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BIOSYNTHESIS OF ANHALONIDINE : ORIGIN OF THE TWO CARBON UNIT

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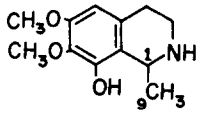
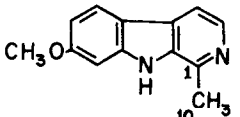
Anhalonidine (I) and its N-methyl derivative pellotine are isoquinoline alkaloids found in the peyote cactus, Lophophora williamsii . It has been established that tyrosine and dopamine are precursors of the phenethylamine portion of these alkaloids (1,2) . It seemed reasonable that the two carbon unit (C-1 and C-9) in these alkaloids would be derived from acetic acid. Battersby (2) found that the administration of acetic acid-1-^{14}C to the cactus yielded radioactive pellotine which had 50 % of its activity located at these two positions. However it was discovered that the activity was equally divided between these positions, suggesting that acetic acid is not a direct precursor of this two carbon unit.



I



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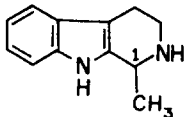

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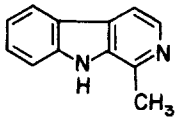

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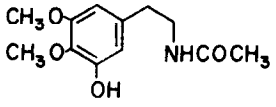

V

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We fed sodium pyruvate-3-^{14}C (16.3 mg, 0.5 mc.) to a peyote cactus and isolated from the phenolic alkaloids, anhalonidine having a specific activity of 1.12 x 10^6 dpm/mM. Radiochemical purity was checked by the preparation of O,N-dimethylanhalonidine methiodide (1.13 x 10^6 dpm/mM.). A Kuhn-Roth oxidation on O,N-dimethylanhalonidine methohydroxide afforded acetic acid, assayed as 1-acetamidonaphthalene (3) (0.67 x 10^6 dpm/mM.). A Schmidt degradation on the acetic acid yielded carbon dioxide (0.19 x 10^6 dpm/mM.) and methylamine assayed as N-methylbenzamide (0.48 x 10^6 dpm/mM.). There was thus a relatively high specific incorporation of C-3 of pyruvate into C-9 of anhalonidine. Stolle and Gröger (4) have similarly found that the two carbon unit (C-1 and C-10) of the β-carboline alkaloid harmine (II) is formed from C-2 and C-3 of pyruvate, whereas unspecific labelling was obtained after feeding acetate-^{14}C to Peganum harmala plants On the other hand O'Donovan and Kenneally (5) reported that the feeding of acetate-1-^{14}C to Eleagnus angustifolia plants yielded eleagnine (III) having 95 % of its activity at C-1 . Slaytor and McFarlane (6) found that N-acetyltryptamine serves as a direct precursor of harman (IV) in Passiflora edulis . It is therefore suggested that the tetrahydroisoquinoline alkaloids having a methyl group at C-1 , are formed from an N-acetylphenethylamine such as V . The failure of acetate to be incorporated directly into the isoquinoline alkaloids found in peyote (2) may be rationalized by suggesting that the plant contains no enzymes capable of utilizing acetic acid directly for the formation of such an acetyl derivative. On the other hand one could conceive of a biosynthetic scheme from pyruvate → acetylcoenzyme A → V.

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