CONTENT OF UBIQUINONE (COENYZME Q) IN THE REGENERATING LIVER OF ALBINO RATS

V. V. Fedurov and I. V. Kuz'menko

UDC 612.6.03 : 612.35.015.11 : 577.158.8.013

The content of ubiquinone in the regenerating liver of albino rats was investigated after single-stage removal of two-thirds of the liver. A statistically significant decrease in the ubiquinone level calculated per gram fresh weight of the regenerating liver was found 3 days after hepatectomy. On the 15th day after the operation, the ubiquinone level was increased when expressed relative to liver protein. The most rapid increase in ubiquinone concentration was observed on the 5th-9th day after operation.

Ubiquinones, or coenzymes Q are widely distributed in animal tissues and in micro-organisms [8], and they are components of their respiratory chain. In their biological role the ubiquinones belong to the same group as compounds such as NAD, folate, and cytochromes. In their molecular structure they are similar to the liquid-soluble vitamins E and K [4]. However, they differ from vitamins in that no ubiquinone deficiency in the diet of animals is observed, for it is synthesized directly by the tissues [11, 12]. Biosynthesis of coenzyme Q takes place by a complex enzyme system and it is closely connected with the biosynthesis of protein and steroids. The reason for this is that amino acids such as phenylalanine and tyrosine are the source of the benzoquinine ring of ubiquinone, while methionine is the source of its methyl and methoxyl groups [11]. The isoprenoid side chain of coenzyme Q is synthesized from acetate via mevalonic acid [11]. A deficiency of protein in the diet of animals leads to a decrease in the ubiquinone concentration [7]. A change in the rate of protein synthesis in the body may perhaps also lead to changes in the ubiquinone level in the organs of animals. The regenerating liver of albino rats is known to differ from the normal liver in its more active protein biosynthesis [2]. In the investigation described below, the ubiquinone content was studied in the regenerating rat liver.

EXPERIMENTAL METHOD

Experiments were carried out on young noninbred male albino rats weighing 120-130 g, kept on the ordinary animal house diet. Partial hepatectomy was performed by the method of Higgins and Anderson [6] under brief ether anesthesia. The animals were decapitated on the 1st, 3rd, 6th-9th, 12th, and 15th days after the operation. The liver was quickly removed, washed with physiological saline, dried with filter paper, and cut up into pieces with scissors. Saponification of the liver was carried out by the method of Mervyn and Morton [10]. Unsaponified lipids were extracted with diethyl ether. The ethereal extract was dried with anhydrous sodium sulfate and evaporated in vacuo. Preliminary isolation of the ubiquinone was carried out on a column with inactive alumina containing 6% water [5]. The ubiquinone was isolated on a thin layer of Velm silica gel by the method of Wagner et al. [13] and determined spectrophotometrically [3]. Protein in the liver also was determined by the method of Lowry et al. [9]. The numerical results were analyzed statistically by Montsevichyute-Éringene's [1] method of direct differences.

Central Research Laboratory, Kiev Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR S. E. Severin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 72, No. 9, pp. 47-49, September, 1971. Original article submitted March 27, 1970.

TABLE 1. Content of Ubiquinone and Protein in Regenerating Liver of Albino Rats

Days after regeneration	No. animals investigated	Mean wt. of liver [M±m(D)]		Ubiquinone content (in μg)(M±m(D)]				% Protein of regenerating liver (M ± m)
				per gram fresh liver		per gram protein	per whole	
		of segmentremoved	of regenerating segment	before hepatectomy	after hepatectomy	before hepatectomy	after hepatectomy	of segmentremoved / of regenerating segment
1	8	3,3 ±0,17	2,4	71,03 ±10,23 not significant	61,5	357,9 ±50,48 not significant	334,5	209,3 ±37,4 / 163,8	17,8 ±0,9
3	15	3,8 ±0,24	4,7	63,7 ±13,8 $P<0,1\%$	38,1	311,7 ±48,6 $P<24\%$	253,7	238,7 ±52,4 / 165,7	15,7 ±0.7
6	9	3,4 ±0,26	5,1	59,9 ±9,72 not significant	47,7	303,4 ±106,6 not significant	263,2	204,9 ±28,9 / 245,7	18,1 ±1
9	6	3,4 ±0,28	5,9	66,4 ±5,73 not significant	62,7	315,3 ±32,6 not significant	351,7	223,5 ±21,8 / 344	17,5 ±0,5
12	8	3,6 ±0,23	5,3	52,8 ±12,24 not significant	60,9	263,8 ±54,5 not significant	318,6	200,1 ±51,8 / 295,2	18,5 ±1,2
15	6	3,5 ±0,14	4,9	67,5 ±10,6 $P<19\%$	82,5	337,3 ±49,1 $P<1,6\%$	478,9	262,9 ±31,4 / 405,7	17,7 ±0,4

EXPERIMENTAL RESULTS

The results are summarized in Table 1. The fact will be noted that 3 days after operation the ubiquinone level in the regenerating liver, calculated per gram fresh weight, was more than one-third lower than in the intact liver. Despite the fact that on the 2nd and 3rd days, the weight of the liver had almost doubled, the ubiquinone content in the liver showed only a very slight increase. It will be noted that on the 3rd day the protein content in the liver was highest. It is known that lipids accumulate most rapidly in the hepatocytes of the regenerating liver during the first 3 days after operation [2]. This evidently explains why the difference between the ubiquinone level observed on the 3rd day, when expressed by gram protein, is not statistically significant. Later, the ubiquinone content in the regenerating liver began to rise steadily, and by the 9th day its level was almost the same as initially, while on the 15th day, it was actually higher than the initial level by a statistically significant margin when expressed relative to liver protein.

On the basis of his experiments to study ubiquinone biosynthesis, Olson [11] calculated the rate of ubiquinone formation and concluded that about 40 μg ubiquinone is formed daily in the rat liver. In the present experiments it was found that from the 3rd until the 6th day the ubiquinone content in the liver increased by 80 μg, and from the 6th to the 9th day by almost 100 μg. Evidently, the rate of ubiquinone formation in the regenerating liver at these periods exceeds the initial rate by several times. Ubiquinone is formed most intensively on the 5th-9th day of regeneration. Subsequently, the rate of ubiquinone synthesis evidently falls somewhat, but by the 15th day after hepatectomy, it still remains fairly high.

LITERATURE CITED

1. E. V. Montsevichyute-Éringene, Pat. Fiziol., No. 4, 71 (1964).
2. V. F. Sidorova and Z. A. Ryabinina, in: L. D. Liozner (editor), Regeneration of Organs in Mammals [in Russian], Moscow (1960), p. 199.
3. F. L. Crane, in: Ciba Foundation Symposium on the Quinones in Electron Transport, London (1961), p. 36.
4. G. D. Davies, Jr., P. Friis, R. K. Olsen, et al., Vitamins and Hormones, 24, 427 (1966).

5. F. W. Heaton, J. S. Lowe, and R. A. Morton, Biochem. J., 67, 208 (1957).
6. G. Higgins and R. Anderson, Arch. Path., 12, 186 (1931).
7. V. C. Joshi, J. Jayaraman, and T. Ramasarma, Biochem. J., 88, 25 (1963).
8. R. A. Morton (editor), Biochemistry of Quinones, New York (1965), p. 1.
9. H. O. Lowry, T. N. Rosebrough, G. A. Farr, et al., J. Biol. Chem., 193, 265 (1951).
10. L. Mervyn and R. A. Morton, Biochem. J., 71, 106 (1959).
11. R. E. Olson, Vitamins and Hormones, 24, 551 (1966).
12. T. Ramasarma, Ind. J. Sci. Indust. Res., 27, 147 (1968).
13. H. Wagner, L. Hornammer, and B. Dengler, J. Chromatogr., 7, 211 (1967).