

EFFECT OF PARENTERAL ADMINISTRATION OF EXOGENOUS CYTOCHROME c ON CYTOCHROME CONTENT IN THE LIVER OF RABBITS WITH CHRONIC CARBON TETRACHLORIDE POISONING

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Administration of exogenous cytochrome c to rabbits with chronic poisoning prevented the decrease in the content of cytochrome c in homogenates and of cytochromes $a + a_3$, b , and $c + c_1$ in the mitochondria of the liver and promoted restoration of the normal histological structure of the organ.

KEY WORDS: carbon tetrachloride; liver; cytochrome c.

Cytochrome c has been used with success in the treatment of various diseases [1], but the biochemical mechanisms of its therapeutic action are still largely unexplained. Previous investigations [3, 4] showed that parenteral administration of cytochrome c has a marked protective action in acute and chronic CCl_4 poisoning, restoring normal energy metabolism in the liver.

In this investigation the effect of parenteral injection of cytochrome c on the cytochrome content in the liver of rabbits with chronic CCl_4 poisoning was studied.

EXPERIMENTAL METHOD

Twenty rabbits weighing 2.5-3 kg each were used. Carbon tetrachloride was injected subcutaneously as a 40% solution in peach oil twice a week for 3 weeks in a dose of 0.25 ml/kg body weight. Cytochrome c ("Cytochrome c for injection," Leningrad Medical Preparations Factory) was injected subcutaneously five times a week for 4 weeks in a dose of 10 mg/kg. Control rabbits received injections of the equivalent volume of physiological saline. The cytochrome c content was determined in homogenates of the liver [8]. Mitochondria were isolated from the liver [5] and their differential spectra were recorded on a modified SF-10 spectrophotometer. The concentrations of cytochromes ($a + a_3$, b , and $c + c_1$) were calculated with the aid of a system of

TABLE 1. Cytochrome Content in Homogenate and Mitochondria of Liver of Rabbits with Chronic CCl_4 Poisoning ($M \pm m$)

Group of animals	Cytochrome c in liver homogenate, in mg %	Cytochromes, $M \cdot 10^{-9}$ /10 mg mitochondrial protein		
		$a + a_3$	b	$c + c_1$
Control (n = 6)	2.37 ± 0.05	1.58 ± 0.12	4.63 ± 0.19	6.18 ± 0.12
CCl_4 (n = 6)	1.46 ± 0.06	0.85 ± 0.13	3.14 ± 0.57	3.40 ± 0.09
CCl_4 + cytochrome C (n = 6)	2.25 ± 0.12	1.59 ± 0.20	4.31 ± 0.53	5.18 ± 0.28

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linear equations [6]. The protein content in the mitochondrial fraction was determined by Lowry's method [7]. Paraffin sections stained with hematoxylin-eosin and Sudan III were examined histologically.

The results were subjected to statistical analysis [2].

EXPERIMENTAL RESULTS

After repeated injections of CCl_4 the animals developed symptoms of chronic poisoning. Of the 14 animals of this group two died at the end of the second week of the experiment.

The cytochrome c content in the liver homogenates from animals with chronic CCl_4 poisoning was sharply reduced ($P < 0.001$; Table 1). Subcutaneous injection of exogenous cytochrome c was followed by restoration of its normal content in the liver of the poisoned rabbits.

The concentration of cytochromes $a + a_3$, b, and $c + c_1$ in the liver mitochondria of the poisoned animals fell ($P < 0.05$). Repeated parenteral injections of exogenous cytochrome c into animals with chronic CCl_4 poisoning prevented the fall in concentration of the cytochromes. The liver of animals receiving cytochrome c differed even in its external appearance from the liver of the animals receiving CCl_4 only. Histological examination of the liver of these animals showed much less intensive signs of fatty infiltration and cloudy swelling than in animals receiving CCl_4 only.

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