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BIOSYNTHESIS OF CACTUS ALKALOIDS

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The cactus Lophophora williamsii produces a range of alkaloids exemplified by mescaline (I), anhalidine (II) and pellotine (III). These contain a β-phenetnylamine residue, combined in tne latter two examples with a one carbon and a two carbon unit, respectively. The origin of these units is of biosynthetic interest, and several possibilities can be considered. These include: a) oxidative cyclisation of the N-methyl derivative of an appropriate β-phenethylamine, which could lead to the anhalidine structure (II). This idea has analogy in berberine-bridge formation (1). Addition of a second one carbon unit would then be required for the pellotine system (III). b) the equivalent of formaldehyde or formic acid, and the equivalent of acetaldehyde or acetic acid could react with the appropriate amine to generate the isoquinoline systems represented by (II) and (III).

It had earlier been shown (2) that [2-^{14}C]tyrosine is incorporated by L. williamsii into pellotine, and when this feeding was repeated, the following radioactive alkaloids were obtained (incorporations are shown in brackets): anhalonidine (IV, 0.01%), lophophorine (V, 0.017%) and mescaline (0.57%). Unambiguous degradation of the latter showed that all the activity (103%) of the original alkaloid was at the α-position, as expected, and degradation of anhalonidine (IV) located essentially all the activity (98%) at position 3. These results are in agreement with Leete's findings (3). Further, 3:4-dihydroxy-β-phen[1-^{14}C]ethylamine is incorporated to the extent of 7.5% into pellotine. It is clear that the phenethylamine portion of the cactus alkaloids

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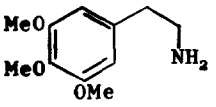
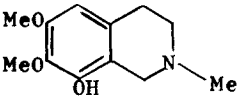
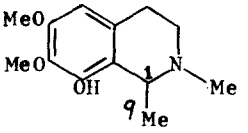
is formed by the well established pathway; cf. the 1-benzylisoquinolines (4) and the Ipecacuanha group of alkaloids (5).



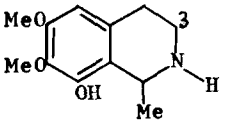
(I)



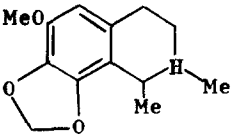
(II)



(III)



(IV)



(V)

[^{14}C-methyl]Methionine fed to the cacti afforded radioactive pellotine (1.8% incorporation), which was degraded by Kuhn-Roth oxidation. This gave radio-inactive acetic acid, proving the absence of labelling at positions 1 and 9. The O-methyl groups of pellotine carried 65% of the total activity.

The pellotine derived from plants fed with sodium [1-^{14}C]acetate (0.084% incorporation) was similarly degraded (two determinations) and the acetic acid carried 53, 49% of the total activity. Further degradation of the acetate by the Schmidt procedure gave methylamine (as N-methyl phthalimide) carrying 26, 25% of the activity of pellotine. Thus, the labelling at C-1 and C-9 is effectively equal. The two O-methyl groups (Zeisel) carry 13% of the activity, and the N-methyl group 5% (Herzig-Meyer). The remaining 30% of the total activity is probably scattered over the eight carbon atoms in the rest of the molecule. It is known that the carboxyl group of sodium [1-^{14}C]acetate can lead to appreciable labelling of O-methyl groups and of residues derived from the shikimic acid pathway (eg. 5).

These results exclude a biosynthesis of the two carbon unit of pellotine from methyl groups derived from methionine. Further, they are not in agreement with direct incorporation of acetic acid. The way in which sodium [1-^{14}C]-acetate contributes a relatively high level of activity to the two carbon unit is the subject of further study. A one carbon pool to which methionine cannot

contribute may be involved; there is analogy for this (6).

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