CONTENT AND BIOSYNTHESIS OF UBIQUINONE-9 IN THE LIVERS OF ALBINO RATS ADAPTED TO ALTITUDE HYPOXIA

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The content and biosynthesis of ubiquinone-9 were studied in thin liver slices from rats adapted to altitude hypoxia. A more than threefold increase in ubiquinone-9 biosynthesis was found in the initial period of adaptation to altitude hypoxia, but this increase 2 weeks after the beginning of adaptation was very slight. The content of ubiquinone-9 in the rat liver showed no significant change during adaptation to altitude hypoxia for 1 month.

KEY WORDS: ubiquinone-9; altitude hypoxia; liver; adaptation.

Ubiquinone is an electron carrier for the NADH and succinate oxidase systems of mitochondria [6]. As well as in mitochondria, ubiquinone is also found in microsomes and other subcellular particles [8]. Ubiquinone biosynthesis is carried out intracellularly by means of a complex enzyme system; the initial stages of its biosynthesis take place in the cytoplasms of the cells but the terminal reactions occur in the inner membrane of the mitochondria [7]. Ubiquinone synthesis in organs is considerably increased during adaptation of animals to cold stress [8], during regeneration of the liver [3], and during compensatory hypertrophy of the kidney after unilateral nephrectomy [4]. The increase in ubiquinone biosynthesis in the organs coincides in time with acceleration of mitochondrial biogenesis [3, 4].

During adaptation of animals to altitude hypoxia the rate of formation of new mitochondria is considerably increased in various organs [1, 5], so that the concentration of mitochondrial protein per unit mass of organs is significantly increased [1]. This explains the need for investigation of the content and biosynthesis of ubiquinone during adaptation of animals to altitude hypoxia.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 180-210 g. Adaptation to altitude hypoxia was carried out in a pressure chamber at 18-26°C for 6 h daily. A reduced pressure was created in the chamber to values corresponding on the first day of adaptation to an altitude of 3000 m, on the second day of 3500 m, on the third day of 4000 m, on the fourth day of 4500 m, on the fifth day of 5000 m, on the sixth day of 5500 m, and on the seventh and subsequent days of 6000 m. During adaptation the animals were used in the experiments 18 h after removal from the pressure chamber. Ubiquinone-9 biosynthesis in the livers of the rats was determined from incorporation of CH_3COONa-2-C^{14} by thin liver slices.

Preparation of the slices, their incubation with labeled precursor, isolation of ubiquinone-9 from the slices, and determination of its content and radioactivity were carried out as described previously [3]. The slices were incubated for 3 h. Control animals (two rats each day) were studied at the beginning of the experiment and 5, 16, and 30 days after the beginning of adaptation of the experimental group. The numerical results were subjected to statistical analysis [2].

EXPERIMENTAL RESULTS

As Table 1 shows, the concentration of ubiquinone-9 in the liver of the rats during adaptation to

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TABLE 1. Content and Biosynthesis of Ubiquinone-9 in Thin Liver Slices of Rats Adapted to a Lowered Barometric Pressure (M ± m)

Time of investigation after beginning of adaptation	Number of rats investigated	Concentration of ubiquinone-9 (in μg/wet weight of slices)	Biosynthesis of ubiquinone-9	
			Incorporation of C^{14} into radioactivity of slices (in counts/min/g slices)	Specific radioactivity of ubiquinone (in counts/min/mg protein)
Control	8	57,90± 7,91	242± 18	4 561± 600
After 2-5 days	6	61,51± 6,59	932± 307*	15 086± 4 108*
After 13-16 days	6	74,60± 11,77	414± 49*	5 903± 879
After 28 days	4	59,76± 23,26	210± 75	4 781± 1 117

$P \leq 0.05$ (compared with control)

altitude hypoxia did not change significantly although a tendency was observed for it to rise a little 13-16 days after the beginning of adaptation.

The biosynthesis of ubiquinone-9 (Table 1) was increased more than threefold in the initial period of adaptation (after 3-5 days). Considerable differences were found in the rates of ubiquinone biosynthesis in different animals. The responses of the rats to altitude stress were evidently not identical. Judging from the rate of incorporation of acetate-2-C^{14}, the rate of ubiquinone biosynthesis 13-16 days after the beginning of adaptation was increased by more than 1.5 times. However, no significant increase in the specific radioactivity of ubiquinone-9 could be found at this period. The rate of ubiquinone-9 biosynthesis 28 days after the beginning of adaptation was practically the same as in unadapted animals. No significant fluctuations in ubiquinone biosynthesis were found in the control rats. A marked increase in ubiquinone biosynthesis was thus observed in the rats only in the initial period of adaptation to altitude hypoxia.

One cause of the increased rate of ubiquinone synthesis in the liver in the initial period of adaptation of rats is activation of the genetic apparatus of the cells [1]. Meerson [1] found a marked increase in the synthesis and concentration of RNA and DNA in the mitochondria of animals in the initial period of adaptation to hypoxia, followed by a slight decrease toward the 30th-40th day of adaptation. However, the rate of nucleic acid synthesis in the adapted animals was appreciably higher than in control animals. In the present experiments an increase in the rate of ubiquinone biosynthesis was observed only in the initial period of adaptation to altitude hypoxia. An increase in the content of acetyl CoA, one of the precursors of ubiquinone, through inhibition of oxidative processes could play an essential role in the activation of ubiquinone biosynthesis in the initial period of adaptation. However, the subsequent increase in the ubiquinone concentration could be an unfavorable factor, for a substantial increase in ubiquinone concentration is accompanied by intensification of free, nonphosphorylating oxidation [4, 8]. During adaptation of animals to altitude hypoxia, normal ubiquinone biosynthesis is therefore restored.

As was stated above, increased ubiquinone biosynthesis in the organs of animals is observed in various other types of stress [3, 4, 8]. Increased ubiquinone biosynthesis under these circumstances is found in the initial period of adaptation to unfavorable environmental factors. During exposure to stressors, activation of ubiquinone biosynthesis is evidently observed initially, but in the course of adaptation to the stress conditions, ubiquinone biosynthesis returns to its normal level.

LITERATURE CITED

1. F. Z. Meerson, Pat. Fiziol., No. 3, 7 (1973).
2. É. V. Montsevichute-Eringene, Pat. Fiziol., No. 7, 71 (1964).
3. V. V. Fedurov and I. V. Kuz'menko, Byull. Éksperim. Biol. Med., No. 8, 109 (1974).
4. V. V. Fedurov and E. F. Shamrai, in: Abstracts of Scientific Proceedings of the Third All-Union Biochemical Congress [in Russian], Vol. 1, Abstracts 7,18, Riga (1974).
5. A. Hamberger and H. Hyden, J. Cell Biol., 16, 521 (1963).
6. A. Kroger and M. Klingenberg, Vitam. Horm., 28, 533 (1970).
7. K. Momose and H. Rudney, J. Biol. Chem., 247, 3930 (1972).
8. T. Ramasarma, J. Sci. Indust. Res., 27, 147 (1968).