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BIOSYNTHESIS OF MESCALINE IN PEYOTE

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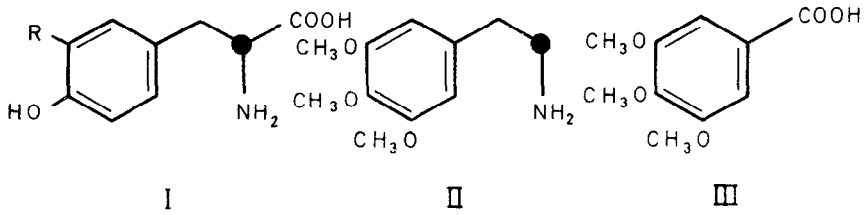
The peyote cactus Lophophora williamsii (Lem.) Coult. (syn. Anhalonium lewinii Hennings) has been used for centuries by Mexican natives as a hallucinogen. This can be attributed to the presence of mescaline. Both mescaline (II) and the tetrahydroisoquinoline alkaloids of peyote bear a close structural relation to tyrosine. Our knowledge concerning the biosynthesis of mescaline is limited to the finding by Leete (1) that tyrosine (I R=H) is a precursor of mescaline and also of anhalonidine. The qualitative incorporation of radioactivity from tyrosine-2-C^{14} into pellotine has also been demonstrated (2). During the preparation of this manuscript, Battersby et al. (3) published results showing the efficient incorporation of 3,4-dihydroxyphenylethylamine (7.5 %) and the methyl group of methionine (1.8 %) into pellotine. We have now investigated the conversion of tyrosine and some of its metabolites to mescaline with special reference to the path leading from tyrosine to mescaline.

The labelled precursors were injected into the cacti, and two weeks later the alkaloid fractions were isolated and separated (1,4) into phenolic and non-phenolic alkaloids by ion-exchange resin (Amberlite IRA 400). Mescaline was isolated by preparative TLC (4) and recrystallized from ethanol as the hydrochloride to constant specific activity, usually without the addition of carrier. The location of the label at the appropriate atom of mescaline was checked by oxidation (1) of the mescaline derived from aromatic precursors to trimethoxybenzoic acid (III)[a]. This acid was in all cases

[a]This degradation will only confine label from dopamine-1-^{3}H to the side chain of mescaline. Oxidation of mescaline carrying tritium label in the nucleus gave trimethoxybenzoic acid retaining 102 % of the label.



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found to carry less than 1 % of the total activity, suggesting a direct conversion of the precursors to mescaline. The predominant labelling of the O-methyl groups (95 % of total activity) of mescaline from methionine-methyl-C^{14} was determined by Zeisel demethylation of mescaline and collection of the evolved methyliodide as tetramethylammonium iodide (3).

TABLE

Incorporation of Radioactive Compounds into Mescaline

	Amount fed Mg	μC	Incorporation into mescaline	Spec. Act. of mescaline μC/mM
DL-Tyrosine-2-C^{14}	0.12	10	0.097%	4.65×10^{-2}
	0.12	10	0.015%	0.84×10^{-2}
Tyramine-1-C^{14}	0.42	10	0.067%	8.78×10^{-2}
	0.42	10	0.35%	9.60×10^{-2}
DL-3,4-Dihydroxy-phenylalanine-2-C^{14}	0.06	10	0.18%	4.26×10^{-2}
	0.06	10	0.59%	17.95×10^{-2}
3,4-Dihydroxy-phenylethylamine-1-H^3 (Dopamine-1-H^3)	0.0003	50	0.048%	3.33×10^{-2}
	0.0003	50	0.052%	4.31×10^{-2}
L-Methionine-methyl-C^{14}	0.25	20	0.802%	51.67×10^{-2}

The results show that both tyrosine (I R=H) and 3,4-dihydroxyphenylalanine (I R=OH) and the corresponding amines[b] are utilized as precursors of mescaline. Kovacs and Jindra (6) have shown that tyrosine may be converted to 3,4-dihydroxyphenylalanine also in plants. The latter compound was particularly effectively incorporated in the present study. The incorporation into mescaline of both tyramine and 3,4-dihydroxyphenylalanine, both presumably products of tyrosine, but on different paths, indicates that alternative routes to mescaline are available.

It was found that the phenolic alkaloid fraction was highly active from fed tyrosine-2-C^{14}. However, the majority of the radioactivity was present in two compounds identified as tyramine and N-methyltyramine.

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REFERENCES

1. E. Leete, Chem. Ind., 904 (1959); J. Am. Chem. Soc., 88, 4218 (1966).
2. A. R. Battersby, Quart. Rev., 15, 272 (1961).
3. A. R. Battersby, R. Binks and R. Huxtable, Tetrahedron Letters, 563 (1967).
4. J. Lundström and S. Agurell, J. Chromatog., in press.
5. R. F. Curtis, P. C. Harries, C. H. Hassall, J. D. Levi and D. M. Philips, J. Chem. Soc., (C), 168 (1966).
6. P. Kovacs and A. Jindra, Experentia, 21, 18 (1965).

[b]The fully O-methylated derivatives of tyramine and dopamine have similar R_F-values as mescaline in TLC. That the activity actually resided in mescaline and not in any contaminating, highly active O-methylated tyramine or dopamine was ascertained by gas chromatography (Aerograph 202, 180°, 6-foot column packed with 20 % SE-52 on DMCS-treated, acid washed Chrosorb W, 60/80 mesh), which well separates the mono-, di- and trimethoxyphenylethylamines. The reisolated mescaline retained all activity.