

THE BIOGENESIS OF HYOSCINE IN DATURA STRAMONIUM L.

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AS previously reported^{1,2,3} the stems and leaves of Datura ferox L. convert hyoscyamine into hyoscyne. An intermediate product in this reaction is an alkaloid V⁴, probably identical with 6-hydroxy-hyoscyamine.

It was assumed that the hyoscyne in other plants e.g. Datura stramonium L. is derived similarly, but it has been established that the stems and leaves of adult plants of Datura stramonium L., Datura innoxia MILL., Datura metel L. and Atropa bella-donna L. are not able to convert hyoscyamine into hyoscyne although this may be possible in the young plants. Marion and Thomas⁵ and Leete⁶ ascertained that 4-5 month old plants of D.stramonium L. cannot synthesize

¹ A. Romeike, Flora 143, 67 (1956).

² A. Romeike, Flora 148, 306 (1959).

³ G. Fodor, A. Romeike, G. Janzso and I. Koczor, Tetrahedron Letters No. 7, 19 (1959).

⁴ A. Romeike, Naturwissenschaften 47, 64 (1960).

⁵ K. Marion and A.F. Thomas, Canad. J. Chem. 33, 1853 (1955).

⁶ E. Leete, J. Amer. Chem. Soc. 82, 612 (1960)

hyoscine.

Although Methyl ^{14}C atropine has been prepared by Werner *et al.*,⁷ owing to the stereospecificity of the enzyme system in Datura to oxidize S - hyoscyamine only,⁴ feeding experiments with S - methyl ^{14}C - hyoscyamine were preferred. The methyl ^{14}C - hyoscyamine was synthesized from nortropine by methylating with ^{14}C -methyl iodide, acylation of the methyl ^{14}C - tropine with S - acetyltropoyl chloride and mild deacetylation.

The feeding experiments with the labelled hyoscyamine were conducted as follows: 26, fourteen day old seedlings of Datura stramonium L.var. stramonium were cultivated for a week in an inorganic nutrient medium containing 500 μg of radioactive hyoscyamine. This solution had a hyoscyamine concentration of 0.004% and the activity, measured in a flow-counter (Frieske and Hoepfner), was 277.500 per minute. After two days all the hyoscyamine had been taken up by the seedlings and during the following five days they were cultivated in a pure nutrient medium.² The results of 26 control seedlings grown under corresponding conditions in the inorganic medium are given in Table 1. The percentage of radioactivity found in the hyoscine and the alkaloid was 27.5 and 9.8 respectively. These analyses were done by paper chromatography and the quantitative estimations according to de Bruyn and van Hall.⁸

In order to examine the role of the shoots in the conversion of hyoscyamine into hyoscine similar experiments were performed with the aerial shoots of Datura stramonium seedlings. The results are recorded in Table 1.

⁷ G. Werner and E. Kassner, Naturwissenschaften 46, 649 (1959).

⁸ J.W. de Bruyn and J.G. van Hall, Mededeling 152 Inst. voor de Veredel. v. Tuinbouwgew., Wageningen (1959).

TABLE 1
Feeding Experiments in *Datura stramonium* L. var. *Stramonium* with ¹⁴C labelled Hyoscyamine (N-CH₃)

	hyoscyamine fed to the plants		alkaloids found after a week						not identified radioactive substances activity (counts/min)
	hyoscyamine		hyoscyamine		hyoscyamine		atracid y		
	activity (counts/min)	quantity	activity (counts/min)	quantity	activity (counts/min)	quantity	activity (counts/min)	quantity	
26 intact seedlings, 14 days old (experiment plants) fresh weight 6,23 g, dry weight 0,29 g	277 500	500 γ	76 300	290 γ	62 570	130 γ	27 100	60 γ	14 500
26 intact seedlings, 14 days old (control plants) fresh weight 6,10 g, dry weight 0,30 g	-	-	-	140 γ	-	20 γ	-	traces	-
alkaloids built by conversion of hyoscyamine			76 300 (27,5 % of the total activity fed to the plants)	150 γ			27 100 (9,8 % of the total activity fed to the plants)	60 γ	14 500 (5,2 % of the total activity fed to the plants)
overground organs of 31 seedlings 14 days old (experiment plants) fresh weight 5,46 g, dry weight 0,28 g	277 500	500 γ	61 400	320 γ	90 200	160 γ	41 400	80 γ	-
overground organs of 31 seedlings 14 days old (control plants) fresh weight 5,30 g, dry weight 0,27 g	-	-	-	220 γ	-	10 γ	-	traces	-
alkaloids built by conversion of hyoscyamine			61 400 (22,1 % of the total activity fed to the plants)	100 γ			41 400 (14,9 % of the total activity fed to the plants)	80 γ	

As the radioactive hyoscyamine was labelled at the methyl-group the possibility existed that the activity resulted from transmethylation in the plant. Scions of adult Datura stramonium L. which are unable to convert hyoscyamine into hyoscine were fed with ^{14}C labelled hyoscyamine and unlabelled hyoscine. After a week hyoscine without any activity was isolated from these plants.

From this it may be concluded that young aerial shoots of Datura stramonium L. are able to convert hyoscyamine into hyoscine. Alkaloid V, an intermediate product, also appears in this conversion. Further investigations will show whether the roots of Datura stramonium L. are likewise synthesizing hyoscine from hyoscyamine and whether other species of Datura and Atropa bella-donna are similarly able to convert hyoscyamine. Further details concerning synthesis of methyl ^{14}C - hyoscyamine⁹ as well as on the isolation of labelled intermediates will be published elsewhere.

⁹ G. Fodor, G. Janzsó, L. Ötvös and D. Bánfi, Chem. Ber. 93, In press (1960).