The Mechanism of Ethionine Antii-
lipotropic Action

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Administration of ethionine to female rats results in a rapid and marked accumulation of triglycerides in the liver. Concomitant with this accumulation, a pronounced drop in plasma lipoproteins, including the phospholipid lecithin, occurs. Thus, the accumulation of triglycerides in the liver may be due to an ethionine-induced inhibition of plasma lipoprotein synthesis in the liver.

Two pathways for the biosynthesis of lecithin are known: (1) By incorporation of preformed, free choline via cytidinediphosphocholine, (2) By methylation of phosphatidylethanolamine.

In vitro experiments have shown that ethionine is an antimetabolite to methionine in protein biosynthesis, and to methionine as a methyl donor in lecithin biosynthesis.

Thus there are two possible mechanisms for the ethionine-induced inhibition of plasma lipoprotein biosynthesis: (1) Interference with the incorporation of methionine into the protein of plasma lipoproteins. (2) Interference with the incorporation of the methionine-methyl group into the lecithin of plasma lipoproteins.

To test the relative importance of the two pathways and lecithin biosynthesis for plasma lipoprotein synthesis, and to test the relative importance of the two possible mechanisms of ethionine inhibition of plasma lipoprotein synthesis, the experiments shown in Table 1 have been performed.

The following points may be made: (1) The specific activity of blood lecithin compared to the specific activity of liver lecithin is nearly the same both when methyl-14C-methionine and when hydroxyethyl-14C-choline is injected, indicating that lecithin synthesized by both pathways enters a common pool in equilibrium with the plasma lecithin. (2) The inhibiting effect of ethionine on the incorporation of radioactivity into liver lecithin is more pronounced with methionine as the precursor. This may in part be due to an increased pool of free, unlabelled methionine in the liver of ethionine-treated rats, and in part to an inhibition of transmethylation. (3) The specific activity of blood lecithin compared to the specific activity of liver lecithin in the ethionine-treated rats.

Studies on Sphingosines. The Isolation and Preliminary Identification of Some Preparative Byproducts of C18-Sphingosine

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With an earlier described method for the dinitrophenyl derivatives of sphingosine in combination with silicic acid column and thin layer chromatography several hitherto unknown byproducts of the acid isolation of sphingosine have been prepared. Two seem to be results of an isomerisation of the allyl group in sphingosine and at least two seem to be dehydration products of sphingosine and of its allylic isomers.


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In the present communication we report results which show that rat liver homogenate subfractions can catalyze the biosynthesis of palmitoylcarmitine from free palmitate and carnitine. Table 1 shows that rat liver microsomes contain the enzyme system catalyzing this reaction. There is an absolute requirement for ATP and CoA, while the addition of albumin-complexed palmitate gives a 5-fold stimulation. The addition of magnesium chloride, glutathione and of sodium fluoride all have small, but significant stimulating effects. These results indicate that the following reactions take place:

$$\text{Mg}^{2+}$$

(1) Palmitate + CoA + ATP $\rightarrow$ Palmitoyl-CoA + AMP + pyrophosphate

(2) Palmitoyl-CoA + carnitine $\rightarrow$ palmitoyl-carnitine + CoA

Isolated mitochondria have also been found to catalyze the formation of palmitoyl carnitine from carnitine.

These results confirm that fatty acid esters of carnitine are intermediates in the carnitine-stimulated oxidation of fatty acids. The results are also in agreement with the idea that carnitine functions as a carrier of activated fatty acids between metabolic compartments within the cell, as previously suggested.