

ABSTRACT

A. Pyruvate dehydrogenase kinase in unlysed but permeable mitochondria was studied after the mitochondria were isolated from tissues of fed, starved or diabetic rats.

1. 24h starvation led to an increase in pyruvate dehydrogenase kinase activity in mitochondria from rat heart and adipose tissue, but not from kidney and brain.

2. Pyruvate inhibited pyruvate dehydrogenase kinase activity in mitochondria from rat heart, adipose tissue, brain and kidney of fed rats.

3. Starvation for 24h led to a loss of pyruvate sensitivity of the kinase in heart and adipose tissue mitochondria. Pyruvate sensitivity of the kinase from heart and adipose tissue mitochondria of starved rats was restored 40min after insulin injection of the animal, and in the case of pyruvate dehydrogenase kinase from heart by pyruvate injection 30min before sacrifice of the animal.

4. Streptozotocin induced diabetes produced a slow loss of pyruvate sensitivity of heart mitochondrial pyruvate dehydrogenase kinase, and a more rapid increased kinase activity in heart and adipose tissue.

It is concluded that the mechanism which controls changes in pyruvate sensitivity of the kinase is different from the mechanism

which controls changes in the uninhibited activity.

B. The possible physiological importance of pyruvate in regulating pyruvate dehydrogenase was further demonstrated in adipose tissue. Injection of insulin into starved rats led to an increase in the ratio of the active form to total pyruvate dehydrogenase activity in extracts of freeze-clamped adipose tissue. Injection of pyruvate as well as insulin into starved rats led to a further increment in this ratio.

C. Addition of carbonylcyanide *m*-chlorophenylhydrazone to the incubation medium of unlysed heart and brain mitochondria, or triton X-100 to the incubation medium of unlysed heart mitochondria or freeze-thawing of brain mitochondria led to an enhancement of pyruvate dehydrogenase kinase activity and loss of pyruvate inhibition compared to pyruvate dehydrogenase kinase of unlysed mitochondria. This may indicate a direct influence of its membrane environment on behaviour of pyruvate dehydrogenase kinase.