INCORPORATION OF S^{35}-CYSTEIN INTO THE LIVER AND SERUM PROTEINS IN TOXIC HEPATITIS CAUSED BY CERTAIN CHEMICAL SUBSTANCES USED IN INDUSTRY

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Various researches have been devoted to the study of the biosynthesis of protein in the different organs and tissues of the animal organism during an attack of toxic hepatitis caused by the action of certain chemical substances. Magee and co-workers [2, 10, 11], for instance, found an appreciable fall in the incorporation of amino acids, labeled by the carbon of their carboxyl group, into the liver proteins of rats treated with dimethylnitrosamine, whereas no similar changes could be detected in the kidneys, the spleen, or other organs. Japanese workers [4] have shown that γ-globulin formation in the spleen of rats poisoned with carbon tetrachloride is considerably reduced. No definite correlation could be established between the amount of γ-globulins in the serum and their formation in the spleen. Definite changes in the biosynthesis of tissue proteins have also been noted as a result of the toxic action of hepatotropic chemical substances.

From our earlier study [1] of some aspects of the mechanism of the toxic action of homologues of carbon tetrachloride – tetrachloropropane, tetrachloropentane, and tetrachloroheptane* , – which also are heptatotropic toxic substances, it seemed likely that in toxic conditions caused by the action of these substances the processes of synthesis, especially the synthesis of the tissue proteins, are disturbed.

The object of the present investigation was to study the biosynthesis of the liver and serum proteins by means of the incorporation of S^{35}-cystein in toxic conditions caused by carbon tetrachloride, tetrachloropropane, tetrachloropentane, and tetrachloroheptane.

EXPERIMENTAL METHOD

As experimental animals we used male white rats weighing 120-170 g, kept in standard conditions in the animal house and receiving a briquette diet and milk. The animals were poisoned by means of three (on alternate days) subcutaneous injections of the test substances in the maximal tolerated doses (CCl_4, each dose 0.6 ml; tetrachloropropane, each dose 0.2 ml; tetrachloropentane, 0.08 ml; and tetrachloroheptane 0.15 ml/100 g body weight of the rats). The substances were injected diluted in an equal volume of sunflower oil. Histological investigations of the liver and kidneys of these animals revealed the presence of lipoid and protein dystrophy.

On the second day after the last injection, the animals were left without food for 18 hours, after which they were given an intraperitoneal injection of S^{35} cystein in a dose of 10,000 impulses/g body weight. Animals of equal weight were chosen for each experiment, the fluctuations not exceeding 5-10 g. The animals were sacrificed by decapitation 3 hours after receiving the injection of S^{35}-cystein. The liver proteins were precipitated by 10% trichloroacetic acid [2] and washed repeatedly with a 5% solution of the same acid until a constant specific activity was obtained. The globulins and albumins were isolated from the blood serum by means of Korner and Debro's method for isolation of albumins [7]. The radioactivity was estimated by means of an end-type counter in 5 mg of protein. In order to detect any disturbances of the formation of stable (peptide) and labile (disulfide, etc.) bonds in the proteins,

*These compounds are widely used at the present time in various branches of industry. They are particularly important in the manufacture of the synthetic fiber "enant."

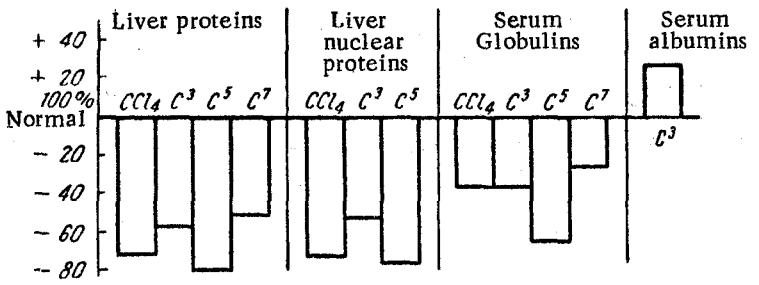

Fig. 1. Incorporation of S^{35}-cystein in the proteins of the liver, of the liver nuclei, and of the blood serum of rats receiving carbon tetrachloride (CCl_4), tetrachloropropane (C_3), tetrachloropentane (C_5), and tetrachloroheptane (C_7).

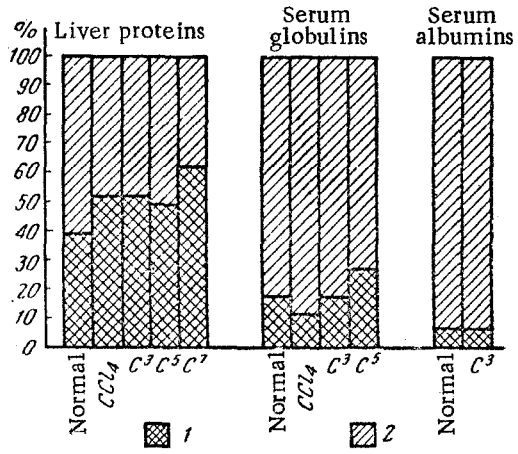

Fig. 2. Distribution of stable (1) and labile (2) bonds in rats in normal conditions and after treatment with carbon tetrachloride (CCl_4), tetrachloropropane (C_3), tetrachloropentane (C_5), tetrachloroheptane (C_7) in the liver and serum proteins.

these were treated with thioglycolic acid [5], formic acid [11], and 0.05 N NaOH solution at room temperature [3]. The incorporation of S^{35}-cystein into the nuclear proteins of the liver was also investigated. The nuclei were isolated from the liver by Marshak's method [3].

The experiments were conducted on four groups of animals, each of which comprised 7 control and 7 experimental rats.

EXPERIMENTAL RESULTS

The results are shown in Figs. 1 and 2. They demonstrate that in toxic conditions caused by carbon tetrachloride, tetrachloropropane, tetrachloropentane, and tetrachloroheptane, the incorporation of S^{35}-cystein into the liver proteins fell by 52-77%, and into the serum globulins by 33-65% by comparison with the control animals. The incorporation of cystein into the serum albumins rose by 27%.

It may be seen from Fig. 2 that the labile bonds are the most sensitive in rats poisoned with the above mentioned tetrachloroalkanes. For instance, whereas in the liver proteins of the control rats the ratio of stable cystein bonds to labile was approximately 1:2, in the liver proteins of the rats treated with chlorinated hydrocarbons this ratio was 1:1.

The reduction in labile bonds was evidently the result of blocking of the sulfhydryl groups by the chlorinated hydrocarbons. It must be pointed out that although the incorporation of the label into stable and labile groups differed in its absolute value in animals poisoned by chlorinated hydrocarbons, the character of these changes remained the same in each case.

The results of our investigations also showed that in poisoning with carbon tetrachloride, tetrachloropropane, tetrachloropentane, and tetrachloroheptane, the incorporation of S^{35}-cystein into the serum proteins was disturbed to a lesser degree than its incorporation into the liver proteins. Despite the total reduction in the incorporation of the label into the serum proteins, the ration between the stable and labile bonds in these proteins remained unchanged after poisoning.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
