The peculiarities of membranotoxic effect of polychlorinated biphenyl and trichlorbenzenes

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Introduction

In the recent years after the revealing of high toxicity level dioxins and related to them compounds investigators have been paying great attention to the clearing up of the pathochemical mechanisms of acute and chronic poisoning by these substances including polychlorinated biphenyls (PB) [1]. Membranotoxic effects of xenobiotics is known to play an important role in the pathogenesis of intoxications and be one of the general mechanism of toxic effect [3]. Due to the character of the effect PB are related to the highly toxic chemical compounds. In a human being clinical signs of intoxication are revealed after the daily administration of PB in a dose of 0.07 mg/kg into the organism [1]. PB are related to the poisons with politropic effect resulting in the structural and functional disorders of many organs and the decrease of body weight. Trichlorbenzenes (TB) [4,5] are hydrophobic possessing irritating and narcotic effects, they are hepatoxic, destroying the hemopoiesis. Acute toxicity of TB after the administration into stomach of rats can be compared with the parameter of PB: LD_{50} is about 1 g/kg. Despite a great number of investigations carried out by different authors on the evaluation of toxic properties of PB and TB the state of biomembrane after the poisoning by these toxicants is insufficiently studied and that is the reason of the present work.

Materials and methods

The experiments have been carried out on 90 white uninbreeding puberal rats. In our research we used an industrial product "Sovtol-10" (the mixture of PB containing 26-31% of TB) as a toxic agent administrated through a probe into the stomach of experimental animals in the doses of 0.5; 1.0 and 1.5 g/kg. Animals were studied for a long time considered loss of animals determined erythrocytes resistance to the hemolytic action of the hydrochloric acid [2] on the 2, 7, 15, 21 and 28 days of the experiment counted the stability index (J) characterizing the erythrocyte decomposition rate and the percentage of low resistance cells (being destroyed during the first minute of hemolysis) of middle resistance cells (being destroyed during the second minute of hemolysis) and high resistance cells (being destroyed after the second minute of hemolysis). The state of membranous structure of hepatocytes were controlled electromicroscopically.

Result and discussion

Sovtol in the dozes of 0.5 and 1.0 g/kg did not cause the loss of the animals up to 30 days of the experiment (Table 1). The effect of this toxicant in the doze of 1.5 g/kg resulted in the loss of 25% of experimental animals on the 21st day of experiment. In connection with the supposed membranotoxic effect of Sovtol we studied the ultrastructure of hepatocytes in animals having received it in the maximal among the studied by us dose of 1.5 g/kg. According to the readings of electronic microscopy the destruction of cellular and subcellular structures was observed of lisis type revealed in the homogenization of heterochromatine and the partial destruction of nuclear membrane.

Table 1.

The effect of different Sovtol doses on the survival of animals

Experimental conditions	Number of the day	Effect (loss/general number of animals)
1. Sovtol 0.5 g/kg	30	0/20
2. Sovtol 1.0 g/kg	30	0/20
3. Sovtol 1.5 g/kg	13	2/20
	21	5/20
	30	5/20

Sovtol increased the erythrocyte resistance index to the hemolytic effect of hydrochloric action (Fig. 1). Thus by its administration in the dose of 0.5 g/kg J increased accordingly by 16 and 30 %; in the dose of 1.0 g/kg – by 25 and 40% in the dose of 1.5 g/kg up to 18 and 40%.

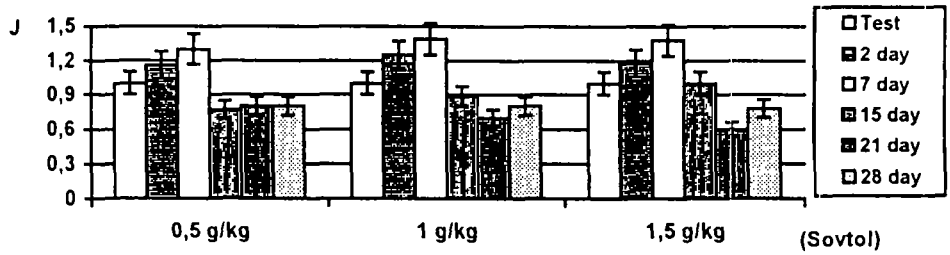

Fig. 1. The effect of Sovtol on the erythrocyte resistance index (J)

By the 15th day of the experiment erythrocyte resistance in the group received the toxicant in the minimal dose decreased and accounted for 77 % of the test indices and pertained this level up to the end of the experiment. In animals exposed to the effect of Sovtol in the doses of 1.0 and 1.5 g/kg on 2nd day J increased accordingly by 25 and 18 % and up to the 7th day it reached 140 % of the test animals indices in both groups. Further the resistance index in both groups decreased up to 0.9 and 1.0 minimal value of J equal to 0.6 was marked in animals received Sovtol in the dose of 1.5 g/kg on the 21st day of the experiment. On the 28th day of the experiment the indices of all experimental groups have been leveled: the acid resistance of erythrocyte made up 80 % of the indices of test animals. Thus in all poisoned animals there was observed the increase of the erythrocyte hemolytic resistance index with the subsequent decrease. It is known from literature that on the whole the resistance index to the hemolytic effect of hydrochloric acid characterizes the state of the lipid matrix of the erythrocyte cellular membrane [2]. That is why the increase of its acid resistance in the stage of the 2-7 days may be conditioned by the immediate penetration of lipofeeling compounds of Sovtol into the hydrophobic compartments of the membrane that caused the changes of its physic-chemical properties evidently into the direction of the increase of microviscosity and consequently plasticity conditioning the increase of resistance to hemolysis. The study of percentage correlation different in hemolytic resistance erythrocytes fractions showed that on the 2nd and 7th days of the experiment in peripheral blood of the poisoned with Sovtol rats the portion of high resistance forms increases considerably. The percentage of these cells considerably increased under the effect of toxicant in the dose of 0.5 g/kg in 4.4 and 12.6 times accordingly (Fig. 2). The portion of high resistance erythrocytes increased in 8.1 time on the 2nd and in 13.3 times on the 7th days of experiment in the poisoning of animals with Sovtol (Fig. 3).

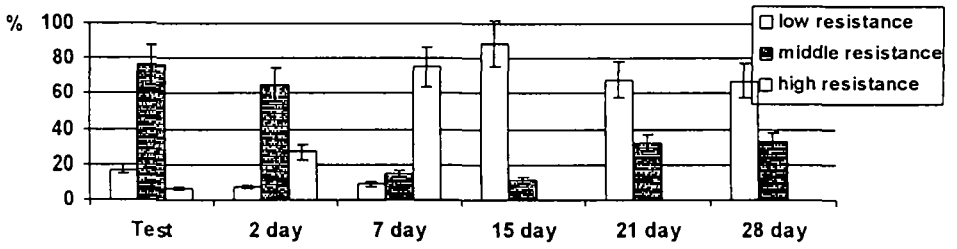

Fig. 2. The effect of 0.5 g/kg Sovtol on the erythrocyte composition

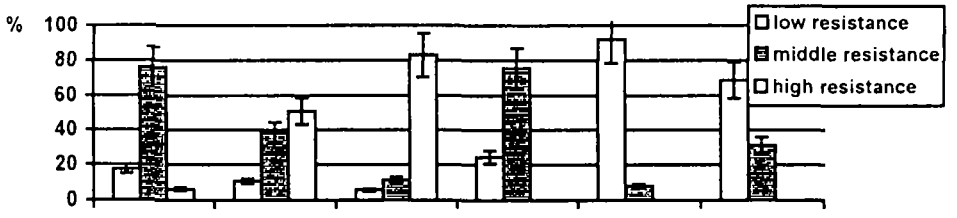

Fig. 3. The effect of 1.0 g/kg Sovtol on the erythrocyte composition

In animal having received the toxicant in the dose of 1.5 g/kg by these terms also the increase of high resistance cells was marked correspondingly by 6.2 and 13.2 times (Fig. 4). However the results obtained on the 15th day of the experiment showed the disappearance of high resistance erythrocyte (Fig. 2-4) in all experimental groups; only low and middle resistance fractions were preserved. By the 21st day of the experiment animals poisoned with Sovtol in a lower dose had the high level of middle resistance cells (32.1 %) while in groups having received the toxicant in the dose of 1.0 and 1.5 g/kg these populations made up 7.9 and 6.3 %.

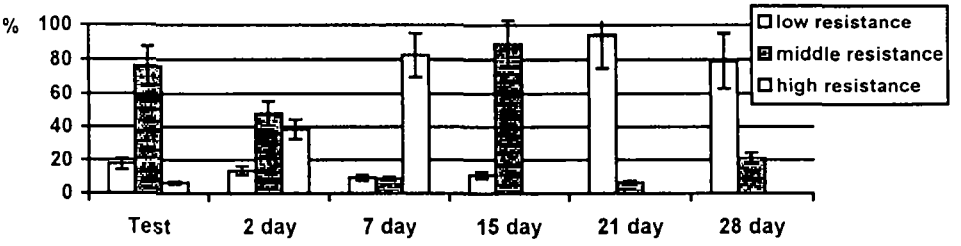

Fig. 4. The effect of 1.5 g/kg of Sovtol on the erythrocyte composition

Nevertheless it should be noted that in animals having received Sovtol in the dose of 1.5 g/kg the sharp decrease of the number erythrocytes with middle resistance took place on the 15th day and made up 11.4 % of the test level. Let's consider the number of erythrocytes in fractions by the 21st day after the poisoning by which the loss of rats having received Sovtol in the dose of 1.5 g/kg has reached 25 %. In the group poisoned with Sovtol in the dose of 0.5 g/kg: low resistance erythrocytes made up 67.9 % middle resistance 32.1 % high resistance were absent. *In animals exposed to the effect of Sovtol (1.0 g/kg), low resistance – 92.1 %, middle resistance – 7.9 %, high resistance were absent too. In rats poisoned with Sovtol in the dose of 1.5*

g/kg low resistance forms – 93.7 %, middle resistance forms – 6.3 %, high resistance forms were absent. In the norm the content of middle resistance forms prevails over other and makes up 76.3 % (low resistance forms – 17.4 % and high resistance forms – 6.2 %) therefore judging by the data received the sufficient number of erythrocyte of middle resistance in the indispensable condition for the normal functioning of erythrocyte system. Probably the obtained results are the evidence of the promising use of the parameter resistance as the prognostic criterion for the evaluation of the obtained dose of PB and the forecast of the intoxication flow. Besides the acute poisoning with Sovtol results in the marked lesion of membranous structures of the liver, erythrocyte and highly probably other organs and tissues. Many authors connect the hemolytic resistance of erythrocytes with their physiological age [2]. By that it has been noted that the younger the cells, the higher the resistance of its external membrane to the acids hemolysis. Hence we can conclude that it, for example after the acute blood loss the hemolytic resistance of erythrocytes increases it is conditioned by the discharge of the young forms from the deposit into the blood stream. Probably in the organism the erythrocyte constantly undergoes different physic-chemical influences such as for example the processes of free-radical oxidation which occurring, on the whole in the lipid membrane matrix. Result in the decrease of unsaturated of its fat acid components and thus in the decrease of its microviscosity and consequently to the plasticity. That is under the normal conditions the value of hemolytic resistance of erythrocyte membrane is inversely proportional to the age of this cells.
Thus in the studied by us acute chemical pathology the poisoning of animals with Sovtol result in the modification of physic-chemical properties of biomembranes increasing their resistance to the acid hemolysis with its destabilization. Obviously membranodestructive effect is one of the leading pathochemical mechanisms of the toxic effects of polychlorinated biphenyls.

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