Immunoprophylaxis with Dimephosphone of Some Negative Aftereffects of 2-Mercaptobenzothiazole in Animals

S.N.Farmonov Samarkand Institute of Veterinary Medicine, Samarkand, Mirzo Ulugbek street, house 82 A, E-mail: sirojiddin.farmonov.77@mail.ru

Y. Salimov Samarkand Institute of Veterinary Medicine, Samarkand, Mirzo Ulugbek street, house 82 A, E-mail: sirojiddin.farmonov.77@mail.ru

ABSTRACT

The results of studies on the toxicological assessment of the chronic effects of 2-Mercaptobenzothiazole on the organism of animals and the possibility of pharmaco-correction of the identified negative effects of this xenobiotic with T-type immunomodulators and, in particular, dimephosphone in combination with polyvinylpyrrolidone are presented.

Keywords:

Actuality. In recent decades, there has been a clear trend towards an increase in environmental pollution due to intensive human activities. Particularly dangerous are products of the chemical and petrochemical industries, including organic accelerators for the sulfur vulcanization of rubbers, one of which is 2-mercaptobenzothiazole.

2-Mercaptobenzothiazole (2-MBT, Captax) is widely used in the production of pesticides, azo dyes, medical and veterinary drugs and, especially, polymeric materials - rubber and latex, there are more and more reports of the negative impact of 2-Mercaptobenzothiazole and some of its derivatives on the environment health of people, animals and other inhabitants. Moreover, the greatest danger is the ability of this xenobiotic to migrate from various polymeric materials for technical, household, medical and veterinary purposes into contacting media, causing undesirable aftereffects on living organisms.

Considering that in the foreseeable future the production and use of 2-mercaptobenzothiazole will undoubtedly increase, it is relevant to conduct detailed and comprehensive studies to study its toxic properties and, especially, long-term effects, information about which is very contradictory and few in number.

Materials and methods. Studies were carried out on the toxicological assessment of the chronic effects of 2-Mercaptobenzothiazole on the body of animals at daily doses of 2.0 (Limch) and 0.2 mg/kg and the possibility of pharmacocorrection of the identified negative effects of this xenobiotic with T-type immunomodulators and, in particular, dimephosphone in combination with polyvinylpyrrolidone.

In the experiments, 140 rabbits were used, including: 16 females and 4 males of 1.5 years of age and 120 rabbits from 1 day of age. , received oral 2-mercaptobenzothiazole at a dose of 2.0 mg/kg, the second - the same dose of the drug and every last decade of the month - dimephosphone (250.0 mg/kg) in combination with

polyvinylpyrrolidone (5.0 mg/kg). These pharmacological agents were used parenterally (IM or subcutaneously), in one solution with an interval of 2-3 days. The rabbits of the third group were given 0.2 mg/kg of xenobiotic daily orally, and the fourth group served as a control. The criteria for assessing the toxic effect of the drug were: the state of the clinical-physiological, hematological and immunological status of animals, as well as their reproductive health.

In this case, the generally accepted methods of hematological and biochemical studies, the recommendations of N.I. Zhavoronkov and I.V. Sanotsky, the statistical method of B.M. Shtabsky et al.

Results and its discussion. It has been established that daily, for 3 months, intake of the indicated drug at doses of 0.2 and 2.0 mg/kg did not cause visible deviations in the state of physiological health in experimental rabbits. Similarly, with chronic exposure to xenobiotics at a dose of 2.0 mg/kg and periodic use of dimephosphone in combination with polyvinylpyrrolidone throughout the entire period of experiments, no significant changes in the clinical status of experimental rabbits were detected.

In the blood of rabbits treated with 2-Mercaptobenzothiazole at a dose of 2.0 mg/kg and animals given a similar dose of xenobiotic and treated with dimephosphone in combination with polyvinylpyrrolidone, the same type of changes were established, manifested by a decrease by 14-15% ($P<0.05$) of the total and 12-13% ($P<0.05$) of reduced glutathione, while increasing more than 3 times ($P<0.05$) the percentage of methemoglobin, indicating the development of chronic intoxication. At the same time, there were no statistically significant disturbances in the morphological and biochemical parameters of rabbit blood after chronic exposure to the study drug at a dose of 0.2 mg/kg.

Consequently, the means of correction did not completely reduce the general toxic effect of 2-Mercaptobenzothiazole on the animal organism. However, dimephosphone in combination with polyvinylpyrrolidone had a positive effect on the state of the immune status of experimental rabbits and, especially, on cellular immunity. Thus, the relative and absolute number of T-lymphocytes in peripheral blood increased by 9% and 49% ($P<0.05$), and these B-cell populations increased by 49% and 38% ($P<0.05$), respectively. There was an increase in the content of whey protein due to albumin and β-globulins. At the same time, the phagocytic activity of neutrophils in untreated animals remained depressed by 39% ($P<0.05$), compared with the control.

In experimental rabbits treated with 2-Mercaptobenzothiazole at a dose of 0.2 mg/kg, no significant deviations in the cellular and humoral immunity, in relation to those of control animals, were found.

Thus, dimephosphon in combination with polyvinylpyrrolidone confirmed its well-known pharmacological properties - to have a directed corrective effect in immunodeficiency states, predominantly of the T-type.

Studies have also been conducted on the possible correction of the reproductive function of rabbits with dimephosphone under conditions of chronic exposure to 2-mercaptobenzothiazole at a dose of 2.0 mg/kg (Limch). For this, after 3 months of daily use of the xenobiotic and appropriate treatment with the indicated immunomodulator, all females were mated with intact (control) males and brought to birth.

It was found that during pregnancy in experimental rabbits there were no visible changes in the clinical and physiological status. The duration of pregnancy was 29-31 days. The results of the round are shown in Table 1. and show that from females under chronic exposure to 2-mercaptobenzothiazole at a dose of 2.0 mg/kg, 28 rabbits were obtained and among them - 2 dead. From females exposed to a similar dose of the drug, but treated with dimephosphone, the number of born offspring was 32 live rabbits. Almost the same fertility was noted from a dose of 0.2 mg/kg in the group of control rabbits.

For 2 months of the postnatal period, 14 rabbits died from the females of the first group, the second - 6, the third - 8 and the fourth - 7 rabbits. At the same time, the dynamics of live weight gain in rabbits from treated sires was 15% ($P<0.05$) higher than that of offspring from untreated females.

It was extremely important to establish a high positive effect of the tested means of correction on the formation of the immunoreactivity of young animals from producers who were chronically exposed to the studied xenobiotic.

Thus, the immunological examination of these rabbits revealed that in the offspring from treated females, the absolute content of T- and B-lymphocytes was increased by 36 and 32% ($P<0.05$), respectively, and the phagocytic activity of neutrophils was more than 1.5 times ($P<0.05$), compared with similar indicators of immunocompetent peripheral blood cells of rabbits from untreated females.

Therefore, dimephosphone in combination with polyvinipirrolidone had a positive effect on the overall fertility of females, the development of newborns and their immune status.

Table 1.

The results of the rounding of experimental females

Groups of rabbits	Doses 2-MBT (mg/kg)	Number of females		Received rabbits			Of them survived h / s (days of research)		
				All	Including:				
		Pgernant	overwhelmed		live	dead			
							20	30	60
Experienced groups:									
1 group ♀оп.+♂r.	2,0	4	4	28	26	2	22	18	12
2 group ♀оп.+♂r.	2,0+ dimephosphone	4	4	32	32	-	30	28	26
3 group ♀оп.+♂r.	0,2	4	4	30	30	-	28	25	22
Control group									
4 group ♀r+♂r.	-	4	4	30	30	-	27	24	23

This is confirmed by the materials of Table 2, which shows that the resistance of rabbits from treated rabbits to pathogens of some common infections and, in particular, pasteurellosis is higher than from untreated breeders. Moreover, immunization of experimental rabbits 2.5 months after birth with a vaccine against hemorrhagic septicemia caused deaths among them, which were: in the group from untreated -50, treated - 8; when exposed to a dose of 0.2 mg/kg - 5 and control 9%, respectively. The resulting spontaneous infection of these young animals with the above infection showed that the protective properties of the vaccine were: for the first group - 0, the second - 62, the third - 82 and the fourth - 83%, respectively.

Table 2

The state of resistance of the body of rabbits to the causative agent of pasteurellosis

Groups of rabbits	Number of live rabbits		
	Total, 2.5 months after birth	After vaccination against hemorrhagic septicemia	After spontaneous infection with pasteurellosis
1 group (from untreated females)	12 100%	6 50%	0 0%
group 2 (from treated females)	26 100%	24 92%	16 62%
Group 3 (♀ - dose 0.2 mg/kg)	22 100%	21 95%	18 82%
4 control group	23 100%	21 91%	19 83%

An analysis of the results obtained allows us to conclude that, apparently, the processes of immunobiological reactivity are among the main ones in the pathogenesis of reproductive dysfunction in females under the influence of chronic exposure to 2-mercaptobenzothiazole.

In this regard, in order to prevent the negative effect of 2-mercaptobenzothiazole on the body, immunobiological reactivity and reproductive function of animals, immunocorrective therapy is indicated through the use of dimephosphone (250.0 mg/kg) in combination with polyvinipyrolidon (5.0 mg/kg), which should be carried out monthly, within 10 days (3 intramuscular or subcutaneous injections in one solution) during the period of exposure to the indicated xenobiotic.

Another way to prevent the negative effect of 2-mercaptobenzothiazole on the animal organism is to reduce its threshold level (Limch) by 10 times - to 0.2 mg/kg of body weight. The latter is recommended by us as the maximum allowable level (MRL) of this xenobiotic in some environmental objects (water and feed).

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