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BIOSYNTHESIS OF APORPHINE - BENZYLISOQUINOLINE ALKALOIDS.
I.RETICULINE AS A PRECURSOR OF THALICARPINE IN THALICTRUM MINUS.

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Abstract: Reticuline considered as the most possible precursor of thalicarpine has been administered into intact plants of Thalictrum minus and its incorporation established in both benzylisoquinoline and aporthine parts of this alkaloid.

Thalicarpine (I.) discovered by Kupchan in Thalictrum Dasycarpum Fisch et Lall[1] is the first representative of aporphine - benzylisoquinoline alkaloids. Later Mollov et al.[2] established that it is present in higher concentration in Thalictrum minus var. elatum, along with other representatives of this type of alkaloids e.g. thalmelatine (II), dehydrothalicarpine, dehydrothalmelatine,adiantifoline and thalmelatidine.

In the present paper we report the results of our tracer experiments for the elucidation of thalicarpine biosynthesis in Thalictrum minus var. elatum. The structure of thalicarpine (I) suggests benzylisoquinoline (III) and aporphine (IV) as direct precursors of that alkaloid, from which it may be derived by intermolecular oxidative coupling in accordance with the established biogenetic theory[3]. Compound (III) laudanidine, was found together with thalicarpine in Thalictrum dasycarpum[4]. Recently, (S)-reticuline, the most important benzylisoquinoline alkaloid from biogenetic point of view, was detected in Thalictrum minus L race B[5]. Its substitution pattern closely resembles that of the supposed precursor (III) of the benzylisoquinoline part of thalicarpine and is identical to the pattern of thalmelatine. For this reason our first task was to study the incorporation of reticuline into the thalicarpine molecule.

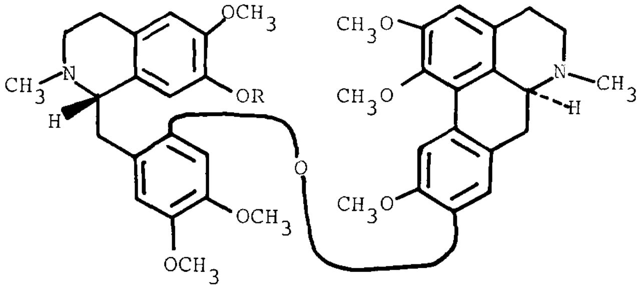
We prepared (±)-1-C^{14}-reticuline hydrochloride[6] with a specific activity 2,57 x 10^7 dpm/mM. It was dissolved in water and administered into a number of intact thalictrum plants using wick - technique.

The plants were harvested after 14 days of incubation and thalicarpine isolated and recrystalized (as picrate) to a constant radioactivity of 1,94 x 10^5 dpm/mM. The significant rate of reticuline incorporation in thalicarpine-1,76% indicates that it is incorporated without randomization.

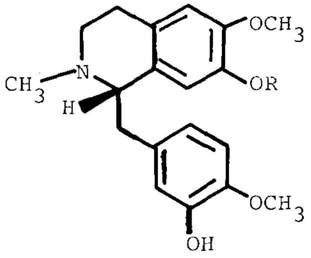
Sodium - liquid ammonia fission of biosynthetic thalicarpine[7], deluted to 4,45 x 10^4 dpm/mM, afforded a mixture of monomeric bases, the major products being VI and VII. The last two were isolated and recrystalized as hydrojodides to a constant radioactivity. Obviously VI and VII originates from benzylisoquinoline and aporphine portions of the thalicarpine molecule respectively.

Both VI and VII proved to be radioactive with specific activities of 2,13 x 10^4 dpm/mM (48%) and 3,11 x 10^4 dpm/mM (70%), respectively.

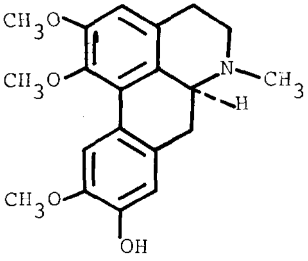
It leads to the conclusion that reticuline is a precursor of both the benzylisoquinoline and aporphine portions of the thalicarpine molecule. The aporphine moiety IV in the plant is plausibly formed by intramolecular oxidative coupling of reticuline.



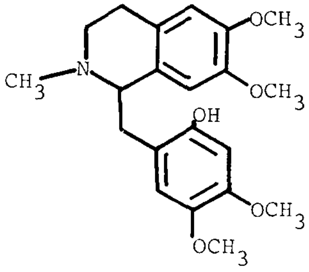
I. R = CH_3
II. R = H



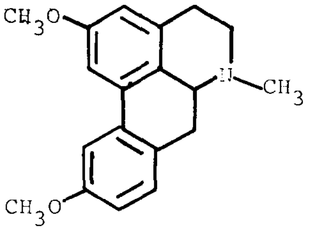
III. R = CH_3
V. R = H



IV.



VI.



VII.

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