

Toxicologic and hygienic characteristics of p-373-2-20; p-5003-ac;p-294-2-35 polyols and prognosis of their potential danger for environment

Zhukov V.¹, Telegin V.¹, Rezunenko Y.¹, Zaytseva O.², Knigavko V.², Grankina S.², Levshenko T.²

¹Kharkiv National Medical University, Kharkiv, Ukraine, Department of Biochemistry

²Kharkiv National Medical University, Kharkiv, Ukraine, Department of Medical and Biology Physics

Email address:

gramatyuk@ukr.net (Zhukov V.)

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Abstract: Studied the toxic effects polyoxipropylene polyols in acute and subacute experiments on warm-blooded animals. It is established that they are pertained to the IV hazard class; have polytropic general toxic effect; on the level of toxic doses they influence on the generative function and the genetic apparatus; inhibit and disrupt the interaction between the cellular and humoral immunity. Experiments were performed on adult Wistar white rats, white mice, guinea pigs, hybrid mouse lines BALB / C, (SBAC57BL) F1, CBA / Lac, and rabbits of the chinchilla race [4-6]. The objects of the investigation were polyoxipropylene triols with molecular masses 5000M (P-5003-AC), and 370M (P-373-2-20), and polyoxipropylene amine with molecular mass 290M (P-294-2-35). Polyoxipropylene polyols P-5003-AC, P-373-2-20 and P-294-2-35 in doses of 1/10 and 1/100 DL50 have a toxic effect on the generative function and the genetic apparatus, and in doses 1/10, 1/100 and 1/1000 DL50 inhibit and disrupt the cooperative interaction of cellular and humoral immunity. In all cases, the dose of 1/10000 DL50 was inoperative, it is equal to 3.23; 3.62 and 1.48 mg / kg of animal weight, respectively, for P-373-2-20, P-5003-AC and P-294-2-35.

Keywords: Xenobiotics, General Toxic Effect, the Specific Types of Biological Effects

Now it is clear that human activity can lead to a profound transformation of the biosphere, which adversely will affect on the vital functions. This requires intensification and expansion of knowledge about the biological effects of chemicals and prognosis ground of their potential danger for flora and fauna. Our knowledge about the possible consequences of xenobiotics effects are limited and are inadequate for the compounds to which people in the process of evolution had never met. Emerged a significant gap between the high capacity of modern civilization to create a new chemical potential of our planet and the disabled man and the biosphere as a whole to accept the action of this potential with reasonable efficiency and without serious adverse consequences [1-3]. Currently, it is created such situation when the influence of combinations of different chemical compounds on humans and wildlife in general is difficult to predict. The uncontrolled use of chemicals can have irreparable

consequences. This fully applies to the products of organic synthesis, which in volume of output and range of goods occupy a leading position in the world. These products include polyols of grades P-373-2-20, P-5003-AC and P-294-2-35, which are widely used in various sectors of the economy to produce polyurethanes, foam rubbers, thermoplastics, lacquers, enamels, hydraulic, and brake fluids, epoxy resins, plastics, artificial leather, etc. [1]. In order to avoid the harmful effects of application of chemicals a system of preventive measures is created, among which one of the main is toxicological assessment of xenobiotics and compounds, including their pre-selection for the postblowing production and use, limiting the exposure levels on the production and the environment.

The aim of this work was to study toxicologic and hygienic characteristics and prognosis of the potential danger to humans of a new group of chemicals - polyols of grades P-373-2-20, P-5003- AC and P-294-2-35.

1. Materials and Research Methods

The research program included the study of the polyoxipropylene polyols effect on the organoleptic properties of water, natural purification processes in reservoirs, and influence on the warm-blooded animals under conditions of acute and subacute exposure [1-3].

1.1. Materials and Research Methods Experiments

Experiments were performed on adult Wistar white rats, white mice, guinea pigs, hybrid mouse lines BALB / C, (SBAC57BL) F1, CBA / Lac, and rabbits of the chinchilla race [4-6]. The objects of the investigation were polyoxipropylene triols with molecular masses 5000M (P-5003-AC), and 370M (P-373-2-20), and polyoxipropylene amine with molecular mass 290M (P-294-2-35). The first priority was to establish the parameters of the toxicity, species sensitivity, cumulative properties of xenobiotics under oral entrance into organism. We used conventional sanitary-chemical, physiological, toxicological, morphological, cytological, biophysical and statistical research methods [4].

1.2. Toxicological

In order to obtain toxicological characteristics of the compounds and to substantiate features of the mechanism of biological action we used a set of techniques for estimation of the status of various organs, systems and organism functions. Taking into account that given substances have a low toxicity, haven't high-cumulative properties, in the subacute experiment we selected doses of 1/10; 1/100; 1/1000 DL50. DL50 for the P-373-2-20, P-5003-AC, and P-294-2-35, respectively, is 32,3 g/kg; 36,2 g/kg and 14,8 g/kg of animal weight.

2. Results of Research and Their Discussion

Experiments have shown that the test substances are low-toxic compounds (IV class of danger), haven't specific sensitivity and skin-irritating properties it is coordinates with results of [5], all compounds have weak skin-resorptive properties. Based on the coefficients of cumulation (Cc), they are low and moderate-cumulative substances (Table 1). The mean effective time (ET50) of the animals death was in the range of the first day of observation.

Table 1. Parameters of polyoxipropylene polyols toxicity

Substance	Species	DL0, g / kg	DL50, g / kg	DL100, g / kg	ET50, h	Cc
P-373-2-20	white rats	70,0	32,3±1,4	45,0	17,3	6,12
	white mice	20,0	33,5±1,7	45,0	15,8	-
	Guinea pigs	20,0	35,0	45,0	16,7	-
P-5003-AC	white rats	20,0	36,2±2,3	50,0	20,3	7,35
	white mice	20,0	38,3±1,6	50,0	19,8	-
	Guinea pigs	20,0	35,0	50,0	20,6	-
P-294-2-35	white rats	10,0	14,8±1,2	20,0	14,7	3,74
	white mice	10,0	15,5±1,3	20,0	15,2	-
	Guinea pigs	10,0	15,0	20,0	16,4	-

Table 2. The enzyme activity in the subacute experiment on the 45th day of observation under the influence of 1/100 DL₅₀ dose ($M \pm m$) mcat / l

The enzyme	P-5003-AC	P-373-2-20	P-294-2-35	Control
CPK	10,46±0,35*	9,62±0,48*	12,30±0,43*	5,20±0,30
LDG	11,63±1,20*	10,34±0,65*	10,72±0,80*	7,80±0,40
AsAT	1,52±0,08*	1,43±0,22*	1,60±0,04*	0,90±0,04
AlAT	0,32±0,04*	0,35±0,06*	0,27±0,01*	0,100±0,001
AIP	10,30±0,43*	11,25±0,56*	9,80±0,30*	6,30±0,20
α -GBDG	6,54±0,15*	5,72±0,28*	5,43±0,20*	9,30±0,08
γ -GT	0,620±0,015*	0,64±0,04*	0,56±0,02*	0,20±0,01

Note: * - difference from control is valid, $p < 0,05$.

The clinical picture of acute poisoning symptoms of disorders in breathing, hemodynamics and central nervous system are dominated. Polyoxipropylene polyols at a doses of 1/10 and 1/100 DL50 reduced the percentage of increase in body weight, contents of erythrocytes, leucocytes, hemoglobin. Changes in the leukocyte formula of blood are not detected. Dose of 1/1000 DL50 had no effect on the indices of white and red blood. At the end of subacute experiment (on the 45th day of observation) there were

significantly altered activities of the creatin phosphokinase (CPK), lactate dehydrogenase (LDG), aspartate and alanine aminotransferases (AsAT and AlAT), alkaline phosphatase (AIP), α -hydroxybutyrate dehydrogenase (α -GBDG), γ -glutamyltranspeptidase (γ -GT). All compounds had a unidirectional effect on the dynamics of the enzyme activity. In serum they increased the activities of CPK, AsAT, AlAT, AIP, γ -GT, LDG and decreased the activity of α -GBDG that witnesses about disorders of the redox

processes in the body and the liver, kidneys, heart functions, that is, organs that play a leading role in the detoxication of xenobiotics (Table 2). Dose of 1/1000 DL₅₀ had no effect on the dynamics of enzyme activity, which allowed to consider this dose inoperative.

An important step in hygienic regulation of harmful chemicals in the environment is to study the effects of the genetic apparatus and the generative function. Gonadotoxic effect of xenobiotics is studied in adult albino rats (males). Experiments have shown that the substances in doses of 1/10 and 1/100 DL₅₀ reduce sperm motility, their number in the suspension of the epididymis, osmotic stability and acid resistance of spermatozoons in the background of increasing number of dead forms of sexual cells.

Morphological evaluation of spermatogenic epithelium showed a reduction in the index of spermatogenesis, the number of tubules with the 12th stage of meiosis, the number of normal forms of spermatogonia and the increase

in the number of tubules with desquamated epithelium (Table 3).

Evaluation of embryonic material obtained at autopsy albino rats (females), showed that the compounds in doses of 1/10; 1/100 DL₅₀ reduced fetal weight and increased the amount of resorptions, the weight of placenta, pre-implantatic, postimplantatic, and total fetal death, rate. Xenobiotics in these doses did not have teratogenic effects. Determination of mutagenic activity of polyoxipropylene polyols detected that the test substances increased the number of bone marrow cells with chromosomal aberrations. Among of them the single and paired fragments, dicentric, translocations, breaks, ring chromosomes were frequently. The increase of chromosomal aberrations under doses of 1/10 and 1/100 DL₅₀ was accompanied by a significant decrease in mitotic activity of bone marrow cells (Table 3).

Table 3. Long-term sequences of polyoxipropylene polyols effect in dose of 1/100 DL₅₀ in white rats ($M \pm m$)

Parameter	P-5003-AC	P-373-2-20	P-294-2-35	Control
The functional state of sperm: motility time, min	137,2±4,8*	141,5±6,2*	129,8±4,5*	168,4±7,3
The number of spermatozoon's, million / ml	14,60±1,05*	12,3±1,2*	11,8±1,3*	21,4±4,4
The number of dead forms,%	9,30±0,67*	10,20±0,93*	8,60±0,72*	4,7±0,5
Osmotic stability,% NaCl	1,86±0,17*	1,9±2,2*	2,10±0,18*	3,70±0,15
Acid resistance, pH	4,50±0,35*	4,20±0,27*	4,60±0,32*	2,50±0,18
Morphological indicators of testicles: the index of spermatogenesis	2,30±0,18*	2,80±0,22*	2,70±0,25*	4,20±0,16
The number of spermatogonia	47,20±2,65*	49,60±1,87*	53,40±1,54*	69,80±3,14
The number of tubules with the 12th stage of meiosis	1,90±0,23*	2,10±0,18*	2,20±0,26*	4,10±0,35
The number of tubules with desquamated epithelium	6,20±0,33*	5,70±0,24*	6,8±0,3*	2,70±0,17
Embryotoxicity: the number of the living embryos	7,10±0,36*	7,60±0,25*	6,80±0,37*	10,20±0,45
The number of resorption	1,7±0,2*	1,40±0,18*	1,80±0,23*	0,60±0,12
The number of yellow bodies of pregnancy	10,5±0,8*	11,3±0,65*	10,90±0,60*	11,3±0,7
Weight of fetus, g	2,90±0,16*	3,1±0,2*	3,20±0,14*	3,90±0,15
Weight of placentas, g	0,77±0,08*	0,78±0,06*	0,74±0,05*	0,51±0,13
Fetal death:				
before implantation	12,4±0,6*	13,20±1,05*	10,4±0,8*	5,30±0,26
after implantation	8,60±0,73*	7,20±0,65*	9,3±0,6*	3,30±0,35
total	21,00±0,65*	20,40±0,83*	19,70±0,65*	8,60±0,29
Influence on gene mutation: the number of cells with chromosomal aberrations,%	6,30±0,42*	5,90±0,35*	6,60±0,28*	0,75±0,10
The mitotic index of cells of bone marrow	2,20±0,18*	3,10±0,22*	2,00±0,16*	6,8±0,4

Note: * - difference from control is valid, $p < 0,05$.

In all cases, the dose of 1/1000 DL₅₀ had no effect on the generative function and the genetic system of warm-blooded animals. Toxicologic and hygienic characteristics of xenobiotics require the study of their influence on the immune system. The results of this research showed that the polyoxipropylene in the doses of 1/10 and 1/100 DL₅₀

reduce the hemolysin-producing, antibody forming, antigen-binding abilities of immune cells and their homotransplantatic activity. In the animals of experimental groups it was observed inhibition of functional activity of T- and B-lymphocytes, and their cooperative interaction in the implementation of the immune response to T-dependent

antigen. At these doses the substances violated the differentiation of immune cells, protein and nucleic acid metabolism in the lymphocytes, inhibited the intensification of these processes during antigenic stimulation and decreased endocytosis formation in tissues of immune system. The test substances in doses of 1/10 and 1/100 DL₅₀ raised in the organism the level of circulating immune complexes and disrupted the morphological, biochemical and cultural properties of the microbiota of the gastrointestinal tract. In all cases the dose of 1/10000 DL₅₀ was inoperative.

Analysis of the results allowed us to obtain toxicological and hygienic characteristics and detect the potential risk of polyoxipropylene polyols for warm-blooded animals and humans.

3. Findings

1. Polyoxipropylene polyols of grades P-5003-AC, P-373-2-20 and P-294-2-35 are low-toxic compounds (IV class of danger), haven't the specific and sexual sensitivities, as well as skin-irritating properties, had the weak skin-resorptive properties. Based on the cumulative coefficients they are low and moderate-cumulative substances. The clinical picture of acute poisoning the symptoms of the disorders in breathing, hemodynamics, and central nervous system, are dominated.

2. Substances in the subacute experiment under the influence of 1/10, 1/100 DL₅₀ doses violate the redox processes, lead to the development of hypochromic anemia and leukopenia, cause structural and metabolic disorders in liver, kidney, heart - organs that play a leading role in the detoxication of xenobiotics.

3. Polyoxipropylene polyols P-5003-AC, P-373-2-20 and P-294-2-35 in doses of 1/10 and 1/100 DL₅₀ have a toxic effect on the generative function and the genetic apparatus, and in doses 1/10, 1 / 100 and 1/1000 DL₅₀ inhibit and disrupt the cooperative interaction of cellular and humoral immunity. In all cases, the dose of 1/10000 DL₅₀ was inoperative, it is equal to 3.23; 3.62 and 1.48 mg / kg of animal weight, respectively, for P-373-2-20, P-5003-AC and P-294-2- 35.

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