Conversion of Caproic Acid to Acetoacetic Acid in the Goat.* (18401)

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Ketosis is a common metabolic disorder of ruminants which is of considerable economic importance. In ketosis of dairy cattle, the blood composition is altered by a marked decrease in blood glucose and an increase in ketone bodies. MacKay *et al.*(1) reported that saturated fatty acids with 4, 6, 8 and 10 carbon atoms were ketogenic when fed to normal rats receiving adequate amounts of carbohydrates. Oral administration to goats of single doses of butyric, caproic, caprylic or capric acid has been shown to cause an increase of the total blood ketone level of 5 to 10 mg % [Schultz, Smith and Lardy(2)]. Maximum concentrations of the ketone bodies were attained 15 minutes after administration of butyric acid and 1 hour after the administration of caproic, caprylic or capric acid. It was not clear from that study whether these acids are converted directly to ketone bodies or merely stimulate their production.

Methods. 10.6 g of caproic acid-1-C^{14} containing 6.9 x 10^8 c.p.m. in 20 cc of water was administered orally by means of a stomach tube to a normal fed mature female goat weighing 107 lb. Blood samples were taken from the jugular vein before administration of the fatty acid and at 15, 30, 60 and 90 minutes thereafter. Perchloric acid was added to a final concentration of 4.5% to deproteinize the blood. Acetoacetic acid was determined on an aliquot of the blood by the method of Behre and Benedict(3). 0.625 mM of acetoacetate per 100 ml of deproteinized filtrate was added as a carrier and acetoacetic acid was degraded as described by Plaut and Lardy(4). All samples of barium carbonate and acetone 2,4-dinitrophenylhydrazone were reprecipitated to constant radioactivity. The substances were plated on aluminum dishes and counted with a Q-gas counter. The counts were corrected for background and self absorption [Calvin *et al.*(5)].

Results and discussion. Fifteen minutes after the administration of the radioactive caproate a rise in the acetoacetate content of the blood was observed. Caproate appears to be converted to acetoacetate as evidenced by the parallelism of the concentration and the radioactivity of this ketone body in the blood (Table I). These results may be of significance in the development of ketosis when considered in view of the recently acquired knowledge of rumen digestion (see Phillipson for review)(6). The short chain fatty acids, acetic, propionic and butyric, are important products of rumen fermentation and are absorbed directly into the blood. Acetic and propionic acids, which are produced in the rumen in greater quantities than butyric, do not cause an appreciable increase in blood ketone levels when fed orally to goats (Schultz, Smith and Lardy)(2). In fact, the intravenous injection of propionate into sheep has been reported (Jarrett and Potter)(7) to produce a fall in blood ketone bodies. Therefore, should conditions arise

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TABLE I. Incorporation of Carboxyl Carbon of Caproate Into Blood Acetoacetate.

Time of blood withdrawal after admin. of of caproate-1-C^{14}, min.	Acetoacetate, μM/ml of blood	Radioactivity of acetoacetate in presence of 'carrier' as c.p.m. per mM			Ratio of radioactivity Carbons 2,3,4 Carbon 1, avg
		Carbon 1	Carbon 2,3,4	Total acetoacetate	
0	22				
15	166	10500 ± 200	3650 ± 65	14060 ± 210	.34
30	110	3920 ± 80	1330 ± 40	5250 ± 90	.34
60	103	3980 ± 70	770 ± 25	4750 ± 75	.19
90	100	2240 ± 55	650 ± 30	2890 ± 63	.29

which would alter the fermentation in the rumen, greater quantities of butyric or longer chain fatty acids might be produced. If this should occur, the acids produced in the rumen might be a factor in the development of ketosis.

It is of interest that the activity of the acetone portion and the carboxyl group of the acetoacetate is not equal, which points to the possibility that when caproate is administered to the whole animal, the recondensation of two-carbon fragments derived from this fatty acid does not occur in a random fashion. This is in accord with the observations of Crandall *et al.*(8,9), in their experiments on the metabolism of fatty acids by washed rat liver homogenates.

Summary. Caproate 1-C^{14} was administered to a goat. The resulting increase of blood acetoacetate is roughly proportional to the rise in radioactivity of this compound. The specific radioactivity per mole of the carboxyl group of the acetoacetate is larger than that of the acetone portion. This is another indication that two-carbon compounds derived from fatty acid do not condense in a random fashion to form acetoacetate.

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Effect of Colchicine on Tumor Growth and Tumor Pyrophosphatase. (18402)

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A new attempt has recently been made to explain the influence of colchicine on tumors. According to this theory the regression of tumors obtained by injections of colchicine is due to the action of this substance on the endothelial cells of growing capillaries of the tumor. This action was very marked in "highly cellular rapidly growing tumors"(1). This explanation compares the action of colchicine to that of polysaccharides obtained from *Seratia marcenses* [Shear and coworkers (2,3)]. In the strain of tumor with which we worked, we were unable to observe this hemorrhagic action of colchicine, and since we found this tumor to contain a highly active enzyme, capable of hydrolysing sodium pyrophosphate, we deemed it worthwhile to examine the dependence of this enzyme system

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