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Notes upon the Isolation of the Alkaloidal Constituent of the Drug "Channa" or "Kougoed" (*Mesembryanthemum anatomicum* and *M. tortuosum*).

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THE "Kougoed" of the Bushmen of Namaqualand is a preparation compounded of the dried, over-ground portions of the plants *Mesembryanthemum anatomicum and Mesembryanthemum tortuosum*. It is chewed and is said to exert a strongly narcotic action in many respects resembling that of cocaine (Watt and Breyer-Brandwyk, 1932. Juritz (1905) observed dilation of the pupil.

Zwicky (1914) examined the preparation and extracted a crude alkaloid which he named "Mesembrin". Neither the free base nor any of its derivatives were obtained in the crystalline state; however, on the grounds of elementary analyses, Zwicky put forward the formula $C_{16}H_{19}NO_4$ for the alkaloid. Certain colour reactions were described.

Since the alkaloids of the Aizoaceae have received very little attention, a reinvestigation of the "Kougoed" seemed highly desirable. Through the kindness of Dr. W. Jordan, in placing at our disposal about 1·5 kilos of a preparation consisting of the dried plants, secured by him recently in Namaqualand, we were enabled to make a preliminary study of the alkaloidal constituents of the drug and to obtain crystalline salts of Mesembrin which establish its correct formula as $C_{17}H_{23}NO_3$. The present paper is a preliminary note upon the isolation and properties of this substance.

ABSENCE OF VOLATILE ORGANIC BASES.

Since piperidine has been found to be a constituent of *Psilocaulon absimile*, another member of the family Aizoaceae, (Rimington 1934) an aqueous acid extract of Kougoed was rendered alkaline and steam distilled into acid. No piperidine was found in the distillate which neutralised only 0·7 c.c. of N alkali per 100 gm. of plant.

Isolation of the alkaloid.

The finely ground drug was extracted with boiling ether and the alkaloid then removed by continuous extraction with boiling chloroform. The dark solution was shaken with decolourising charcoal and evaporated to dryness, the residue being stirred up with dilute hydrochloric acid and a quantity of tarry material rejected. The aqueous solution containing the hydrochloride was again treated with charcoal, evaporated to dryness, and chloroform added to the dry residue when the hydrochloride of the base passed easily into solution. The filtered liquid was poured into several volumes of petroleum ether which precipitated the crude alkaloidal salt as a somewhat hygroscopic, pale buff-coloured powder. Attempts to crystallise it were not successful neither was the free base, which is moderately soluble in water, obtained in the crystalline state, although a crystalline picrate and platinichloride were readily obtained and the methylated free base was also crystallised with ease. From the composition of these crystalline derivatives, that of the free base was deduced.

Precipitation and colour reactions.

An aqueous solution of the alkaloidal hydrochloride gave amorphous precipitates with all of the usual alkaloidal reagents. Millon's reagent produced a pale red colouration and diazobenzenesulphonic acid in sodium carbonate solution an intense orange red colour indicating the presence in the molecule of phenolic groups. The dry material was dissolved by concentrated sulphuric acid with production of a yellow-brown colour. Mandelin's reagent, (Vanadium-sulphuric acid gave a greenish-blue colour on warming.

Preparation of derivatives.

No attempt was made to prepare an exhaustive series of alkaloidal salts; since the amount of material available was very limited, attention was paid particularly to the picrate and platinichloride.

Picrate.

Aqueous picric acid in excess was added to an aqueous solution of the hydrochloride and the amorphous precipitate removed, washed and dissolved in sufficient warm 60 per cent. alcohol. On cooling, a little tarry matter separated and was filtered off. The filtrate in the ice-chest yielded crystals of the picrate consisting of prisms aggregated into clumps or rosettes. It is insoluble in ether, sparingly soluble in water and sparingly soluble in hot benzene but does not separate very well from the latter solvent alone. Recrystallisation was effected by adding excess of ether to a hot benzene solution and allowing the mixture to stand for some days. M.P. 193-4°.

*Microanalysis :**

		C	H	N
$C_{17}H_{23}NO_3 + C_6H_3N_6O_7$.....	Found	53·54	5·13	10·71
	requires	53·28	5·02	10·81

* Microanalyses by Dr. Backeberg of the University of the Witwatersrand, to whom we wish to express our thanks.

Picrolonate.

Prepared by the addition of aqueous picrolonic acid to a solution of the hydrochloride picrolonate is an amorphous yellow precipitate soluble in warm dilute alcohol but not crystallising readily. The material analysed contained some white ash which was allowed for in the calculations.

Microanalysis:

		C	H	N
	Found	57·82	5·76	12·02
$C_{17}H_{23}NO_3 + C_{10}H_8N_4O_5$.....	requires	58·56	5·64	12·66

Platinichloride.

Two forms of this salt were obtained. The amorphous precipitate produced when aqueous platinic chloride and alkaloidal hydrochloride are mixed separates, when crystallised from dilute alcoholic solution, in the form of small prisms having the melting point 151-3°, and containing neither water nor alcohol of crystallisation (see Fig. 1). On slow crystallisation in the ice-chest from aqueous alcohol, however, irregularly octagonal plates are obtained which contain two molecules of alcohol of crystallisation. Heated under the melting point microscope, softening is seen to occur with the evolution of bubbles at 170° but true melting does not take place before 181° is reached.

Microanalysis:

Salt with M.P. 181° dried in vacuo over P_2O_5 at 105°

	Per Cent.
Loss of weight.....	8·03
Calculated for 2x C_2H_6O.....	8·52

		C	H	N	Pt.
Above dried material.....	Found	41·20	4·84	3·12	20·48
Salt with M.P. 151-3°.....	Found	40·52	4·95	3·33	19·64
$(C_{17}H_{23}NO_3)_2H_2PtCl_6$.....	requires	41·28	4·90	2·83	19·74

A determination of methoxyl, CH_3O, and N-methyl,N-CH_3, carried out upon the crystalline platinum salt showed the presence of 2 methoxyl and 1 N-methyl group per molecule of base, thus:—

		CH_3O	CH_3 as N-CH_3
	Found	12·22	2·25
$(C_{17}H_{23}NO_3)_2H_2PtCl_6$ requires for 4 groups.....		12·54	3·03*

* For 2 groups.

Methylation.

Since colour reactions indicated the presence of a phenolic hydroxyl group, an attempt was made to obtain the fully methylated base by treating the alkaloidal hydrochloride dissolved in water with an excess of dimethyl sulphate and sodium hydroxide in the usual manner. The methylated derivative crystallised from the resulting reaction mixture in colourless four-sided prisms of M.P. 220-2° (see Fig. 2). The material so obtained contained a little ash which proved difficult to remove, therefore the platinichloride was prepared for analysis.

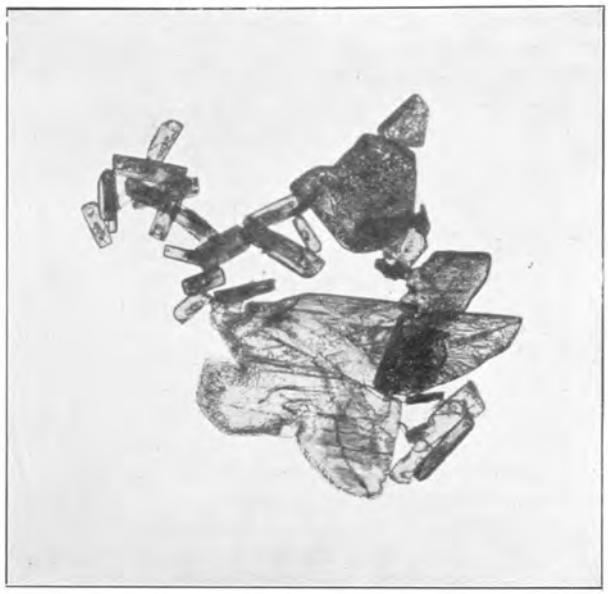

Fig. 1. Mesembrin Platinichloride M.P. 151-3°. ×75

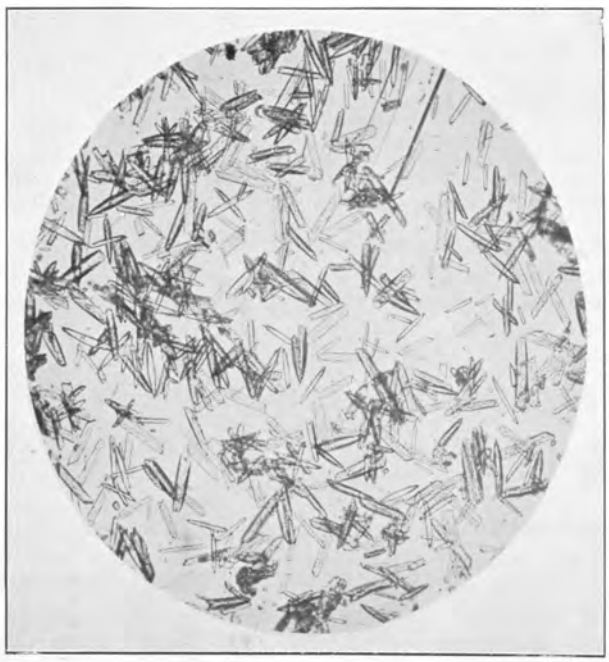

Fig. 2. Methyl-Mesembrin M.P. 220-2°. ×85.

Microanalysis:

		Pt	CH_3O
$(C_{18}H_{25}NO_3)_2\ H_2Pt\ Cl_6$	Found	18·72	18·85
	requires	19·21	18·31*

* For 6 methoxyl groups.

An addition of one methoxyl group per molecule of base has thus been brought about. Methyl-Mesembrin gives a red colour with concentrated nitric acid and a crystalline precipitate with Wagner's reagent (Iodine in potassium iodide).

It would appear from the above considerations that the molecular formula of the alkaloid is $C_{17}H_{23}NO_3$ which can further be written

$$C_{14}H_{13}\begin{cases}-OH\\-OCH_3\\-OCH_3\\-NCH_3\end{cases}$$

It is of interest to compare this with the provisional formula put forward by Zwicky, namely $C_{16}H_{19}NO_4$. His material was impure and the error has fallen mainly upon the CH determination as might have been expected.

The molecular formula of Mesembrin, $C_{17}H_{23}NO_3$, is identical with that of Atropine and of Hyoscyamine. In view of the narcotic properties and reported mydriatic action possessed by Mesembrin, the question arises whether it may also belong to the series of Tropane alkaloids. Unfortunately very little material was available for the investigation of this point but a test hydrolysis was carried out upon a small quantity of the hydrochloride, using boiling saturated baryta as the hydrolytic agent, and the resulting reaction mixture separated definitely into an acidic fraction, crystallising in prismatic needles, and a basic fraction.*

The suggestion that Mesembrin belongs to the group of tropane ester alkaloids would thus appear to be strengthened.

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* We wish to thank Mr. P. Symons for carrying out this experiment.