A CONSTANT-PROPORTION GROUP IN THE ENZYME ACTIVITY PATTERN OF THE EMBDEN-MEYERHOF CHAIN

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In a previous study the activity patterns of enzymes of the Embden-Meyerhof chain were compared in three different types of muscles of the desert locust (Vogell et al. 1959). Each of these muscles could be characterized by the specific arrangement of its enzymes on the scale of absolute activity. From this point of view the activity patterns of the three muscles were different. On the other hand, a certain congruence of the patterns was established by the fact that five enzymes - triosephosphate isomerase (TIM), glyceraldehyde-phosphate dehydrogenase (GAPDH), phosphoglycerate kinase (PGK), glycerate mutase (GPM) and enolase (EN) - showed a striking constancy in the ratio of their activities in these three muscles.

We have tried to confirm this phenomenon of a "constant-proportion group" of extramitochondrial enzymes by extending the range of investigated tissues beyond the realm of insects and of muscles (Bücher and Pette, 1961). A further improvement in the technique of tissue extraction (Pette, 1962), as well as standardized and optimal conditions for the measurement of the different enzymic activities, were basic requirements in this comparative study. The results obtained are shown in figures 1 to 3 in the form of activity patterns (Bücher and Klingenberg, 1958; Delbrück et al., 1959; Vogell et al., 1959; Bücher et al., 1959; Bücher, 1960; Bücher and Pette, 1961), i.e., the extramitochondrial enzymes extracted from one gram of tissue and tested in vitro are plotted in a logarithmic scale. As can be seen, the

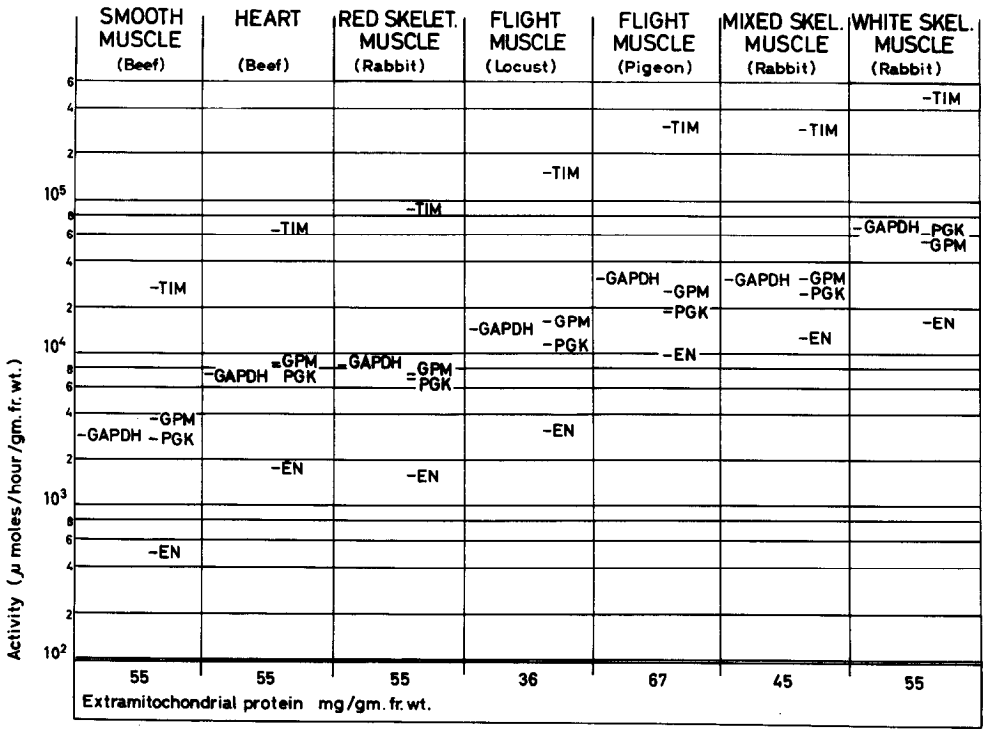

Figure 1

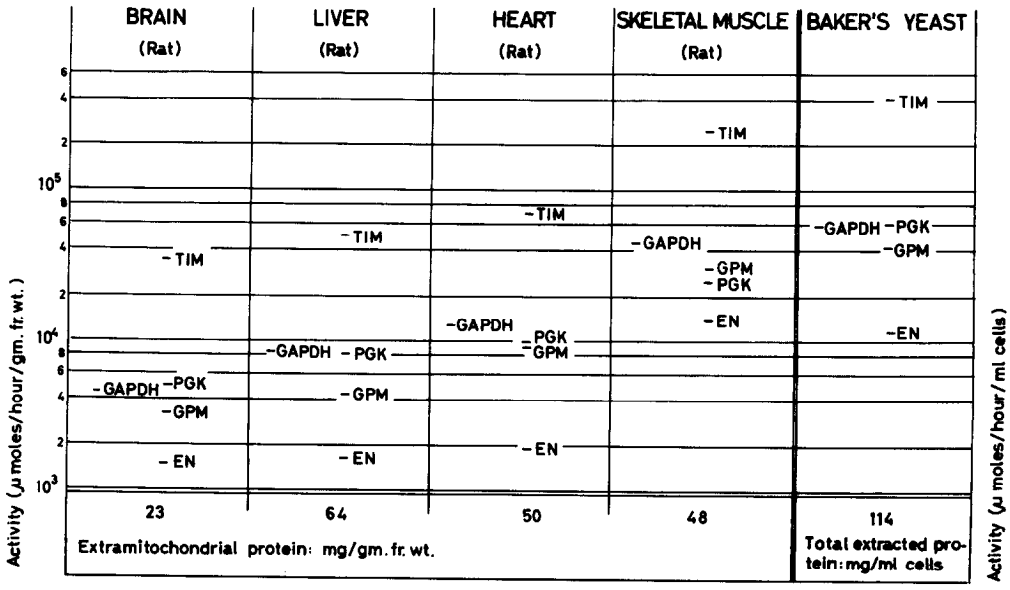

Figure 2

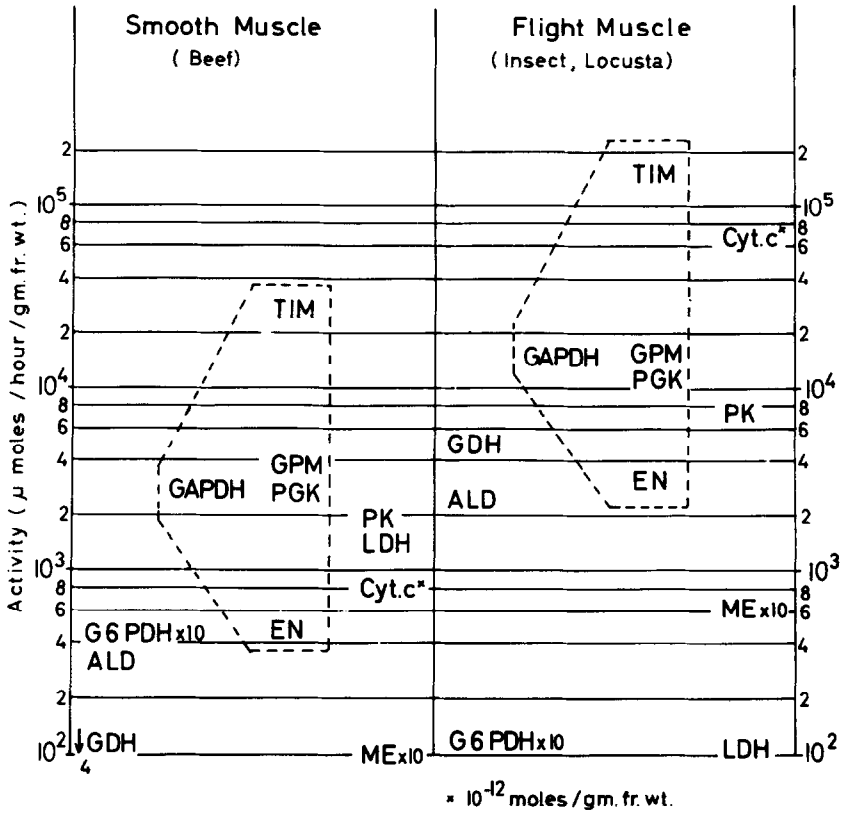

Figure 3

proportions of the activities of the five enzymes mentioned above are comparable in various types of muscle from phylogenetically different animals (fig.1) as well as in various organs of the rat as well as in yeast (fig.2). In the great number of tissues investigated, the ratio of activity to that of GAPDH is 6 to 12 for TIM, 0.6 to 1.2 for PGK and GPM and 0.15 to 0.3 for EN. On the other hand, the level of this group varies by orders of magnitude, the absolute activity of GAPDH in the smooth muscle being 5 % of that in white muscle.

Besides this group of five enzymes, a great number of extramitochondrial enzymes of energy-producing metabolism, including the complete sequence of the EMBDEN-MEYERHOF chain, was tested in all tissues. The characteristic situation of the "constant proportion group" within the enzyme pattern of

energy-producing metabolism is shown by the more complete activity patterns in figure 3. By comparing these patterns in two extreme types of muscle it can be seen that great differences exist in the activities of lactate dehydrogenase (LDH) and glycerol-1-P dehydrogenase (GDH). An almost total lack of LDH and a high activity of the DPN-specific GDH is characteristic of the insect flight muscle (Zebe et al., 1956; Zebe and McShan, 1957; Sacktor and Cochran, 1957; Chefurka, 1958; cf. reviews Klingenberg and Bücher, 1960; Sacktor, 1961). The reciprocal proportion of the activities of these **dehydrogenases** is found in the smooth muscle of the first stomach in beef. Similar differences of the relative activities are found with glucose-6-P dehydrogenase (G6PDH) as a representative of the oxidative shunt and cytochrome c (Cyt.c), representing the activity of the respiratory chain. With respect to these enzymes, the patterns are dissimilar in terms of absolute activities as well as in the relation of their activities to that of the "constant-proportion group". On the other hand, aldolase (ALD), pyruvate kinase (PK), malic enzyme (ME) and other enzymes which are not plotted in the patterns, such as phosphoglucomutase, fructose-6-P kinase and the extramitochondrial malate dehydrogenase, show, independently of the varied levels of their absolute activities, comparable proportions to this quintet of enzymes in both muscles. This holds for the majority of the muscles investigated, but not for all the other tissues.

The significance of the constant-proportion group dealt with in this paper may be seen in the fact that it fits exactly between two junction points of the network of carbohydrate metabolism. With respect to the organisational plan of the Embden-Meyerhof chain, the quintet forms the only major unbranched segment. It seems to be significant that the group is formed by these five enzymes arranged one after another in that segment of the chain which metabolizes the phosphorylated 3-carbon compounds. The close functional interconnection of the enzymes of the "phosphotriose-glyceratephosphate group" (PTG-group) may explain the limited variability of their relative activities. However, other constant proportion groups in the system of the key-pathways of metabolism may be found, even including enzymes which are dealt with in different

chapters of the textbooks (Bücher and Pette, 1961; Pette et al., 1962; Pette and Luh, 1962). Fitch and Chaikoff (1960) recently reported an inductional rise of the levels of three enzymes which are linked by the extramitochondrial TPN-system (glucose-6-P dehydrogenase, 6-P-gluconate dehydrogenase, malic enzyme) by a factor of 10 in approximately constant proportions.

So far, our experiments concerning the PTG-group do not account for the phenomenon of "isozymes" and differences in catalytic properties which may exist in corresponding enzymes from different organs and species. However, the nearly constant ratio of the activities of the PTG-group suggests that the phenomenon is a result from a co-ordination at the molecular levels. Co-ordinate pleiotropy at the level of enzyme patterns has been found in micro-organisms. Mechanisms for the co-ordinate control of enzyme synthesis have been proposed by Szilard (1960) as well as by Jacob et al. (1960) in their operon hypothesis.

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