P-FRUCTOKINASE AND THE CONTROL OF THE CITRIC ACID CYCLE*

Janet V. Passonneau and Oliver H. Lowry

The Department of Pharmacology and the Beaumont-May Institute of Neurology, Washington University School of Medicine, St. Louis 10, Missouri

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It was reported earlier (Passonneau and Lowry, 1962a, 1962b) tha the strange kinetic properties of P-fructokinase (PFK) provide a reasonable explanation for the control of glycolysis beyond fructose-6-P (F6P). PFK is strongly inhibited by high levels of one substrate ATP (Lardy and Parks (1956), Bueding and Mansour (1957), Mansour and Mansour (1962)), and this inhibition is counteracted by the other substrate and both products as well as by AMP, P_i, and cyclic 3',5'-AMP.[1] Increases in activity of 10 or 20-fold are produced by small increases in these compounds, and combinations of some of them are particularly effective. These results have been confirmed for heart PFK (Mansour, 1963); and yeast PFK has been shown to exhibit a number of the same kinetic phenomena (Viñuéla et al., 1963).

It has now been found simultaneously in this and two other laboratories that citrate is a potent inhibitor of PFK from skeletal muscle (Parmeggiani and Bowman, 1963), heart (Garland et al., 1963),

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[1]In a more thorough study of the kinetics of PFK to be reported elsewhere it has been found that ADP, AMP and 3'5'-cyclic AMP act chiefly by enhancing activity at all ATP levels, whereas P_i, F6P, and fructose diphosphate overcome ATP inhibition. It has also been found, in confirmation of Muntz (1953), that NH_4^+ and K^+ enhance PFK activity but they are not effective in antagonizing ATP inhibition.