

# Study of Some Toxicological Properties of Sorbent from Plant Cellulose

Denis A. Grachev<sup>1</sup>, Said S. Ksembaev<sup>2</sup>, Elimina A. Agatieva<sup>3</sup>

<sup>1,2,3</sup>Kazan State Medical University, Butlerova St. 49, Kazan, 420012, Russia

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## Abstract

When studying the acute toxicity of a new agent based on plant cellulose, it was found that a single oral administration of a test sample of cellulose sorbent in doses of 2000; 4000; 6000 mg/kg of live weight did not have a negative effect on clinical and pathological parameters, animal survival, body weight gain and organ weight. The studied doses of experimental sample of cellulose sorbent do not cause death in rats, therefore, the average lethal dose has not been determined. The maximum dose administered was 6000 mg/kg. The facts revealed allow us to attribute experimental sample of cellulose sorbent substances of hazard class 4 - low-hazard substances.

A single cutaneous application of a test sample of cellulose sorbent in doses of 1000 mg/kg, 2000 mg/kg and 3000 mg/kg also did not have a negative effect: it did not lead to the death of rats, and no signs of intoxication were noted. Cumulative properties of a new plant sorbent have been studied. The data obtained from the research results indicate that the studied agent, when used for 28 days, does not exhibit a toxic effect on the body. Intra-gastric administration of the studied sorbent sample in increasing doses did not cause death of experimental rats. In experimental rats that received the test sample, the morphological and biochemical parameters of the blood do not differ from those of control animals and reference values characteristic of this species. According to the autopsy and macroscopic examination of the organs under study, no differences were found between the animals that received distilled water and the test agent. Analysis of the absolute weight of the internal organs of animals with subchronic administration of the plant sorbent did not reveal reliable differences between the groups of animals.

**Keywords:** sorbent, cellulose, acute toxicity, cumulative properties, rats

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## INTRODUCTION

Currently, one of the most important problems in surgical dental practice is purulent inflammatory odontogenic diseases of the facial area, which is associated with widespread prevalence, as well as the risk of development and rapid spread of complications and pathological process [1,2,3,4,5, 6].

Among the numerous agents used in the local treatment of purulent-inflammatory odontogenic diseases, a group of medical sorbents that provide an active cleansing effect on a purulent wound is very promising. The development of methods for local wound treatment using them has led to the development of an independent direction called sorption-application therapy [7,8,9,10]. However, modern sorbents are rarely used in clinical dentistry. The drug "Celoform" for sorption-application therapy, made from cotton cellulose, is known, which has shown high efficiency associated with the creation of optimal conditions in the wound for the course of reparative processes due to pronounced bactericidal, anti-inflammatory and analgesic effects. Currently, a preclinical study of a new sorbent made of plant cellulose, previously not used in existing analogous drugs, is underway. Therefore, the issues of studying its toxicological properties are becoming relevant. The basis of drug toxicology is the assessment of the ratio of the therapeutic value of a drug and the undesirable effects that may arise from its use. This means that an experimental study of the safety of a new drug is no less important than an assessment of its pharmacological activity.

The aim of the present studies was to determine the acute and chronic toxicity of a new plant sorbent upon parenteral administration and cutaneous application.

## MATERIALS AND METHODS

The experimental animals were kept in standard conditions of keeping and feeding according to the pan-European requirements for animals used for experimental and other scientific purposes (Strasbourg, 1986), sanitary and epidemiological requirements for the arrangement, equipment and maintenance of experimental biological clinics (vivariums). The animals were kept in individual cages with free access to food and water. The animals were fed in accordance with zootechnical standards.

Animals with no signs of deviations in appearance were selected into experimental groups using the analog method. The groups were formed by random selection using body weight as the leading characteristic (the spread in initial weight between and within groups did not exceed  $\pm 10.0\%$ ).

To study the acute intragastric and cutaneous toxicity of the experimental sample of cellulose sorbent, 4 groups of rats of both sexes were formed for each type of administration/application ( $n=6$ ) with a live weight of 185-205 g. Administration/application was carried out once in doses of 2000, 4000, 6000 mg/kg/ 1000, 2000, 3000 mg/kg, respectively. The animals of the control group were given distilled water intragastrically when studying acute intragastric toxicity. When studying acute cutaneous toxicity, an area of skin 6 x 6 cm<sup>2</sup>. The experimental sample of cellulose sorbent was pre-mixed with vaseline oil. The rats of the control group were given vaseline oil in its pure form. Clinical observation of the animals was carried out for 14 days. The consumption of food and water, the condition of the fur and mucous membranes, and behavior were recorded. The rats were weighed at the beginning of the experiment and on the 14th day of the study on electronic laboratory scales "HIGHLAND" type "HCB 602H", designed for static measurement of weight.

On the 14th day after a single intragastric administration/cutaneous application of the experimental sample of cellulose sorbent, rats of each group were euthanized for pathomorphological studies. Organs were weighed on an Aczet CY-124 C analytical scale, the condition of the internal organs was assessed macroscopically.

The study of the cumulative properties of the experimental sample of cellulose sorbent by the subchronic toxicity method was carried out on 12 white nonlinear rats of both sexes (6 per group) with a live weight of 130-150 g, divided into 2 groups (experimental and control). The animals of the experimental group were administered a sample of cellulose sorbent intragastrically for 28 days. The initial dose was 1/10 (600 mg/kg) of the maximum administered during the study of acute toxicity. In each subsequent 4 days, the dose was increased by 1.5 times. The control group received distilled water. The total duration of observation during the assessment of subchronic toxicity was 28 days and 30 days of post-observation. The clinical picture and the timing of possible death were recorded. On the 28th and 58th days, the most complete examination of the animals was carried out using hematological and biochemical tests. Blood was collected after a 14-15-hour fast. Blood serum was analyzed using an ARD-200 analyzer with special Chronolab reagent kits. Hematological parameters were determined in whole blood using a Mythic 18Vet automatic analyzer. Three rats from each group were euthanized on day 28 and all remaining animals on day 58 for pathomorphological studies with an assessment of the macroscopic picture of internal organs. Organs were weighed using an Aczet CY-124 C analytical scale.

## RESULTS AND DISCUSSIONS

A single intragastric administration of the experimental sample of cellulose sorbent in doses of 2000 mg/kg, 4000 mg/kg and 6000 mg/kg did not cause death of rats, no signs of intoxication were noted. Immediately after the administration of the plant sorbent, animals of all groups showed depression, which passed in 10-15 minutes, which can be explained by the reaction to manipulations. During the 14-day observation, the activity of animals of all groups was preserved, they readily consumed food and water, the fur remained smooth and shiny.

The body weight of the experimental groups of rats did not differ significantly from the indicators of the control group of rats. Thus, none of the studied doses of the cellulose sorbent caused signs of intoxication or had a negative effect on the increase in live weight (Table 1).

**Table 1:** The effect of a single intragastric administration of a sorbent on the dynamics of live weight in rats, g ( $n=6$ )

Research period, days	Group of animals			
	Group 1 (Biological control)	Group 2 (2000 mg/kg)	Group 3 (4000 mg/kg)	Group 4 (6000 mg/kg)
Background	197.36 $\pm$ 2.66	195.07 $\pm$ 3.37	193.37 $\pm$ 3.73	196.44 $\pm$ 2.50
14	247.69 $\pm$ 3.25	241.73 $\pm$ 4.47	237.13 $\pm$ 4.77	239.51 $\pm$ 3.19

According to the autopsy and macroscopic examination of the organs studied, no differences were found

between the animals that received distilled water and the sorbent.

Analysis of the absolute weight of the internal organs of animals that received a single intragastric administration of the sorbent in different doses did not reveal any significant differences between the groups of animals (Table 2).

**Table 2:** Effect of a single intragastric administration of the sorbent on the organ weight of white rats, g (n=6)

Organ under study	1 Group 1 (Biological control)	2 (2000 mg/kg)	3 (4000 mg/kg)	4 (6000 mg/kg)
Heart	0.98±0.04	1.00±0.04	1.01±0.05	1.16±0.19
Lungs	3.08±0.11	3.26±0.14	3.13±0.13	3.16±0.13
Liver	10.22±0.40	10.31±0.54	10.16±0.50	10.08±0.44
Spleen	0.74±0.03	0.76±0.03	0.73±0.04	0.74±0.03
Kidneys	1.05±0.04	1.09±0.04	1.17±0.05	1.09±0.05
Stomach	2.13±0.07	2.25±0.11	2.10±0.09	2.18±0.09
Intestines	22.11±0.83	22.86±0.72	22.23±0.83	21.98±0.93
Testicles	0.84±0.01	0.84±0.01	0.85±0.00	0.84±0.02
Ovaries	0.05±0.00	0.04±0.01	0.04±0.01	0.04±0.00

During the autopsy and macroscopic examination of the heart, lungs, liver, kidneys, spleen, testicles, and ovaries, no visible changes in the morphostructure were detected. The organs had their characteristic color, shape, and consistency.

Thus, a single oral administration experimental sample of cellulose sorbent rats in doses of 2000; 4000; 6000 mg/kg of live weight did not have a negative effect on clinical and pathological indicators, animal survival, body weight gain and organ weight. It was established that the studied doses experimental sample of cellulose sorbent do not cause death in rats, therefore, the average lethal dose has not been determined. The maximum dose administered was 6000 mg/kg. The facts revealed allow us to attribute experimental sample of cellulose sorbent substances of hazard class 4 - low-hazard substances.

A single cutaneous application of the experimental sample of cellulose sorbent in doses of 1000 mg/kg, 2000 mg/kg and 3000 mg/kg did not cause death of rats, no signs of intoxication were noted. During the 14-day observation, the activity of animals in all groups was preserved, they readily consumed food and water, the fur remained smooth, no skin pathologies were noted on the shaved area, and restoration of the fur was observed. The body weight of the experimental groups of rats did not differ significantly from that of the control group. Thus, none of the studied doses of the sorbent caused signs of intoxication and did not have a negative effect on the gain in live weight.

According to the autopsy and macroscopic examination of the organs under study, no differences were found between the animals in the biological control group and the experimental groups. Analysis of the absolute weight of the internal organs of animals that were given single skin applications of sorbent suspensions in different doses did not reveal any reliable differences between the animal groups. No visible changes in morphostructure were found during autopsy and macroscopic examination of the heart, lungs, liver, kidneys, spleen, testicles, and ovaries. The organs had their characteristic color, shape, and consistency.

Since the cutaneous application of the experimental sample of cellulose sorbent at a dose of more than 2500 mg/kg did not cause changes in the physiological state of rats or their death, the studied sorbent, according to the classification, belongs to substances of hazard class 4 - low-hazard substances.

Intragastric administration of the studied sorbent sample in increasing doses during the study cumulative properties did not cause death of experimental rats. The behavior, appearance and physiological state of the rats in the experimental group did not differ from those in the control group. There was no mortality in the groups (Table 3).

**Table 3:** Cumulative properties of the cellulose sorbent sample

Days of introduction	Daily dose, mg/kg	Total dose, mg/kg	Total dose by periods of administration,	Number of dead animals

			mg/kg	
1-4	600	2400	2400	0
5-8	900	3600	6000	0
9-12	1350	5400	11400	0
13-16	2025	8100	19500	0
17-20	3037,5	12150	31650	0
21-24	4556	18224	49874	0
25-28	6834	27336	77210	0

No statistically significant changes in the rats' body weight were detected when various doses of the plant sorbent were administered, compared to the control group of animals. Thus, the studied agent does not have a negative effect on live weight gain (Table 4).

**Table 4:** Dynamics of live weight of rats in the study of cumulative properties, g (n=6)

Animal group, drug dose	Research period, days		
	Background	28	58
Control (distilled water)	142.79±3.43	241.43±4.69	312.07±7.54
Experimental (sorbent)	144.39±3.12	239.79±8.49	302.82±9.31

When studying hematological parameters, it was established that there were no statistically significant differences relative to the values of the control group, and that they were within the reference values established for this type of animal.

According to the autopsy and macroscopic examination of the organs under study, no differences were found between the animals that received distilled water and the test agent. Analysis of the absolute weight of the internal organs of animals with subchronic administration of the plant sorbent did not reveal reliable differences between the groups of animals. During diagnostic autopsy of the animals at the end of the experiment, one rat showed mild hyperemia of the gastrointestinal mucosa. No other visible changes in the organs and tissues of the rats in the experimental group were observed compared to the control animals. Thus, long-term administration of the test sample in increasing doses from 600 to 6834 mg/kg did not have a negative effect on the clinical status, body weight, hematological and biochemical blood parameters of animals. As a result of morphometric analysis and macroscopic examination of the internal organs of animals, it was established that the plant sorbent has weakly expressed cumulative properties.

## CONCLUSION

The results of toxicological studies have established that the studied product based on plant cellulose belongs to the classification of class 4 - low-hazard substances, does not have a negative effect on the growth and development of laboratory animals, does not cause a negative effect on hematological blood indices. When autopsied, the laboratory experimental and control groups did not reveal any pathological changes in the internal organs.

## REFERENCES

- Gadicherla S., Manglani K., Pentapati KC, Kudva A., Aramanadka C., Chandravel R. Profile of patients with maxillofacial space infections and associated risk factors. *TheScientificWorldJournal*; 2024:9304671 (2024).
- Isola, G. Antibiotics and antimicrobials for the treatment of the oral microbiota: myths and facts in research and clinical practice. *Antibiotics (Basel)*, Vol. 9 (2). - P. E95 (2020).
- Klein DA, Lee BH, Bezhani H., Droukas DD, Stoffels G. The clinical utility of MRI in evaluating for osteomyelitis in patients presenting with uncomplicated cellulitis. *J. Foot Ankle Surg*, Vol. 59(2), 323-329 (2020).
- Ritwik P., Fallahi, Q. S. Yu. Management of facial cellulitis of odontogenic origin in a pediatric hospital. *Int. J. Paediatr. Dent*, 10(1111), 12613 (2020).
- Tüzüner Öncül AM, Uzunoğlu E., Karahan ZC, Aksoy AM, Kişnişci R., Karahmetoğlu Ö. Detecting gram-positive anaerobic cocci directly from the clinical samples by multiplex polymerase chain reaction in odontogenic 174 infections. *J. Oral Maxillofac. Surg.*, 73, 259-266 (2015).

6. Treviño-Gonzalez JL, Acuña-Valdez F., Santos-Santillana KM Prognostic value of systemic immune-inflammation index and serological biomarkers for deep neck infections. *Medicina oral, patología oral y cirugía bucal.* 29(1) (2004).
7. Aindow, D., Butcher, M. Films or fabrics: is it time to re-appraise postoperative dressings? *Br. J. Nurs,* 14(19), 15 - 16 (2005).
8. Bishop, S.M., Walker, M., Rogers, A.A., Chen, W.Y. Importance of moisture balance at the wound-dressing interface // *J. Wound Care.* 2003. Vol. 12, N 4. P. 125 - 128. 9. Carter, K. Hydropolymer dressings in the management of wound exudate. *Br. J. Com. Nurs,* 8(1), 10 - 16 (2003).
9. Martineau, L., Shek, PN Evaluation of a bi-layer wound dressing for burn care I. Cooling and wound healing properties. *Burns,* 32(1),70 - 76 (2006).
10. Martineau, L., Shek, PN Evaluation of a bi-layer wound dressing for burn care. II. In vitro and in vivo bactericidal properties. *Burns,* 32(2),172 - 179 (2006).