THE INHIBITION OF SATURATED FATTY ACID DEHYDROGENATION BY DIETARY FAT CONTAINING STERCULIC AND MALVALIC ACIDS[1]

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This study is a test of the hypothesis that dietary fats containing fatty acids with a cyclopropene ring in the chain (I), such as malvalic and sterculic, inhibit the desaturation of tissue saturated fatty acids to the corresponding monoenes (Reiser et al. 1963a, 1963b).

In one experiment 150 gm rats on stock ration were given 50 mg per day of sterculia foetida oil containing about 50% sterculic acid or corn oil. After seven days they were administered sodium acetate-1-C^{14} intraperitoneally three hours after dosing with the oil, and sacrificed one hour later. The specific activities of the palmitic, palmitoleic, stearic and oleic acids of the epididymal fat pads were determined. The ratios $\frac{\text{dpm/mg palmitic}}{\text{dpm/mg palmitoleic}}$ and $\frac{\text{dpm/mg stearic}}{\text{dpm/mg oleic}}$ were found to be 1.8 and 2.5 respectively in the corn oil controls, but 1.0 and 1.9 respectively in the test animals.

The higher ratios in the control animals is contrary to the hypothesis and actually suggests that the monoenoic acids are formed independently of the saturates and possibly even more rapidly in the test animals.

In a second experiment 250 gm rats maintained on a fat-free diet for 3 weeks were administered by stomach tube 10-20 μc of methyl stearate-1-C^{14} dissolved in either 0.25 ml of corn or sterculia foetida oil. The animals were sacrificed after 4 hours and the fatty acids of the liver and epididymal fat pad triglycerides were assayed for the specific activities of

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stearic and oleic acids.

The results of this study are given in Table 1.

Table 1

The effect of sterculia foetida oil administered with methyl stearate-1-C^{14} on the conversion of the stearate to oleic acid

	Adipose tissue triglycerides			Liver triglycerides		
Controls						
0.25 ml corn oil with methyl stearate-1-C^{14}	Stearic dpm/mg	Oleic dpm/mg	Ratio	Stearic dpm/mg	Oleic dpm/mg	Ratio
	468	149	3.1	1322	479	2.8
	317	92	3.4	1972	817	2.5
	289	85	3.4	11436	3531	3.2
	1275	110	11.6	18264	7104	2.6
Average			5.4			2.8
Test Animals						
(a) 0.25 ml sterculia foetida oil with methyl stearate-1-C^{14}	26222	607	43	12404	196	63
	385	11	35	7405	169	44
	277	9	31	9117	37	246
Average			36			118
(b) 0.5 ml sterculia foetida oil with methyl stearate-1-C^{14}	921	5	184	15550	7	2221

In control rats the stearate had about 3 times the activity of the oleate, showing a high rate of conversion of dietary stearic to oleic acid. Similar results have been reported with lactating cows and goats (Glascock et al. (1956) and in cow's udder perfusion studies (Lauryssens et al. 1961). The activity of palmitic acid was too low to measure, demonstrating that the oleic acid did in fact originate by desaturation of stearic acid and not by β-oxidation and re-synthesis. In the test animals the liver stearate had from 44 to 246 times the activity of the oleate and the adipose tissue stearate from 31 to 43 times. In one rat administered 0.5 ml of sterculia foetida oil the desaturation was almost completely inhibited.

These data indicate that I in the diet inhibit the conversion of stearic to oleic acid and support the hypothesis that the increase in the saturated

fatty acids at the expense of the corresponding monoenes in animals which ingest small amounts of I is due to inhibition of the desaturation mechanism.

Since the ratios of the label from acetate were not different in the contr and test animals, it must be concluded that there are two routes for the biosynthesis of oleic acid in animals, one which does not go through stearate and which is not inhibited by I and one through stearate which is. It is quite possible that the direct route from acetate may be similar to the anaerobic one suggested by Scheuerbrandt et al. (1961) to function in autotropic organisms. Murty et al. (1962) postulated that such a mechanism also operates on the conversion of cis-2-octenoic acid to linoleic acid by laying hens.

Recently, Kircher (1964) studied the addition reaction of I derivatives with methyl mercaptan and β-mercaptopropionic acid and suggested that this reaction of sulfhydryl groups may have its counterpart in the animal body and could cause the physiological effects that are observed when I derivatives are fed to animals. In addition, Holloway et al. (1963) reported that the fatty acid desaturating enzyme from rat liver may be a thiol enzyme as indicated by the ability of para-hydroxymercurybenzoate at very low concentrations to completely inhibit the enzyme activity. The addition of a thiol compound, such as mercaptoethanol, to the inhibited system, restored full activity. These findings suggest that I may add to the thiol group of the fatty acid desaturating enzyme, thereby limiting the conversion of fatty acids to their corresponding monoenes. This hypothesis also explains why I do not inhibit the direct route which does not involve dehydrogenation.

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