ETHIOPIAN INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 11, Issue 04, April-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

STUDYING THE CHRONIC TOXICITY OF SULFOPARIN

Kutlikova G.M.
Department of Internal medicine
Andijan State Medical Institute

ABSTRACT: For the first time, a set of preclinical experimental studies of the new drug "Sulfoparin", developed by the Institute of Chemistry and Physics of Polymers of the Academy of Sciences of the Republic of Uzbekistan, was carried out. It has been established that with chronic exposure for 3 months, the drug in doses of 500, 100 and 25 mg/kg b.w. does not cause pathological changes in the body of experimental animals. Morphological studies have established that no significant differences were found in the structure of internal organs between the experimental and control groups, meaning Sulfoparin does not cause dystrophic, necrobiotic and inflammatory changes in animals.

Key words: Drug Sulfoparin, chitosan, chronic toxicity, cumulative properties.

Throughout the world, there is an increasing interest in preparations based on chitin, its derivatives (chitosan and chitosan sulfate) and the possibilities of their use in various fields of medicine today[6]. Of particular interest stands the preparation of chitosan sulfate from chitosan. The study of the sulfation of chitosan established the regularity of this reaction from the standpoint of high-molecular compounds. The physicochemical characteristics of the obtained chitosan derivatives were revealed at the molecular and supramolecular levels. The formation of chitosan sulfate was analyzed through identification experiments using IR and NMR spectroscopy, X-ray diffraction analysis, polarization microscopy and sorption in water [6].

The problem of creating highly effective domestic medicines is very relevant today. One of these drugs is Sulfoparin, which has antisclerotic properties [2,3,5]. The drug Sulfoparin was developed at the Institute of Chemistry and Physics of Polymers of the Academy of Sciences of the Republic of Uzbekistan [6]. There is limited information in the literature about the low toxicity of Sulfoparin and its use in medicine in experiments on laboratory animals. However, there is no information about the nature and severity of the damaging effect of Sulfoparin on the body of experimental animals and an assessment of its safety.

The purpose of this work: to study the chronic toxicity of the drug Sulfoparin.

Material and research methods. Object of research – Sulfoparin, which is a drug intended for use as an anti-atherosclerotic agent. The drug Sulfoparin was developed at the Institute of Chemistry and Physics of Polymers of the Academy of Sciences of the Republic of Uzbekistan. Toxicological studies of Sulfoparin were carried out on 80 white rats weighing 110-120 grams, which received aqueous solutions of the drug intragastrically daily for 3 months [1,4,7]. The animals were divided into 4 groups of 20 animals per group: 1st group of animals received Sulfoparin at a dose of 500 mg/kg; Group 2 received Sulfoparin at a dose of 100.0 mg/kg; Group 3 received Sulfoparin at a dose of 25 mg/kg; Group 4 served as control. The toxicity indicators were: animal behavior, survival rate, time of death, appearance of intoxication symptoms, body weight dynamics, hemoglobin content, erythrocytes and leukocytes in peripheral blood, activity of alkaline phosphatase, AST and ALT, catalase. Indicator studies were carried out after completion of the experiment. The content of hemoglobin, erythrocytes and leukocytes in peripheral blood was studied in a classical, generally accepted way; activity of enzymes alkaline phosphatase, AST, ALT in blood serum was carried out

eISSN: 2349-5715 pISSN: 2349-5707
Volume: 11, Issue 04, April-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

by biotests from Lachema (Czech Republic). The obtained research results were subjected to statistical processing.

Results and its discussion. Chronic toxicometry parameters of Sulfoparin had not been previously studied, which was the basis for the research. During the experiment, the general condition of the experimental animals was not disturbed, no symptoms of intoxication were detected, and there was no death of the animals. No local changes were found on the skin; no areas of focal baldness or ulcers were noted. The animals were neat, their coats were smooth and shiny, they readily ate food, were active, and responded adequately to external stimuli.

As can be seen from the data presented in Table 1, no statistically significant lag in body weight gain was established in all experimental animals compared to control animals.

Table 1.

of Sulfoparin in various doses for 3 months , g .

animal groups	Stat. indicators	Research time (months)				
		Background	1	2	3	Restore period
Control	M±m	140 ±4.1	148 ±4.3	157 ±4.2	165 ±7.6	173 ±7.9
Sulfoparin , dose 500 mg/kg	M±mR	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 , dose 100 mg/kg	M±mR	141 ±9.9 >0.05	149 ±12.2 >0.05	155 ±4.8 >0.05	167 ±5.8 >0.05	170 ±7.2 >0.05
Sulfoparin , dose 25.0 mg/kg	M±mR	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

The dynamics of the content of hemoglobin, erythrocytes and leukocytes in the peripheral blood was studied, which did not reveal statistically significant differences in the animals of the experimental group compared to the control data (Table 2).

Table 2.

of Sulfoparin for 3 months

Name of animal groups	Statistician, indicators	Hematological parameters		
		Hemoglobin content, g /l	RBC content, 10^{12} /l	Leukocyte content, 10^{9} /l
Control	M±m	127.0 ±5.8	4.90 ±0.19	8.09 ±0.3
Sulfoparin , dose 500 mg/kg	M±mR	130.0 ±5.5 >0.05	4.87 ±0.25 >0.05	8.16 ±0.31 >0.05
Sulfoparin , dose 100 mg/kg	M±mR	129.0 ±3.6 >0.05	4.85 ±0.44 >0.05	8.17 ±0.17 >0.05

eISSN: 2349-5715 pISSN: 2349-5707
Volume: 11, Issue 04, April-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

Sulfoparin , dose 25.0 mg/kg	M±mR	131.0 ±9.1 >0.05	4.82 ± 0.4 >0.05	8.14 ±0.32 >0.05

Data from the study of biochemical parameters of the blood serum of experimental and control animals are presented in Table 3. The data obtained in experimental animals for studying the activity of the enzymes alkaline phosphatase, AST, ALT and catalase in the blood did not differ from the control values. From the data presented in Table 3, it is clear that statistically significant differences in the activity of the studied enzymes in the blood of experimental rats compared to control results have not been established.

Table 3.

of Sulfoparin for 3 months

Name of animal groups	Stat. indicators	Biochemical indicators			
		Alkaline phosphatase activity, mol/l .h	AST activity , mmol / l.h	ALT activity , mmol / l.h	Catalase activity, mcat /l
Control	M±m	0.37 ±0.01	0.31 ±0.02	0.23 ±0.025	23.01 ±2.14
Sulfoparin , dose 500 mg/kg	M±mR	0.34 ±0.01 >0.05	0.33 ±0.04 >0.05	0.21 ±0.019 >0.05	20.05 ±1.36 >0.05
Sulfoparin , dose 100 mg/kg	M±mR	0.35 ±0.01 >0.05	0.35 ±0.06 >0.05	0.19 ±0.017 >0.05	22.04 ±1.49 >0.05
Sulfoparin , dose 25.0 mg/kg	M±mR	0.38 ±0.02 >0.05	0.30 ±0.04 >0.05	0.22 ±0.013 >0.05	21.04 ±1.16 >0.05

Results of studies of the functional state of the kidneys of rats 3 months after intravenous administration of Sulfoparin in doses of 500.0 mg/kg b.w., 100.0 mg/kg b.w. and 25.0 mg/kg b.w. showed that the diuresis of experimental rats was not statistically different from control rats. The state of nitrogen metabolism, the criterion of which is the urea content in the blood, had no deviations from the control. Glucose and protein in urine as in The experimental and control groups were absent during the entire experiment. The acidity of urine in all studied groups did not change during the entire experiment and its acidity (pH) was 7.0 (Table 4).

Table 4

Some indicators of kidney function in experimental and control rats, 3 months after intravenous administration of Sulfoparin in doses of 500.0 mg/kg, 100.0 mg/kg and 25.0 mg/kg

Groups of animals	Drug dose mg/kg	Diuresis after 4 hours, %	Blood urea, mmol /l
Control	0	91 ±1.6	4.6 ±0.13
Sulfoparin	500.0	90 ±1.3 P >0.05	4.7 ±0.12 P >0.05

eISSN: 2349-5715 pISSN: 2349-5707
Volume: 11, Issue 04, April-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

Sulfoparin	100.0	89 ±1.88 P >0.05	4.8 ±0.13 P >0.05
Sulfoparin	25.0	89 ±1.45 P >0.05	4.5 ±0.31 P >0.05

Note: P >0.05 relative to control

No pathological changes in the content of urine sediment were detected.

The results obtained allow us to conclude that the drug does not have a toxic effect on kidney function. Thus, it was established that Sulfoparin does not have a toxic effect at all doses studied.

A general examination of the bodies of white rats after intragastric administration of Sulfoparin for 3 months showed the absence of macroscopically recognizable abnormalities compared to animals in the control group. All animals had a regular physique, a neat appearance, a shiny coat, no areas of baldness or ulcers were found. The visible mucous membranes are moist, pale pink, shiny and smooth in appearance. The mass of the internal organs of white rats during a macroscopic pathological examination during autopsy of animals after the end of the experiment showed that no changes were detected in the experimental animals. A light-optical microscopic examination of the internal organs and brain of all experimental groups of animals showed the absence of deviations.

Conclusions

1. With a long-term chronic intragastric administration, Sulfoparin does not affect the behavior and dynamics of body weight of animals.

2. The drug does not have a toxic effect on hematological parameters, kidney and liver function, as well as a negative effect on the morphology of organs and tissues.

Literature Index:

1. Guskova T.A. Toxicology of medicinal substances. Moscow, 2008. - pp. 27-30.
2. Inoyatova F.Kh., Kutlikova G.M., Milusheva R.Yu. and others. Some mechanisms of the hypocholesterolemic action of sulfaporin // Bulletin of TMA. - 2011. - No. 3. - P. 19-22.
3. Inoyatova F.Kh., Rashidova S.Sh., Kutlikova G.M. Correction of endothelial dysfunction with sulfaporin in rabbits with hypercholesterolemia // Intern . J. Of applied and fundamental research.- 2013.- No. 1.- P. 36-40.
4. Instructions for preclinical testing of the safety of pharmacological agents. - Tashkent - 2000
5. Kutlikova G.M. The effect of sulfaporin on the parameters of the nitric oxide system during experimental hypercholesterolemia // Postgraduate doctor. - 2012. - No. 4 (53). - P. 39-43.
6. Rashidova S.Sh., Milusheva R.Yu. Chitin and chitosan . Bombyx mori . Synthesis, properties and application. - Tashkent .- 2009.- P. 193-242.
7. Guide to experimental (preclinical) study of new pharmacological substances, methods of pharmacological preclinical research (edited by R.U. Khabriev). - Moscow. - 2005. P. 699-709.