SPECIFICITY OF TYROSINE METABOLISM DEPENDING ON THE STATE OF MELANINOGENESIS

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UDC 612.398.192:547.587.42

The study of excretion of tyrosine metabolites (p-hydroxyphenylpyruvic acid, homogentisic acid, total keto compounds) and of the tyrosine-aminotransferase activity of the organs and tissues of albino and black rabbits showed that the initial levels of the tyrosine metabolites in the urine of the black and albino rabbits differ only very little from each other. After oral administration of L-tyrosine the quantity of p-hydroxyphenylpyruvic acid excreted by the albino rabbits increased sharply, whereas that of homogentisic acid fell. In the case of black rabbits, increased excretion of homogentisic acid was observed whereas the level of excretion of p-hydroxyphenylpyruvic acid remained comparatively constant. Of the organs tested, only in the skin and liver of the albino rabbits was a sharp increase in the initial activity of tyrosine-aminotransferase found after the administration of L-tyrosine, indicating adaptive synthesis of the enzyme. Analysis of the results suggests that tyrosine metabolism is dependent on the state of melaninogenesis.

KEY WORDS: *tyrosine; melaninogenesis.*

Melanins of animal origin are synthesized from tyrosine. According to the generally accepted scheme, tyrosine is oxidized and converted through a series of compounds into indole-5,6-quinone, which in turn is polymerized into a melanin polymer. The initial and, to some extent, the final stages of this pathway of tyrosine metabolism have been studied both in model systems and in vivo sufficiently well [6, 7, 16, 17]. The properties of tyrosinase, catalyzing only the initial stage of tyrosine oxidation along the path of its conversion into melanin, have been described [9, 11, 12, 15]. A connection was demonstrated by the writers previously between the rate of deamination of histidine in the skin and the state of melaninogenesis [2] and changes also were discovered in tyrosine catabolism during pathology of melanin metabolism [3].

The object of this investigation was to study the oxidative breakdown of tyrosine in animals differing in their degree of melaninogenesis.

EXPERIMENTAL METHOD

Experiments were carried out on albino and black rabbits weighing 2-2.7 kg, usually in the summer months (July and August). All the rabbits were kept under identical laboratory conditions on a similar diet. The 24-h excretion of tyrosine metabolites—p-hydroxyphenylpyruvic acid (PHPP) [10], homogentisic acid (HGA) [8], and total keto compounds (KC) [4]—, activity of tyrosine-aminotransferase in the liver and various other tissues [5], and also the protein level in those tissues [14] were deter-

Department of Biochemistry, Turkmenian Medical Institute, Ashkhabad. Department of Biochemistry, Patrice Lumumba Peoples' Friendship University, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR S. S. Debov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 80, No. 8, pp. 44-47, August, 1975. Original article submitted October 10, 1974.

TABLE 1. Tyrosine-Aminotransferase Activity in Organs and Tissues of Albino and Black Rabbits before and after Loading (0.5 mmole/kg) with DL-Tyrosine (M ± m)

Organ and tissue	Albino rabbits		Black rabbits	
	initial level (6)	after loading (9)	initial level (6)	after loading (9)
Liver	3,39±0,170	4,19±0,380	3,80±0,380	3,93±0,210
Kidneys	0,26±0,025	0,20±0,026	0,30±0,022	0,29±0,029
Spleen	0,16±0,021	0,24±0,033	0,22±0,011	0,25±0,021
Adrenals	0,36±0,014	0,33±0,050	0,39±0,037	0,31±0,032
Skin	0,045±0,019	0,195±0,062	0,144±0,019	0,302±0,084

Note. Number of animals in parentheses.

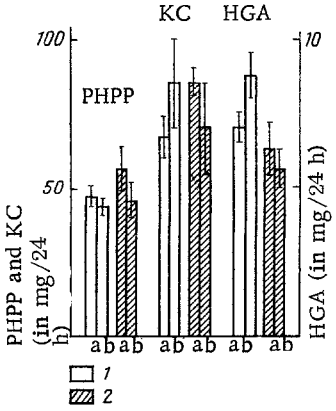

Fig. 1

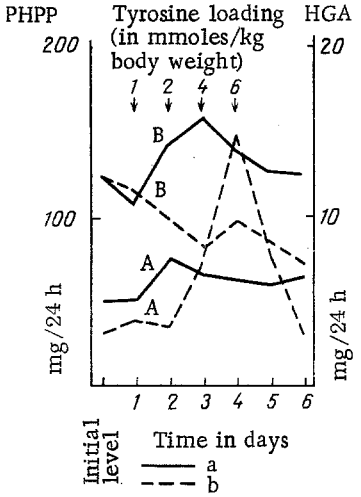

Fig. 2

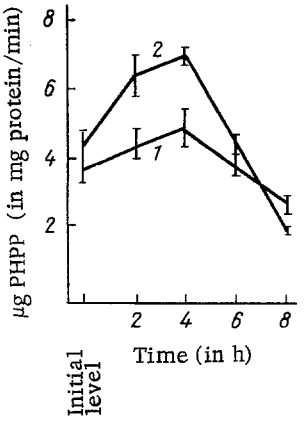

Fig. 3

Fig. 1. 24-Hourly excretion of PHPP, KC, and HGA in urine of rabbits: a) initial level; b) after oral administration of DL-tyrosine (0.5 mmole/kg); 1) albino rabbits, 2) black rabbits.

Fig. 2. Dynamics of 24-h excretion of PHPP (A) and HGA (B) in urine of albino and black rabbits after repeated administration of L-tyrosine (1-6 mmoles/kg): a) black rabbits, b) albino rabbits.

Fig. 3. Dynamics of tyrosine-aminotransferase activity in liver of black (1) and albino (2) rabbits after single dose of L-tyrosine (2 mmoles/kg).

mined in the animals. Enzyme activity was expressed in µg PHPP/mg protein/min.

Investigations were carried out before and after injection of L-tyrosine through a tube into the stomach. After determination of the volume of the 24-h sample of urine, 50-60 ml of it was frozen and kept for not more than 3-4 days before determination of the tyrosine metabolites.

EXPERIMENTAL RESULTS AND DISCUSSION

In the experiments of series I on 30 rabbits the excretion of tyrosine metabolites and activity of tyrosine-aminotransferase in the liver, kidneys, spleen, adrenals, and skin and the effect of DL-tyrosine in a single dose of 0.5 mmole/kg body weight on these indices were studied (Table 1; Fig. 1). Clearly excretion of tyrosine metabolites was almost identical in the rabbits of both groups, and loading with a small quantity of substrate likewise caused no appreciable change in excretion of the tyrosine metabolites. However, it will be noted that after loading some differences

(although not reaching statistical significance) in the character of excretion of the metabolites did appear, depending on the state of melaninogenesis. For instance, whereas the decrease in PHPP excretion by the albino rabbits was negligible, in the black rabbits it was almost 20% of the initial level, whereas the excretion of HGA by the black rabbits after loading showed a tendency to decrease, but in the albino rabbits it increased by about 24% ($P = 0.1$).

Tyrosine-aminotransferase activity in all the organs of the albino and black rabbits investigated, except skin, was about the same (in the skin of the albino rabbits the initial enzyme activity was only about one-third that in the black rabbits), and after tyrosine loading its activity in the skin of the black rabbits was doubled but in the skin of the albino rabbits it was increased by nearly 5 times.

Latent differences in tyrosine metabolism depending on melaninogenesis thus exist in rabbits and are manifested after loading with the substrate.

According to data in the literature [13] increased activity of liver tyrosine-aminotransferase and the excretion of large quantities of HGA in the urine are observed after administration of large doses of L-tyrosine. Accordingly, in the next series the dynamics of excretion of tyrosine metabolites after prolonged and repeated loading with L-tyrosine was investigated in the course of 1 week.

After collection of the original 24-h sample of urine, L-tyrosine was given to albino and black rabbits (5 animals of each color) by gastric tube in doses of 1 mmole/kg on the 1st day, 2 mmoles/kg on the 2nd day, 4 mmoles/kg on the 3rd day, and 6 mmoles/kg on the 4th day. The urine was collected during the 4 days of the experiments and the 2 days after the end of substrate administration. These experiments (Fig. 2) showed significant differences in the dynamics of excretion of both PHPP and HGA depending on the state of melaninogenesis. On the first day of loading of the animals with L-tyrosine a slight increase in the excretion of PHPP and HGA by the black rabbits was observed, but the figures for the albino rabbits were either unchanged (PHPP) or even slightly reduced (HGA). With an increase in the dose of L-tyrosine to 4 and 6 mmoles/kg the excretion of PHPP in the urine increased sharply in the albino rabbits but remained comparatively steady in the black rabbits. HGA excretion by the black rabbits, on the other hand, showed a tendency to rise and reached a maximum on the 3rd day after loading, whereas increased substrate loading of the albino rabbits led to a decrease in HGA excretion, and after the loading was discontinued, the HGA excretion remained significantly lower than in the black rabbits. Excretion of PHPP in the urine returned rapidly to its initial level in the albino rabbits after the end of substrate loading, but in the black rabbits it remained higher.

The liver tyrosine-aminotransferase of the albino rabbits reacted more actively to administration of 2 mmoles/kg L-tyrosine. The maximal increase in activity was found 4 h after administration of the substrate (Fig. 3).

During administration of small doses of L-tyrosine (up to 2 mmoles/kg body weight) to the animals the increased quantity of PHPP formed as a result of adaptive synthesis of tyrosine-aminotransferase in the liver was evidently oxidized to HGA by the action of specific PHPP oxidases in the tissues is relatively high [1]. After administration of large doses of L-tyrosine (4 and 6 mmoles/kg) to the animals a considerable increase in PHPP content was observed as the result of a sharper increase in liver tyrosine-aminotransferase activity in the albino rabbits, but the potential capacity of the PHPP oxidases did not permit conversion of the whole of the PHPP into HGA. In albino rabbits the excretion of PHPP thus rose sharply. The comparatively stable level of PHPP in the urine of the black rabbits can be explained by the small increase in liver tyrosine-aminotransferase activity, which evidently led to the formation of a moderate amount of PHPP, not more than could be successfully oxidized to HGA by the action of the oxidase. Another possibility is that some tyrosine in black rabbits is incorporated into the melanin metabolic pathway, for the increase in liver

tyrosine aminotransferase activity in their liver is less than in that of albino rabbits for the same L-tyrosine loading. It has been shown, for example, that the increased melaninogenesis during exposure to sunlight is accompanied by a decrease in the tyrosine content in the skin [17].

Analysis of these findings suggest that tyrosine metabolism evidently depends on the state of melaninogenesis.

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