acetyl-CoA formed was converted into ketone bodies. With increasing concentrations of inorganic phosphate this percentage was greatly increased. At 30mM-phosphate it was 68%. The amount of palmitoylcarnitine broken down was lowered by 29%; the oxygen uptake was 55% lower; ketone-body production was doubled; the tricarboxylic acid-cycle activity was lowered by 70%. These observations are in good agreement with the inhibition by inorganic phosphate of palmitoylcarnitine oxidation observed by Van Tol, De Jong & Hülsmann (1969). However, when palmitate was oxidized in the presence of dinitrophenol, 10mM-ATP and 10 μ g of oligomycin (Van den Bergh, 1965), no effect of the inorganic phosphate concentration was observed.

When 2 μ mol of palmitate was oxidized in the presence of 30mM-phosphate and a phosphate-acceptor system, the addition of 1.5% bovine serum albumin lowered the percentage of acetyl-CoA converted into ketone bodies from 78% to 17% in a typical experiment. The addition of albumin lowered by 11% the amount of palmitate broken down; oxygen uptake was 70% increased; tricarboxylic acid-cycle activity was increased 3.3-fold; ketone-body production was 80% decreased. The effect of albumin was much smaller, however, when palmitoylcarnitine was the substrate.

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Effects of an Acylcarnitine Analogue, 2-Bromomyristoylthiocarnitine, on Mitochondrial Respiration

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The CoA thiol esters of long-chain 2-bromo acids are powerful inhibitors of carnitine palmitoyltransferase and hence of the carnitine-dependent mitochondrial oxidation of palmitoyl-CoA, but, presumably because of a permeability barrier, they do not inhibit palmitoylcarnitine oxidation (Tubbs & Chase, 1967). This is, however, very strongly inhibited by 2-bromoacyl derivatives of the new compound thiocarnitine:

S-Acetylthiocarnitine is a good substrate for

carnitine acetyltransferase, and longer-chain esters are rapidly oxidized by liver or heart mitochondria. Thiocarnitine itself can substitute for carnitine in supporting the mitochondrial oxidation of palmitoyl-CoA. Rat liver mitochondria briefly incubated with very low concentrations of S-2-bromomyristoylthiocarnitine cannot oxidize palmitoylcarnitine, although pyruvate (+ malate) or succinate still support rapid respiration. The simple explanation would be that bromoacylthiocarnitine inactivates the carnitine palmitoyltransferase of the mitochondria, by analogy with the effect of bromoacetylthiocarnitine on carnitine acetyltransferase (Chase & Tubbs, 1969). However, when mitochondria are treated with 50 μ M-palmitoyl-L-carnitine after exposure to 3 μ M-2-bromomyristoyl-DL-thiocarnitine they become incapable of oxidizing pyruvate, α -oxoglutarate or hexanoate, although succinate oxidation is unimpaired. The oxidation of these substrates, but not of palmitoylcarnitine or palmitoyl-CoA, is restored by the addition of 2mM-L-carnitine. These observations suggest that some of the carnitine palmitoyltransferase is still active, and that a metabolite of bromoacylthiocarnitine, presumably 2-bromoacyl-CoA generated within the 'carnitine permeability barrier', inhibits the β -oxidation of long-chain fatty acyl groups. Thus the further addition of palmitoyl-carnitine leads to extensive acylation of mitochondrial CoA and prevents the CoA-dependent oxidation of substrates such as pyruvate, unless sufficient carnitine is present to act as an acyl sink.

The apparent immunity of the 'inner' pool of carnitine palmitoyltransferase to bromoacylthiocarnitine is of interest; whether this is an intrinsic property of the enzyme or is due to its environment within the mitochondrion remains to be determined.

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Translocation of Protons and Alkali-Metal Cations Accompanying the Uptake of Neutral Amino Acids by Yeast

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Eddy (1966) drew an analogy between the effects of varying extracellular $[\text{H}^+]$ and $[\text{K}^+]$ on the rate of uptake of glycine by yeast and the effects of varying $[\text{Na}^+]$ and $[\text{K}^+]$ on glycine uptake by mouse ascites-