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SUCCINIC ACID AS A PRECURSOR OF THE TROPANE ALKALOIDS

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In a study of succinic acid we have attempted to find how its inclusion in the biosynthesis of the alkaloids of Datura innoxia Mill. takes place. Under mild conditions close to those that exist in the plant (temperature and pH), the formation of tropinone from succindialdehyde, methylamine, and acetone is observed [1]. Atoms 1, 2, 3, and 4 of succindialdehyde form carbon atoms 1, 7, 6, and 5, respectively, of the tropane nucleus. In its turn, succindialdehyde can be formed by the reduction of succinic acid.

A treatment of the plants exerting a stimulating effect on their growth did not affect the weight content of alkaloids in the plant as a whole. The radioactivity levels of the alkaloids in the different variants were very close to one another (Table 1).

Table 1

Specific Radioactivity of the Alkaloids, μCi/g

Method of treatment	Alkaloid	Roots	Stem	Leaves	Generative organs	Plant as a whole
Succinic-1,4-^{14}C acid	Hyoscyamine	0.05	0.10	0.10	0.02	0.05
	Scopolamine	0.03	0.04	0.02	0.04	0.03
	Sum	0.04	0.05	0.04	0.03	0.04
Succinic-2,3-^{14}C acid	Hyoscyamine	0.01	0.11	0.04	0.10	0.04
	Scopolamine	0.02	0.18	0.10	0.00	0.03
	Sum	0.02	0.16	0.07	0.02	0.03

The alkaloids in the stems have the greatest sensitivity to radioactivity. The inclusion of ^{14}C in the alkaloids was greatest in the roots (Table 2). Both types of succinic acid were used for the biosynthesis of the alkaloids. Similar radioactivities of the alkaloids are possible only if the whole of the succinic acid molecule or half of it is used.

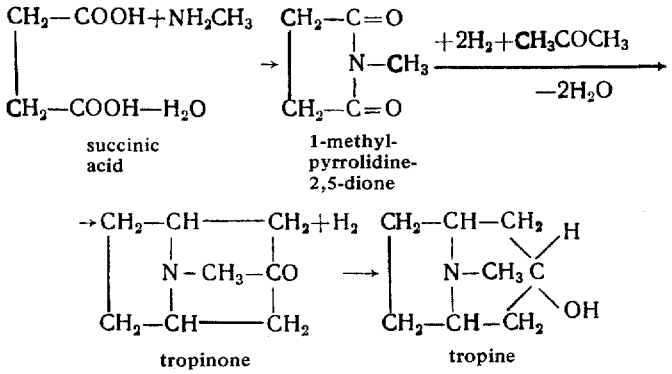
Table 2

Inclusion of ^{14}C in the Alkaloids, %

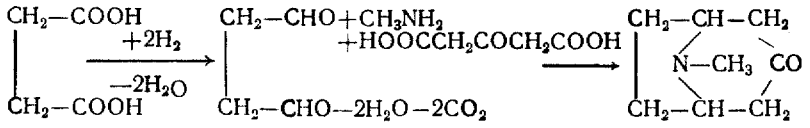
Method of treatment	Alkaloid	Roots	Stem	Leaves	Generative organs	Plant as a whole
Succinic-1,4-^{14}C acid	Hyoscyamine	1.31	0.27	0.07	0.23	0.16
	Scopolamine	1.07	0.32	0.05	0.38	0.17
	Sum	2.38	0.59	0.12	0.61	0.33
Succinic-2,3-^{14}C acid	Hyoscyamine	0.23	0.15	0.03	0.31	0.09
	Scopolamine	2.30	0.46	0.07	0.03	0.18
	Sum	2.58	0.61	0.10	0.34	0.27

Let us consider what the radioactivity level should be when various parts of the molecule of succinic acid are used. When the carboxyl groups are used, the alkaloids will be radioactive only in the experiment with succinic-1, 4-^{14}C acid. This is not confirmed by the experimental results. If the succinic acid residue containing the two neighboring atoms is included in the alkaloids, they will be radioactive only where succinic-2, 3-^{14}C acid is used, which is also not in accordance with the experimental results. If half the succinic acid molecule (acetate) is used, the greatest radioactivity of the alkaloids must be found where succinic-2, 3-^{14}C acid is used and only a small amount with succinic-1, 4-^{14}C acid, since acetate is used for methlating the amino group of γ-aminobutyraldehyde. In this process the acetic acid undergoes decarboxylation. Carbon dioxide may also be used but it takes part in a large number of reactions of the biosynthesis of various substances of the plant and will be incorporated in the alkaloids in only small amount. All that has been said above compels us to reject these hypotheses.

The results of the use of the whole of the molecule of succinic acid in the stepwise formation of tropine can be represented by the following formulas:



It is possible that before being incorporated in the molecule of the alkaloid succinic acid is reduced to succindialdehyde. Then the formation of tropinone would take place in the following way:



Experimental

The plants were sprayed three times with a 0.05% solution of succinic acid in vegetation vessels. In the last spraying, succinic-1,4-^{14}C and -2,3-^{14}C acids with activities of 0.2 μCi were used. After 5 days, the plant was separated into its organs, fixed at 105° C for 15 min, dried, and ground. The plant material was moistened with 25% ammonia, covered with ether and chloroform (1:1) and steeped for 2 days with periodic shaking. The raw material was exhaustively extracted with ether and chloroform. The organic phase obtained was exhaustively extracted with 0.5 N hydrochloric acid. The hydrochloric acid solution was washed with ether, made alkaline with ammonia, and exhaustively extracted with chloroform.

The alkaloids were transformed from solution in chloroform into citrate-phosphate buffer with pH 6.5. Practically all the scopolamine passed from the buffer into chloroform after eight extractions and the hyoscyamine remained in the buffer. The alkaloids were freed of impurities on plates of alumina containing gypsum in chloroform.

Summary

The succinic acid used for the biosynthesis of the tropane alkaloids is probably included in their molecule as a whole, and forms the fragment of the alkaloid molecule consisting of carbon atoms 1, 7, 6, and 5.

REFERENCE

V. A. Kretovich, Principles of Plant Biochemistry [in Russian], Moscow, 1966.

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