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PREPARATION OF A NEW ENTEROSORBENT BENTORB AND DETERMINATION OF ITS TOXICOLOGICAL PROPERTIES

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ABSTRACT

This article presents the results of several studies of the new Bentorb sorbent, which is produced from wine-making waste - adhesive deposits of yellow blood salt. It was found that oxygen, carbon, silicon, aluminum, iron, nitrogen, and magnesium occupy the largest percentage in the sorbent sample. Studies of the toxicological properties of Bentorb sorbent were carried out on laboratory animals. Studies of the acute toxicity of the Bentorb sorbent were conducted on 60 white mongrel rats weighing 237 ± 7 g. Experiments found that the general clinical condition of rats from all experimental and control groups did not change significantly, all animals remained alive. Studies of the chronic toxicity of Bentorb sorbent were conducted on 60 white mice and 40 Wistar rats weighing 185±12 g. During the study period, no significant differences in the general condition and survival of control and experimental animals were observed. The study of the effect of Bentorb sorbent on the function of the digestive tract was carried out on piglets 40-80 days old. The study of the effect of Bentorb sorbent on the function of the digestive tract was carried out on piglets 40-80 days old. The embryotoxic effect of Bentorb sorbent was studied on pregnant Wistar rats with an average body weight of 200-240 g. In addition, a study of body weights and some internal organs of laboratory animals, a control group, and an experimental one taking Bentorb sorbent was conducted.

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Introduction

The intensive development of industry is accompanied by an increase in the level of pollution of natural environments with exotoxins [1]. The possibility of contamination of atmospheric air, water, soil, food, and food raw materials with potentially dangerous chemicals allows us to consider the chemical factor as universal and one of the determinants of the degree of degradation of the environment as a whole [2-4]. Persistent organic substances classified as particularly dangerous (dioxins, dibenzofurans, etc.) are detected in the environment almost everywhere [5]. The level of pollution in many regions with household waste, heavy metals, and pesticides is high [6].

Various pollutants entering the body by inhalation or parenteral route can lead to the development of diseases of various etiologies [7]. Exposure to adverse environmental factors often leads to metabolic reorientation of the body and clinically

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pronounced metabolic changes [8]. As a result of environmental problems, human morbidity and mortality increase, and reproductive function is impaired [9]. In connection with large-scale radionuclides and increasing technogenic pollution, the search for means and methods of detoxification of the human body is relevant [10].
For this purpose, intracorporeal methods of enterosorption are increasingly used [11]. These methods are considered convenient to use, physiological, non-complicating, and do not require significant material costs. The essence of enterosorption consists of the oral administration of several sorbent substances, the properties of which are aimed at retaining toxic components of the chyme on their surface [12].

Materials and Methods

The determination of organic acids in the extract from the adhesive residues of yellow blood salt was carried out by capillary electrophoresis on the device "Kapel-105" R52841-2007. The report was issued by the Multichrome program for Windows.
The toxicity of adhesive precipitates of yellow blood salt, from which the Bentorb sorbent was produced, was determined by rapid biotesting using infusoria from the order of equidistant paramecia (Paramaecium candatum) as biotests. The toxicity of the finished Bentorb sorbent was evaluated on white mongrel mice and Wistar rats.
To study the effect of adhesive precipitation of yellow blood salt on infusoria, various dilutions of solutions of the mineral environment of Lozin-Lozinsky were introduced into the round-bottomed wells of a serological tablet (the volume of the well was 2.5 cm3), 2.0 ml of a solution of adhesive precipitation of yellow blood salt and 0.5 ml of 3 daily cultures of paramecia or Stylonychia according to variants. As a control, the mineral environment of Lozin-Lozinsky was used without the introduction of a sorbent, into which infusoria was introduced in the same amount. The exposure time ranged from 15 minutes to 4 days.
Studies of the new Bentorb sorbent were conducted on laboratory animals: acute toxicity studies on 60 white mongrel rats weighing 237 ±7 g, chronic toxicity studies on 60 white mice and 40 rats weighing 185±12 g of the Wistar line, divided into 4 similar groups of 10 animals each, taking into account body weight. The study of the effect of Bentorb sorbent on the function of the digestive tract was carried out on piglets 40-80 days old. The embryotoxic effect of Bentorb sorbent was studied in pregnant Wistar rats with an average body weight of 200-240 g.
The physicochemical properties of feces were studied by determining the pH using litmus paper, for the presence of blood – a benzidine sample, bilirubin – a Fouche sample, bile pigments – a Terquay sample, fat and starch – microscopically with Sudan III and Lugol solution.

Results and Discussion

Wine-making wastes are used as raw materials for the production of sorbents - adhesive precipitates of yellow blood salt formed during the demetallization of wine materials [13].
Demetallization of wine with potassium hexacyanoferrate (II) (yellow blood salt) is carried out to a residual iron content of up to 3 mg / dm3. At the same time, copper, lead, zinc, and aluminum ions are removed. The treatment with potassium hexacyanoferrate (II) is carried out to remove excess heavy metal cations (mainly iron) from the wine, which hurt the taste properties and stability of the wine [14].
Data on the composition of organic acids in raw materials for the production of ferrocyanide-bentonite sorbents are shown in **Table 1**.

Table 1. Concentration of organic acids in adhesive precipitates of yellow blood salt

Name	Acid concentration	
	mg/l	%
Wine Room	1645	78.5
Apple	67.7	1.5
Lemon	114.9	2.5
Dairy+acetic	801.3	17.3
Total	4629	100.0

As can be seen from the data presented in **Table 1**, tartaric acid occupied the largest amount of organic acids in the adhesive precipitates of yellow blood salt - 78.7%, followed by lactic + acetic and citric acids in decreasing concentration.
Thus, the elemental composition of the adhesive precipitates of yellow blood salt was mainly represented by trivalent and divalent iron ions, and the composition of organic acids was mainly tartaric acid.
When technological and capacitive equipment made of ferrous metal is used in wineries, due to dissolution in an acidic environment, iron ions accumulate in wine materials. After processing wine materials with hexacyanoferrate (yellow blood salt), ferrocyanide is formed.
The resulting precipitate is a gel-like mass containing, in addition to ferrocyanides, many other organic and mineral compounds. The sediment of winemaking contains 5-10% bentonite, 5-7% yeast, 0.5-2.5% ferro-ferricyanide, adhesives, dyes,

tannins, alcohols, has an acidic reaction of the medium (pH=4-4.5). The average humidity of the waste is 85-93%. The solids content in the sediment is 15-20%, Prussian blue is 0.5-6%. It is difficult to filter and dehydrate, which complicates its neutralization and disposal [15].

For the production of sorbents, adhesive precipitates of yellow blood salt are collected from dumps at primary plants for the production of building materials.

The technological process of production of Bentorb sorbent includes the following operations: dewatering (drying) of the feedstock to an air-dry state and grinding (grinding) dried raw materials.

For dehydration (drying), the feedstock is distributed in a uniform layer 5-10 cm thick under a canopy to protect against precipitation and direct sunlight. Drying is carried out in air at a temperature of 15-30 ℃ for 10-20 days. During the drying process, the raw materials are periodically mixed and the residual moisture is controlled. The raw material is considered to have reached an air-dry state if the residual humidity does not exceed 2-5%. The dried raw materials are stored at a temperature of 18-20 ℃ for no more than 1 month. With longer storage, its humidity is checked again and, if necessary, additional drying is carried out to the required humidity.

Table 2 shows the requirements for the Bentorb sorbent. **Table 3** shows the results of laser mass spectrometric analysis of a sample of Bentorb sorbent.

Table 2. Requirements and standards for Bentorb sorbent

Indicator	The norm
Appearance	Fine powder of gray-blue color
Bulk weight, kg/dm3	0.6-1.2
Quantitative content, %	
of iron (II)	0.3-5.0
iron (III)	0.4-10.0
potassium	0.1-15.0
Sorption activity, % not lower	70

Table 3. Results of laser mass spectrometric analysis of the Bentorb sample

Chemical elements	Content, %	Chemical elements	Content, %
Boron	3.5×10^{-3}	Scandium	9.0×10^{-4}
Carbon	19.2	Titanium	1.1×10^{-1}
Nitrogen	3.0	Chrome	5.0×10^{-3}
Oxygen	44.2	Manganese	8.4×10^{-2}
Fluorine	7.3×10^{-2}	Iron	3.7
Sodium	3.2×10^{-1}	Cobalt	6.4×10^{-4}
Magnesium	1.3	Nickel	5.5×10^{-3}
Aluminum	5.4	Copper	2.3×10^{-2}
Silicon	14.0	Zinc	6.0×10^{-2}
Phosphorus	2×10^{-1}	Gallium	1.4×10^{-3}
Sulfur	2×10^{-1}	Bromine	2.6×10^{-3}
Chlorine	1.6×10^{-1}	Rubidium	5.6×10^{-2}
Potassium	7.8×10^{-2}	Strontium	2.8×10^{-3}
Calcium	2.0×10^{-1}	Yttrium	5.3×10^{-4}
Barium	6.4×10^{-3}	Zirconium	4.4×10^{-3}
Lanthanum	1.7×10^{-3}	Niobium	4.3×10^{-4}
Cerium	1.0×10^{-3}		

It can be seen from the table materials that oxygen, carbon, silicon, aluminum, iron, nitrogen, and magnesium occupy the largest percentage in the sample (from 44.2 to 1.3%). This is followed in descending order (from 3.2 to 1.1×10^{-1} %) by sodium, phosphorus, sulfur, chlorine, calcium, titanium; (from 8.4 to 2.3×10^{-2} %) - manganese, potassium, fluorine, zinc, rubidium, copper; (from 6.4 to 1.0×10^{-3} %) – barium, nickel, chromium, zirconium, boron, bromine, strontium, lanthanum, gallium, cerium; (from 9.0 to 4.3×10^{-4} %) – scandium, cobalt, yttrium, niobium. As, Cd, Pb, and Hg at the level of 3.0×10^{-4}% of the mass were not detected.

Determination of Acute and Chronic Toxicity

The results of studies of adhesive deposits of yellow blood salt have shown their beneficial effect on the growth, reproduction, and activity of paramecia and Stylonychia. The environment with a concentration of adhesive precipitates of yellow blood salt

$\times 10^{-2}$ turned out to be the most optimal for the vital activity of Stylonychia. It was noted that the infusoria settled on the substrate of adhesive deposits of yellow blood salt, and then actively moved in the nutrient medium. After 72 hours, there was a decrease in the amount of liquid in the wells of the tablet due to evaporation, but the number of Stylonychia did not decrease. The reproduction of cells by dividing infusoria was observed, the number of their individuals was 3-4 times higher than the initial one.

The paramecia felt better in a less concentrated solution ($\times 10^{-4}$). Unlike Stylonychia, they live in the surface layer of water and have more pronounced negative chemotaxis to the salt content of organic matter. In the control, a decrease in the activity of the infusoria was noted, but their number did not increase.

The experimental material showed that the waste from the technological processing of wine turned out to be a favorable environment for protozoa, which was confirmed in the number of infusoria and the change of generations in comparison with the control.

The results of the study of the microflora of adhesive deposits of yellow blood salt showed a high content of mesophilic aerobic and facultative anaerobic microorganisms. Bacteria of the genus Bacillus subtilis – Bac. mesentericus, Bac. megaterium has been isolated. This association of bacteria is characteristic of soils and substrates with high mineralization and, high content of sulfates, and iron oxides. On the bismuth-sulfite medium, the growth of colonies with a brown color in the center was noted, and the surface of the colony was wrinkled; colonies typical of the genus E. coli were isolated on the Endo medium.

Studies of the acute toxicity of the Bentorb sorbent were carried out on 60 white mongrel rats weighing 237 ± 7 g. The sorbent was administered to animals in the form of a 50% aqueous suspension at a concentration of 400 mg/ml using a probe. Given the small volume of the stomach of rats, the sorbent suspension was administered at an interval of 1 hour in a volume of 5 ml per injection: to rats of the second group - once; the third - twice; the fourth - four times; the fifth - five times and the sixth - sevenfold. The control animals of the first group were injected sevenfold with 5 ml of water. The total amount of the introduced sorbent was conditionally taken as a single intake into the body. The animals were monitored for 14 days.

Experiments showed that the general clinical condition of rats from all experimental and control groups did not change significantly, all animals remained alive **(Table 4)**.

Table 4. Acute toxicity of Bentorb in rats

Group	Suspension volume, ml	The amount of the drug, mg/kg	Number of rats	
			Total	Died
1	5	8370	10	-
2	10	16735	10	-
3	20	33473	10	-
4	15	41841	10	-
5	35	58577	10	-
6	35 (control)		10	-

Studies of the chronic toxicity of Bentorb sorbent were conducted on 60 white mice. For 2 months, 0.3 ml of sorbent suspension in 2.5% starch gel was administered daily to the animals. The mice of the 1st group were injected with Bentorb sorbent with a shelf life of 3 years, the mice of the 2nd group were injected with sorbent stored for 13 years, the 3rd group was a control, and the mice were injected with pure starch gel. Groups 1.1 and 2.1 were given the drug at a concentration of 100 mg/ml, groups 1.2 and 2.2 – at a concentration of 200 mg/ml, and groups 1.3 and 2.3 – 400 mg/ml. The toxicity of the drug was assessed by the survival rate of mice during the experiment.

The results of studying the chronic toxicity of Bentorb when administered to mice are presented in **Table 5**.

Table 5. Chronic toxicity of Bentorb in mice

Shelf life	Group	Drug quantity		Number of mice	
		Suspension concentration, mg/ml	Total amount, mg	Total	Died
3 years	1.1	100	21600	10	2
	1.2	200	43200	10	2
	1.3	400	86400	10	4
13 years	2.1	100	21600	10	2
	2.2	200	43200	10	2
	2.3	400	86400	10	4
Control	3	Starch gel	0	10	4

During the study period, no differences in the general condition of the animals were observed. The mortality rate of mice injected with the sorbent did not exceed the mortality rate among mice treated with pure starch gel. The causes of death of all

mice were of the same type and were the result of perforation of the stomach wall with a metal probe. Therefore, the Bentorb sorbent is non-toxic. In groups of mice treated with the drug of different shelf life in the same concentrations, no differences in survival were found. This indicates that long-term storage of the finished sorbent does not lead to an increase in its toxicity.
The chronic toxicity of Bentorb sorbent was studied on 40 Wistar rats weighing 185±12 g, divided into 4 similar groups of 10 animals each, taking into account body weight. The sorbent was injected inside with a syringe using a probe daily for 60 days in a volume of 5 ml per day. Animals of groups 1, 2, and 3 were injected with an aqueous suspension of sorbent with concentrations of 100, 200, and 400 mg/ml. Over the entire study period, the total doses corresponded to 30,000, 60,000, and 120,000 mg per animal. Group 4 rats received 5 ml of water daily.
During the study period (60 days), no significant differences in the general condition and survival of control and experimental animals were observed.

Investigation of the Effect of the Ferrocyanide-Bentonite Sorbent Bentorb on the Function of the Digestive Tract
The study of the effect of Bentorb on the function of the digestive tract was carried out on piglets 40-80 days old. The effect of the sorbent on the function of the digestive system of animals was characterized by the physico-chemical properties of feces, which were collected at the beginning of the experiment and the next 20 days before the end of the research. During this time, a sensory assessment was performed, paying attention to the consistency, smell, color, and presence of impurities.
Studies have found that the acts of defecation in piglets of the experimental and control groups were carried out in a natural position, painlessly and without tension. Fecal masses were formed, cement-gray in color (similar to the color of the sorbent), with a specific odor. Impurities of blood, gas bubbles, and mucus were not found in the studied stool samples, and helminth eggs, and protozoa were absent.
Microscopic examination characterizing the digestive ability of the gastrointestinal tract revealed fat droplets and single starch grains.
The pH reaction was neutral and ranged from 7.0 to 7.3, ensuring the vital activity of the intestinal microflora.
Biochemical studies have isolated bile pigments in feces within the normal range.
During auscultation of the gastrointestinal tract in the experimental group of piglets, there was no decrease in gastric and intestinal motility.
The conducted studies have established that the Bentorb sorbent in therapeutic doses (1% in the diet) did not negatively affect the digestive processes with prolonged administration.

Study of Embryotoxic and Teratogenic Properties
The embryotoxic effect of Bentrob sorbent was studied in pregnant Wistar rats with an average body weight of 200-240 g. 20 animals were used in the experiment, of which 10 were selected during implantation (5th day of pregnancy) and 10 during ontogenesis (10th day of pregnancy). Bentorb sorbent in 2.5% starch gel at a dose of 10,000 mg/ kg body weight was injected once into the stomach of five animals from each group. The remaining females in the groups served as controls. They were injected with 2.5% starch gel in the same volume.
The slaughter of animals (two rats from each group) was carried out by decapitation on the 20th day of the experiments. The section took into account overall fertility, early and late fetal resorption, the number of yellow pregnancy bodies, as well as the presence of living and dead embryos.
As a result of the external examination of the fruits, no deviations from the norm were revealed. No skeletal abnormalities, internal organs, or deformities were found. The Bentorb sorbent did not affect the number of yellow bodies in the ovary. The number of live and dead fetuses in the rats of the experimental groups did not differ significantly from the control ones. Differences in the weight of the fruits, their length, the mass of the placentas, and their diameter were not reliable. Macroscopic external examination of fetuses and their placentas revealed no differences between the groups. The ratio of the number of females and males in the litter of experimental animals did not differ from the control ones.
Offspring were obtained from the remaining females, the development of which was continued to be monitored.
The conducted studies have established that the administration of Bentorb sorbent in a therapeutic dose to pregnant animals does not have a toxic effect on the course of pregnancy and childbirth. Labor in both experimental and control rats occurred on the 23-24 days of pregnancy. The litter size of females treated with Bentorb was similar to the litter size of control animals (the number of born rats per female in the experimental group was 12.6±0.653, in the control group – 12.4±0.72). The baby rats were born alive, without external abnormalities. During the experiment, their weighing, measurements of body length, tail, and ears were carried out; the timing of ear detachment, eye eruption, overgrowth, sucking reflex, mobility, and motor activity was taken into account. Thus, the average body weight of one rat at birth was 30.2±0.51 g (experiment) and 29.9±0.62 g (control), respectively.
The peeling of the ears occurred 4-5 days after birth. On days 5-6, the rats of both groups had a partial appearance of hair, and complete overgrowth of hair occurred by the 16th day after birth, and on the 15th-17th day, the eyes opened.
Studies have shown that offspring born from rats treated with ferrocyanide-containing sorbent during pregnancy did not differ from control animal pups. There were no differences in their growth, development, and behavior.
The results of the examination of the morphology of the wound and internal organs of the fruits allow us to conclude that there is no embryotoxic and teratogenic effect of the ferrocyanide-containing sorbent, which indicates the absence of its toxic effect on the body of rats.

The Effect of the Sorbent on the Body and Organs of Animals

The sorbent suspension was injected into rats (50 heads divided into 5 similar groups) with a syringe through a metal probe of 5 ml per injection: group 1 – once, group 2 – twice with an interval of 1 hour, group 3 – four times, groups 4 and 5, respectively 5-ti and 7 times with the same interval, the 6th group of animals (10 heads) did not receive sorbent and served as a control.

There were no significant differences in the general condition of the experimental and control rats: all animals had a characteristic appearance for healthy rats, the condition of the coat, visible mucous membranes, attitude to food, mobility, and respiratory rate.

The body weight of all experimental rats tended to increase but without significant deviations from the initial values **(Table 6)**.

Table 6. Body weight and hematological parameters of rats once treated with Bentorb sorbent (M= m; n=60)

The duration of the study, day	Group	Body weight, g	Leukocytes, thousand/μl	Lymphocytes, thousand/μl	Erythro-cytes, million/μl	Platelets, thousand/μl
Before the administration of the drug	1	236.7±2.0	19.0±4.1	9.5±1.9	8.6±1.4	475±39
	2	233.3±16.7	22.6±2.1	14.0±1.7	8.6±1.0	460±44
	3	233.3±19.7	20.5±3.2	12.3±2.2	7.5±0.9	393±60
	4	243±22.5	19.7±3.3	11.7±2.1	7.3±0.2	338±13
	5	211.7±8.2	23.8±3.5	14.3±2.0	7.4±0.4	387±55
	6	265.0±40.2	19.6±3.3	11.1±3.8	6.6±0.4	405±13
1	1	235±3.5	23.8±1.4	15.4±1.8	6.8±1.2	415±76
	2	243.3±24.8	15.8±0.*	10.5±1.0	7.2±0.2	466±39
	3	233.3±8.9	16.7±0.9	10.5±1.5	6.2±0.3	323±20
	4	248.3±25.6	20.5±2.1	13.1±1.5	6.6±1.1	274±86
	5	201.7±8.9	18.6±1.8	8.8±1.3	7.3±0.3	423±43
	6	256.7±36.8	15.0±2.3	9.9±2.2	7.6±0.6	333±45
7	1	230.0±1.0	27.1±3.3	16.8±1.3	7.9±0.7	463±45
	2	246.7±30.9	23.1±4.7	12.6±2.7	7.0±0.5	427±91
	3	230.0±3.5	24.6±2.6	13.3±4.5	6.4±0.7	333±57
	4	251.7±26.5	26.5±6.9	16.2±4.5	7.60.3	32466
	5	206.78.2	20.02.0	13.3±2.7	7.4±0.5	349±30
	6	265.0±43.4	17.0±1.8	10.1±1.5	7.0±0.5	360±19
14	1	241.7±2.0	22.5±3.8	13.9±1.6	7.4±0.4	440±49
	2	250.0±28.9	19.6±3.2	11.6±1.9	6.6±0.4	441±37
	3	240.0±6.1	24.1±4.6	12.4±3.1	6.9±0.5	343±27
	4	258.3±31.7	24.1±4.9	14.3±2.8	8.0±0.6	242±26
	5	215.0±9.4	18.9±2.6	11.6±2.3	7.1±0.8	380±7
	6	273.3±47.5	20.6±1.0	14.8±1.4	7.6±0.4	357±71

There are also no patterns in the change in the number of erythrocytes and platelets in animals of the experimental and control groups. For leukocytes, there was a tendency to increase their number in the period from day 1 to day 7, however, changes in the content of blood cells were not statistically significant.

As can be seen from the table materials, Bentorb sorbent, when injected into the gastrointestinal tract of rats in doses from 2000 to 14000 mg per animal, did not significantly affect body weight and peripheral blood picture, all animals survived.

The results of the study of the cellular composition of the venous blood of rats (4 groups of 10 animals each) treated with Bentorb repeatedly for 60 days are presented in **Table 7**.

Table 7. Hematological parameters of the blood of rats treated with Bentorb for 60 days (M± m; n=40)

The duration of the study, day	Group	Body weight, g	Leukocytes, thousand/μl	Lymphocytes, thousand/μl	Erythro-cytes, million/μl	Platelets, thousand/μl
before administration of the drug	1	261±29	16.4±1.7	11.3±1.6	7.1±0.6	343±64
	2	238±11	14.9±0.9	10.2±0.8	6.8±0.6	255±26
	3	246±8	19.1±2.7	13.4±1.7	7.7±0.3	328±46
	4	238±10	21.6±5.1	12.8±2.8	6.6±0.5	298±43

10	1	265±10	22.0±1.3	15.2±2.0	7.5±0.5	390±51
	2	248±12	18.1±2.3	13.3±2.1	7.4±0.1	380±31
	3	255±6	23.6±4.2	16.0±3.1	6.5±0.3	278±28
	4	265±15	18.9±3.1	13.3±2.9	7.3±0.5	330±57
20	1	255±22	21.4±2.3	13.9±2.1	7.8±0.2	358±41
	2	258±13	13.7±1.7	8.4±0.7	7.1±0.3	350±36
	3	263±9	22.7±6.3	12.4±2.6	7.1±0.5	391±44
	4	269±19	26.3±2.6	18.3±2.3	7.5±0.6	343±22
30	1	261±28	20.1±1.5	12.8±2.4	7.2±0.4	403±29
	2	260±12	17.0±1.1	11.8±1.7	6.9±0.4	360±34
	3	271±8	21.1±1.4	14.0±1.1	7.7±0.4	353±51
	4	261±29	23.0±3.0	13.8±0.83.	7.3±0.3	356±31
45	1	253±21	20.6±3.7	14.2±2.9	7.4±0.6	401±22
	2	263±12	13.0±1.0	8.2±0.8	7.8±0.6	391±30
	3	261±5	19.8±2.3	13.9±1.7	8.0±0.8	359±40
	4	248±17	24.9±2.4	18.0±1.5	7.7±0.1	347±66
60	1	249±17	21.6±3.9	14.3±3.9	7.7±0.8	357±35
	2	250±21	14.6±2.0	10.0±1.2	7.5±0.9	297±25
	3	270±7	21.3±5.2	11.0±2.2	7.8±0.7	322±19
	4	245±13	19.4±2.2	13.0±3.2	7.6±0.6	377±25
90	1	250±17	16.6±3.6	11.4±2.8	6.3±0.4	340±48
	2	255±16	16.7±1.5	10.8±0.9	6.3±0.2	357±32
	3	272±7	16.7±4.9	9.8±3.7	7.1±0.4	366±64
	4	250±23	24.5±0.9	17.5±2.5	7.1±0.2	360±68

It can be seen from the table that in rats of the 1st group, from the 10th to the 60th day, there was a tendency to decrease body weight without a significant difference about the initial level. The number of erythrocytes and platelets in animals of different groups varied equally and did not differ significantly from the norm. By the 10th day, the number of leukocytes and lymphocytes in the animals of the experimental groups increased significantly. In general, venous blood counts fluctuated during the study period without significant difference from those of the control group.

The data obtained indicate that with chronic administration of the drug into the body in amounts from 30,000 to 120,000 mg per animal, there are no violations of the physiological state of rats.

Conclusion

During the study of the acute toxicity of the Bentorb sorbent, it was found that the general clinical condition of rats from all experimental and control groups did not change significantly, all animals remained alive. In a study of the chronic toxicity of the Bentorb sorbent, it was found that the mortality of mice injected with the sorbent did not exceed the mortality of mice in the control group. In groups of mice treated with the drug of different shelf life in the same concentrations, no differences in survival were found. This indicates that long-term storage of the finished sorbent does not lead to an increase in its toxicity. During the study period of laboratory rats (60 days), no significant differences in the general condition and survival of control and experimental animals were observed.

When studying the Bentorb sorbent on the function of the digestive tract, it was found that Bentorb sorbent in therapeutic doses (1% in the diet) with prolonged administration did not adversely affect the digestive processes.

The results of the examination of the morphology of the external and internal organs of fetuses allow us to conclude that there is no embryotoxic and teratogenic effect of ferrocyanide-containing sorbent on the body of rats.

Investigation of the effect of Bentrob sorbent on animal organs has shown that with chronic administration of the drug into the body in amounts from 30,000 to 120,000 mg per animal, there are no violations of the physiological state of rats.

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Ethics statement: The protocol for experiments with laboratory animals complied with the requirements of the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes.

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