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0 A BIOSYNTHETIC SEQUENCE FROM TRYPTOPHAN TO PSILOCYBIN

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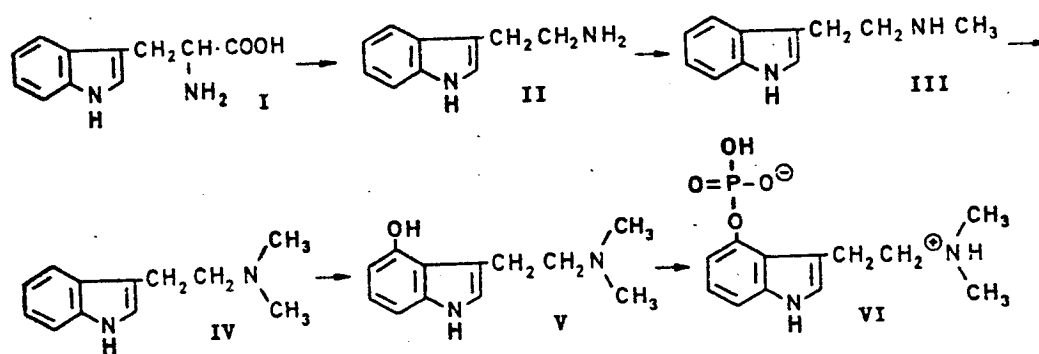
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Psilocybin (VI) and psilocin (V) are two hallucinogenic compounds present in a number of mushrooms mainly members of the genus *Psilocybe* (cf.1). The compounds are closely related 4-hydroxylated indoles and it has been shown by Brack *et al.* (2) and us (1) that psilocybin may biosynthetically derive from tryptophan and tryptamine. The tryptophan molecule (I) requires the following modifications in a definite or alternative order for conversion to psilocybin: decarboxylation, methylation, hydroxylation and phosphorylation.

We have now obtained experimental results consistent with the sequence of biosynthesis for psilocybin in *Psilocybe cubensis* shown in the scheme below. However, this is apparently not the only pathway to psilocybin which the fungus may utilize.



This and other pathways have been examined by previously used techniques (1) *viz.* investigating the incorporation of H^3 - and C^{14} -labelled hypothetical

intermediates into psilocybin in submerged cultures of P. cubensis. Full details will be published subsequently (3).

Incorporation of labelled Precursors into Psilocybin

<u>Precursor introduced</u>	"Dilution"
	(Spec. activity of precursor/ spec. activity of psilocybin)
L-Tryptophan-H ³	132
Tryptamine-C ¹⁴	33
N-Methyltryptamine-H ³	2
N,N-Dimethyltryptamine-C ¹⁴	31
Psilocin-H ³	6
DL-4-OH-Tryptophan-H ³	>500

The results (Table) show that 4-OH-tryptophan in contrast to tryptophan (I) does not function as a precursor. Tryptamine (II) which is readily formed from tryptophan by P. cubensis (3) serves as a better precursor of psilocybin than tryptophan. N-Methyltryptamine (III) is a still better progenitor of psilocybin but N,N-dimethyltryptamine (IV) is rather poorly incorporated as judged from the dilution figures. However, if the poor absorption of this compound by the fungus (less than 5%) is taken into account, the high dilution factor does not make it an unlikely intermediate. Psilocin (V) is effectively converted into psilocybin. 4-Hydroxytryptamine-C¹⁴ is also incorporated into psilocybin but the introduction of this compound led to the formation of one or two other minor products not normally detectable in the cultures. Thus, it may be questioned if this route via 4-hydroxytryptamine is normally occurring in the fungus.

REFERENCES

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