH_3; N = 10.54.
Hyoscine picrate $C_{17}H_{21}O_4N.C_6H_2(NO_2)_3OH$ required N = 10.53.

The free base, liberated from either the hydrobromide or the sulphate was a syrup, soluble in ordinary organic solvents.

Hyoscyamine $C_{17}H_{23}O_3N$.

The alcoholic mother liquor of the hyoscine hydrobromide obtained as above, was evaporated to dryness over water bath and the residue taken up with water and filtered. The clear aqueous solution was then made alkaline with sodium carbonate and the liberated base extracted with ether. The ethereal solution was dried and concentrated to a small volume when hyoscyamine separated out in fine needles on standing for the day. When crystallised pure from little alcohol with addition of ether, it formed long silky needles, m.p. 108°. When mixed with hyoscyamine of E. Merck, its melting point remained unchanged. A one per cent solution in alcohol gave in 2 dm tube a specific rotation of −0.42°, whence $[\alpha]_{D}^{20} = -21°$: when analysed, it gave the following results:—

0.1039 g substance gave 0.2688 g CO_2 and 0.0770 g H_2O
C = 70.56; H = 8.29

Hyoscyamine $C_{17}H_{23}O_3N$ required C = 70.54; H = 8.02.
Its salts were prepared, being identical in all respects to those of hyoscyamine: the picrate, plates, m.p. 165°; the aurichloride, hexagonal plates; m.p. 165°; the sulphate, silky needles, or sometimes rhombic prisms, m.p. 208°.

Atropine $C_{17}H_{23}O_3N$

The ethereal mother liquor, after the removal of hyoscyamine as above, was evaporated to dryness and the residue converted into its oxalate in alcoholic solution which crystallised out on long standing. When crystallised pure from alcohol, it formed hard warty masses of small prisms, m.p. 192°. Its aqueous solution was found to be optically inactive. The free base, liberated from the oxalate and recrystallised from chloroform with addition of light petrol ether in prisms, m.p. 116°, being identical to atropine. When mixed with atropine of E. Merck, its melting point remained unchanged. Evaporated to dryness

over water bath with little concentrated HNO_3, it gave a residue which became violet on adding a drop of KOH in alcohol. It formed a picrate, rectangular plates, m.p. 176° and an aurichloride, minute crystals, m.p. 138°.

Isolation of the neutral principles, Datugen and Datugenin.

The crude material obtained from hot benzene extract, was redissolved in chloroform, decolorised with a little animal charcoal and filtered. The chloroform solution, when dried and concentrated deposited datugen as soft needles, whilst datugenin remained in chloroform solution and crystallised out on addition of alcohol.

Datugen $C_{13}H_{20}O_2$.

Datugen crystallised from chloroform in soft silky needles, melting at 295°. It is easily soluble in hot chloroform, less so in alchohol, acetone or benzene and insoluble in water. It dissolves in conc. HNO_3 (D = 1.42) to a colourless solution and with conc. H_2SO_4, it produces a violet coloration becoming reddish brown on standing. A 0.6 per cent solution in chloroform gave in 2 dm tube a specific rotation of +0.50, whence $[\alpha]$ 26/D = +41.6°. Its molecular formula was found to be $C_{13}H_{20}O_2$ according to the following analysis:—

(1) 0.1030 g substance gave 0.2826 g CO_2 and 0.0899 g H_2O

C = 74.82 ; H = 9.77

(2) 0.1103 g substance gave 0.3024 g CO_2 and 0.0964 g H_2O

C = 74.77 ; H = 9.78

(3) 0.0211 g substance in 0.3024 g Camphor : 7°△.

Mol. wt = 209.7

Calculated for $C_{13}H_{20}O_2$, C = 74.94; H = 9.68; Mol. wt = 208

Datugenin $C_{16}H_{22}O_5$.

When crystallised pure from chloroform with the addition of alcohol, datugenin forms colourless prismatic needles or orthorhombic prisms according to the concentration of the solvent. It melts at 265° and is very soluble in chloroform, less so in alcohol, benzene or ether and insoluble in water. Like datugen, it produces a violet colouration with conc. H_2SO_4 and dissolves in conc. HNO_3 to a colourless solution. When boiled with dilute acids or alkalies, it undergoes change, but no sugar could be found in its decomposition products. A one per

cent solution in chloroform gave in 2 dm tube a specific rotation of $+1.50°$, whence $[\alpha]\ 26/D = +75°$. It has a molecular formula of $C_{16}H_{22}O_5$ according to the following analysis:—

(1) 0.1323 g substance gave 0.3165 g CO_2 and 0.0904 g H_2O
C = 65.24 ; H = 7.64

(2) 0.1494 g substance gave 0.3577 g CO_2 and 0.1014 g H_2O
C = 65.30 ; H = 7.59

(3) 0.0215 g substance in 0.2005 g Camphor : 14.5° △.
Mol. wt = 295.8

Calculated for $C_{16}H_{22}O_5$ C = 65.27; H = 7.54; Mol. wt. = 294.

SUMMARY

From European *Datura strammonium* cultivated in China, there was isolated, besides the alkaloids hyoscine, hyoscyamine and atropine, two neutral principles named Datugen and Datugenin to the extent of 0.3 per cent of the air dried plant. Datugen has a molecular formula of $C_{13}H_{20}O_2$, a melting point 295° and a specific rotation +41.60. Datugenin has a molecular formula of $C_{16}H_{22}O_5$, a melting point 265° and a specific rotation + 75°.

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蔓陀羅化學成分之研究

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本篇所用蔓陀蘿 *Datura stramonium* 之原料，其種子得自奧國皇家植物研究所而在上海附近所種植者．研究結果，發現亥俄辛 hyoscine，莨菪素 hyoscyamine，及阿刀平 atropine 三種植物鹼多存在，惟含量極少，共只約千分之一．此外又發現兩種中性結晶物，定名爲蔓陀芹 datugen，及蔓陀芹引，datugenin，乃前人所尚未發現者，其在植物中之含量共約千分之三．蔓陀芹之化學分子式，爲 $C_{13}H_{22}O_2$，熔點爲 295°，旋光度爲 +41·6°．蔓陀芹引之化學分子式，爲 $C_{16}H_{22}O_5$，熔點爲 265°，旋光度爲 +75°．二者之生理作用，俟作藥理研究後，再行報告．