PHARMACOLOGICAL AND BIOCHEMICAL EFFECTS OF SULFOPARIN ON THE HUMAN BODY

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Anotation: Currently, there is an increasing global interest in chitin-based drugs, its derivatives, and their potential applications in various fields of medicine (1,2). One such medicinal product is *Sulfoparin*, which possesses anti-sclerotic properties. Sulfoparin is a complex of chitosan with sulfo groups, developed by researchers at the Institute of Chemistry and Physics of Polymers of the Academy of Sciences of the Republic of Uzbekistan(3). At the same time, it should be noted that the development of highly effective domestic pharmaceutical agents remains very relevant today, since many anti-sclerotic drugs, along with their main therapeutic properties, cause a number of undesirable effects associated either with their toxic characteristics or with side effects.

Keywords: Sulfoparin, sulfo group, drug, animal, solution, interval, administration, assistant, probe.

ФАРМАКОЛОГИЧЕСКОЕ И БИОХИМИЧЕСКОЕ ВЛИЯНИЕ СУЛЬФОПАРИНА НА ОРГАНИЗМ ЧЕЛОВЕКА

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Аннотация: В настоящее время во всем мире отмечается возрастание интереса к препаратам на основе хитина, его производным и возможностям их использования в различных областях медицины (1,2). Одним из таких лекарственных средств является сульфопарин, который обладает противосклеротическими свойствами. Сульфопарин является комплексом хитозана с сульфогруппами, разработанный сотрудниками института химии и физики полимеров АН РУз (3). Вместе с тем, следует отметить, что на

сегодняшний день проблема создания отечественных высокоэффективных лекарственных средств весьма актуальна, т.к. многие противосклеротические препараты наряду с основными свойствами вызывают ряд нежелательных явлений, связанных либо токсическими свойствами, либо побочными действиями этих препаратов.

Ключевые слова: Сульфопарин, сульфогруппа, препарат, живот, раствор, интервал, прием, помощ, зонд.

SULFOPARINNING INSON ORGANIZMIGA FARMOKOLOGIK VA BIOXIMIK TASIRLARI

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Annotatsiya: Hozirgi vaqtda butun dunyoda xitin asosidagi dori vositalari, uning hosilalari va ularni tibbiyotning turli sohalarida qo‘llash imkoniyatlariga bo‘lgan qiziqish ortib bormoqda (1,2). Ushbu dori vositalaridan biri — **Sulfoparin** bo‘lib, u anti-sklerotik xususiyatlarga ega. Sulfoparin — O‘zbekiston Respublikasi Fanlar akademiyasi Polimerlar kimyosi va fizikasi instituti xodimlari tomonidan ishlab chiqilgan sulfogruppalar bilan bog‘langan xitozan kompleksidir (3). Shu bilan birga, shuni ta’kidlash lozimki, yuqori samarali mahalliy dori vositalarini yaratish masalasi bugungi kunda ham dolzarbdir, chunki ko‘plab anti-sklerotik preparatlar o‘zining asosiy terapevtik xususiyatlari bilan bir qatorda ularning toksikligi yoki nojo‘ya ta’sirlari bilan bog‘liq bo‘lgan bir qator noxush holatlarni keltirib chiqaradi.

Kalit so‘zlar: Sulfoparin, sulfoguruhlari, preparat, hayvon, eritma, interval, qabul qilish, yordamchi, zond.

Materials and Methods

Acute intragastric toxicity of Sulfoparin was studied in 60 white mice of both sexes, weighing 18–22 g. The animals were divided into 6 groups, 10 animals in each group. The mice in the five experimental groups received the aqueous solution of the drug intragastrically on an empty stomach using a syringe with a metal probe, at doses of 1000, 1500, 2000, 2500, and 3000 mg/kg of body weight. The larger doses were administered in two portions with an interval of 1 hour. The sixth group served as the control and received physiological saline administered in the same manner. The animals were observed throughout the first day of the experiment and dynamically for 2–3 weeks. In assessing the acute toxicity of the drug, the maximum tolerated and absolutely lethal doses were taken into account. The LD_{50} error was calculated using the method proposed by Miller and Tainter, through determining LD_{34} and LD_{86}. Based on the obtained data, LD_{50} values were calculated using the statistical method of V.B. Prozorovsky (4).

Chronic toxicity of Sulfoparin was studied in 80 white rats of both sexes, weighing 110–120 g. The animals were divided into 4 groups, 20 rats per group.

- Group 1 received Sulfoparin at a dose of 500 mg/kg.
- Group 2 received 100 mg/kg.
- Group 3 received 25 mg/kg of the drug intragastrically once daily for 3 months.
- Group 4 served as the control (5,7).

Indicators of toxicity included animal behavior, survival rate, time of death occurrence, appearance of intoxication symptoms, dynamics of body weight, hemoglobin level, activity of alkaline phosphatase, AST, ALT, and catalase. Hemoglobin, erythrocytes, and leukocytes in peripheral blood were assessed using classical standard methods, while the activity of alkaline phosphatase, AST, and ALT in blood serum was determined using Lahéma (Czech Republic) biochemical test kits. Hematological and biochemical parameters were examined after completion of the experiment (6). The obtained results were subjected to statistical analysis using

methods of variational statistics, including calculation of the arithmetic mean (M), standard deviation, standard error of the mean (m), relative values (%), and statistical significance of differences. Comparisons of mean values were performed using Student's t-test (t), with probability of error (P) determined after checking for normal distribution (kurtosis test) and equality of variances (Fisher's F-test). Changes were considered statistically significant at $P < 0.05$.

Results of the study and their discussion

The results of our research showed that in the intact animals of Group 1, after the administration of an aqueous solution of the drug at a dose of 1000 mg/kg, no changes in behavior or functional condition were observed. However, as the dose increased, the animals became lethargic, less active, and reacted sharply to external stimuli. Their appetite was disturbed, their general appearance worsened, and their fur became ruffled. The death of the animals occurred due to respiratory arrest (Table 1).

Table1

Dependence of the survival time of white mice on the administered dose of Sulfoparin.

Dose of the drug, mg/kg	Number of animals	Time of death			Total deaths	% Death
		Within the first 24 hours	Within 3 days	In the following days		
1000	10	0	0	0	0	0
1500	10	0	1	1	2	20
2000	10	0	3	1	4	40
2500	10	1	4	1	6	60
3000	10	2	7	1	10	100

The maximum tolerated dose and the absolutely lethal dose of the drug were determined to be 1000 mg/kg and 3000 mg/kg, respectively (Table 2). It was found that the median lethal dose (LD_{50}) of Sulfoparin is 2150 (2425.4–1874.6) mg/kg. Therefore, according to the toxicity classification of medicinal substances, the drug belongs to low-toxicity substances (Class IV) (3,4,5).

Table 2

Parameters of acute toxicity of the drug Sulfoparin during single intragastric administration to white mice.

Species of animals	LD_{16}	LD_{50}	LD_{84}
White mice	1450	2150(2425,4 ÷1874,6)	2800

When studying the chronic toxicity of the drug Sulfoparin, no disturbances in the general condition of the experimental animals were observed during the experiment; no symptoms of intoxication were detected, and no deaths occurred. No local skin changes were found, and no areas of focal alopecia or ulcers were noted. The animals were clean, their fur was smooth and shiny, they were active and responded adequately to external stimuli. No statistically significant delays in body weight gain were observed in any of the experimental animals compared to the control animals (Table 3).

Table 3

Dynamics of body weight in white rats during repeated intragastric administration of the drug Sulfoparin, in grams.

Names of animal groups and administered drug dose	Statistical indicators	Duration of the study (months)				
		Background	1	2	3	Recovery period
Control	M±m	140±4,1	148±4,3	157±4,2	165±7,6	173±7,9

Sulfoparin, 500 mg/kg	M±m, P	142±6,6 >0,05	151±10,1 >0,05	159±7,8 >0,05	164±6,1 >0,05	171±6,5 >0,05
Sulfoparin, 100 mg/kg	M±m, P	141±9,9 >0,05	149±12,3 >0,05	155±4,8 >0,05	167±5,8 >0,05	170±7,2 >0,05
Sulfoparin, 25 mg/kg	M±m, P	143±7,9 >0,05	147±5,6 >0,05	158±7,2 >0,05	163±4,9 >0,05	174±7,4 >0,05

Next, the dynamics of hemoglobin, erythrocytes, and leukocytes in peripheral blood were studied. As can be seen from the data presented in Table 4, these hematological parameters in peripheral blood did not show statistically significant differences in the experimental group animals compared to the control group.

Table 4

Hematological parameters in peripheral blood of white rats during repeated intragastric administration of the drug Sulfoparin.

Names of animal groups and administered drug dose	Statistical indicators	Hematological parameters		
		Hemoglobin content, g/L	Erythrocyte count, million/L	Leukocyte count, T/L
Control	M±m	127,0±5,8	4,90±5,8	8,09±0,3
Sulfoparin, 500 mg/kg	M±m, P	130,0±5,5 >0,05	4,87±0,25 >0,05	8,16±0,31 >0,05
Sulfoparin, 100 mg/kg	M±m, P	129,0±3,6 >0,05	4,85±0,44 >0,05	8,17±0,17 >0,05
Sulfoparin, 25 mg/kg	M±m, P	131,0±9,1 >0,05	4,82±0,4 >0,05	8,14±0,32 >0,05

Additionally, in the experimental conditions, the activity of alkaline phosphatase, AST, ALT, and catalase enzymes in the blood of rats was studied. According to the

obtained data, it was found that in the experimental animals, the activity of alkaline phosphatase, AST, ALT, and catalase enzymes in the blood did not differ from the control values (Table 5).

Table 5

Biochemical parameters of the blood serum of white rats during repeated intragastric administration of the drug Sulfoparin.

Names of animal groups and administered drug dose	Statistical indicators	Biochemical parameters			
		Alkaline phosphatase activity, mol/L·h	AST activity, mol/L·h	ALT activity, mol/L·h	Catalase activity, μkat/L
Control	M±m	140±4,1	148±4,3	157±4,2	165±7,6
Sulfoparin, 500 mg/kg	M±m, P	142±6,6 >0,05	151±10,1 >0,05	159±7,8 >0,05	164±6,1 >0,05
Sulfoparin, 100 mg/kg	M±m, P	141±9,9 >0,05	149±12,3 >0,05	155±4,8 >0,05	167±5,8 >0,05
Sulfoparin, 25 mg/kg	M±m, P	143±7,9 >0,05	147±5,6 >0,05	158±7,2 >0,05	163±4,9 >0,05

From the data presented in Table 5, it can be seen that no statistically significant differences in the activity of the studied enzymes in the blood of experimental rats were observed compared to the control results.

Conclusions:

1. The study of acute intragastric toxicity of the drug in white mice showed that Sulfoparin belongs to low-toxicity substances.
2. During prolonged chronic intragastric administration, Sulfoparin does not have a negative effect on the behavior or body weight dynamics of the animals.

3. The drug does not exhibit toxic effects on the hematological and biochemical parameters in the bodies of the experimental animals.

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