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EVALUATION OF THE SKIN-RESORPTIVE EFFECT OF THE DRUG "SULFOPARINE"

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ABSTRACT: Research results. For the first time, a set of preclinical experimental studies of the new drug "Sulfoparin" developed at the Institute of Chemistry and Physics of Polymers of the Academy of Sciences of the Republic of Uzbekistan was carried out. It was revealed that Sulfoparin does not have a resorptive and irritating effect on the skin and mucous membranes of the eyes, does not cause sensitization of the guinea pigs organism. The drug does not have a cumulative effect. On an experimental model on white rats, it was established that Sulfoparin does not have a sensitizing effect.

Keywords: Sulfoparin preparation, chitosan, skin-resorptive and locally irritating effect, sensitizing effect.

The problem of creating domestic highly effective medicines is very relevant today. One of such drugs is Sulfoparin, which has anti-sclerotic properties [2,3,4]. 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]. Sulfoparin is a complex of chitosan with sulfo groups. The exceptional role of sulfo groups in the vital processes of a living organism is well known [6]. The latter opens up new opportunities for the correction of various pathological conditions of the body. Chitosan is a universal sorbent capable of binding a huge range of substances of organic and inorganic nature, which determines the widest possibilities of its application in human life [6]. Chitosan, soluble in acidic solutions, has wide possibilities for application in various sectors of the national economy and, in particular, in medicine. In the literature there are isolated data on the low toxicity of Sulfoparin and its use in medicine in an experiment on laboratory animals. However, there is no information on the nature and severity of the damaging effects of Sulfoparin on the body of experimental animals and an assessment of its safety.

The purpose of this work: studying skin-resorptive and sensitizing action of sulfated chitosan.

Material and research methods. The study of the skin-resorptive action of the drug "Sulfoparin" was carried out on 6 white rats weighing 140-160 g, which were fixed in special machines, the tails of the animals were immersed in test tubes with the test drug by 2/3 of the tail length [1,5,7]. The tubes were placed in a water bath with a temperature of 28-30 ° C. The exposure time was 4 hours. After the end of the experiment, the skin of the tails was washed with warm water and soap. The animals were observed for 3 weeks. The study of a single local irritant effect of the drug "Sulfoparin" was carried out on 6 white rats weighing 130-145 g, to which the drug in the form of a solution was applied to a shaved area

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of the skin measuring 2x2 cm. The animals were fixed for 4 hours. The skin reaction was recorded at the end of the exposure, 1 and 16 hours after the application. Studies of the multiple local irritant effect of the drug "Sulfoparin" on the skin were conducted on 10 white rats weighing 130-140 grams, to which the drug was applied to a 2x2 cm shaved skin area in the form of a solution once a day for 20 days. The animals were fixed for 4 hours. The skin reaction was recorded at the end of the exposure 1 and 16 hours after application. The digital material was processed by the method of variation statistics.

Results and their discussion. When applying the drug "Sulfoparin" to the skin, the goal was to find out whether the substance has a skin-resorptive, local-irritant effect in single and multiple exposures. The results of the assessment of the skin-resorptive effect of the drug "Sulfoparin" showed that during the observation period of 3 weeks, no symptoms of intoxication in the experimental animals and their death were detected. The animals remained active, willingly ate food, and responded adequately to external stimuli. Consequently, the drug "Sulfoparin" does not have a toxic skin-resorptive effect.

When applying the preparation "Sulfoparin" to the skin of white rats on the shaved area once or multiple times, it was found that the substance does not cause skin irritation, no symptoms of intoxication or death of animals were noted. Thus, it was determined that the preparation "Sulfoparin" does not have a local irritant effect.

To evaluate a single local irritant effect of the drug "Sulfoparin" on the mucous membranes of the eyes, 2 drops of "Sulfoparin" solution were introduced into the conjunctival sac of the left eye of 3 rabbits. The right eye served as a control. When applying, the inner corner of the conjunctival sac of the eye was pulled back, the drug was instilled, and then the lacrimal canal was pressed for 1 minute. Observation was carried out for 7 days. No irritation was detected during the entire observation period. The condition of the eyelids, sclera, cornea, and the width of the pupil of the experimental left eye did not differ from the right control eye. Therefore, the drug does not have an irritating effect on the mucous membranes of the eyes.

The study of the sensitizing properties of the drug Sulfoparin was carried out using a conjunctival test.The conjunctival test is a very sensitive test and in some cases even allows identifying the reaction of animals to an allergen with weak allergization and negative skin tests [5]. The experiment was conducted on 10 rabbits weighing 2.5-3.0 kg, in whose left eye 0.01 and 0.1% solution of the drug was instilled, in the second eye (control) 1 drop of physiological solution was introduced. The reaction was taken into account after 15 minutes (rapid reaction) and after 24-48 hours(delayed-type hypersensitivity) and were assessed using the following scale(in points) [7]:1-slight redness of the tear duct;2-redness of the lacrimal duct and sclera towards the cornea;3-redness of the entire conjunctiva and sclera. In addition, the degree of hyperemia, edema, and lacrimation were taken into account.

The results of observations showed that Sulfoparin does not cause even slight redness either after 15 minutes or after 24 and 48 hours. Based on this, it can be concluded that the drug Sulfoparin in 0.1% and 0.01% concentrations does not have an irritating effect.

The study of the effect of Sulfaporin on the development of anaphylactic shock was conducted on 30 guinea pigs weighing220±20 g [5]. 6 in each group (5 groups). Guinea pigs

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were administered Sulfoparin intramuscularly at doses of 1 mg/kg and 10 mg/kg. Sensitization was performed according to the following scheme: the first injection subcutaneously; two subsequent intramuscularly, every other day in the thigh. A resolving injection intravenously on the 21st day after the sensitizing injection (2 mg/kg and 20 μg/kg). After the resolving injection, observation was carried out for 30 minutes. Its severity was assessed in indices according to the W.O. Weigl scale. The severity of anaphylaxis after intravenous administration of Sulfoparin correlated with the results recorded in the group of guinea pigs prepared for shock (group 3). 100% mortality of animals in this group occurred as a result of subcutaneous injection of 0.1 ml of horse serum 3 weeks before the resolving dose of 0.3 ml (positive control, group 3). At the same time, the resolving dose of the test substance was administered to animals that, instead of sensitizing injections of the drug, were given the corresponding volume of physiological solution (negative control)(4-I and the 5th group) During the experimental period and after the introduction of the resolving dose in the experimental groups and the "negative" control groups, no changes in weight, temperature, or behavior were detected. The drug Sulfoparin in doses of 1 mg/kg and 10 mg/kg does not cause anaphylactic shock.

To study the effect of the drug Sulfaporin on the course of delayed-type hypersensitivity reactions were used 24 guinea pigs weighing 220±10 g, 6 in each group (group 4) [5]. Animals of the experimental groups were sensitized by a single injection into the pads of 4 paws of the drug mixed with complete Freud's adjuvant (CFA) in a volume of 0.5 ml in a ratio of 1:1. The drug was administered in doses of 1 and 10 μg/kg (groups 1 and 2). Control animals were administered CFA in a similar manner (groups 3 and 4). On the 21st day of the experiment, the animals were intradermally injected with a resolving dose of the drug (2 and 20 μg/kg) in a volume of0.05ml. Skin reactions were determined after 1, 6, 24 and 48 hours. Skin reactions were visually assessed in points according to the following scheme: 0 - no visible reaction;1 - pale pink erythema over the entire area or its periphery, 2 - bright pink erythema over the entire area or its periphery;3 - red erythema throughout the area;4 - infiltration and swelling of the skin;5 - erythema, severe infiltration, focal ulcerations.

Sulfoparine at doses of 1 and 10 mg/kg did not cause any reactions on the clipped area of the skin surface of guinea pigs, which allows us to conclude that Sulfoparine does not cause delayed-type hypersensitivity.

To investigate the effect of Sulfaporin in topical applications, the experiments were conducted on 10 guinea pigs weighing 220±10 g, 5 in each group. Three drops of a 0.1% (Group 1) and 1% (Group 2) solution of the preparation prepared in physiological saline were applied to a trimmed area of the skin on the lateral surface closer to the middle of the body. The preparation was applied 5 times a week for 4 weeks. The skin reaction was taken into account daily according to the skin test scale given above. This experiment allows us to identify the risk of developing non-allergic contact dermatitis depending on the dose of the preparation. The sensitizing effect of Sulfoparin was studied by 20 repeated applications. The first testing was conducted after 10 applications and if the result was negative, the number of applications was increased to 20. The preparation Sulfoparin in 0.1% and 1% concentrations did not cause any reactions on the trimmed area of the skin surface of the guinea pigs throughout the experiment (20 applications). Thus, it can be concluded that the substance does not have the ability to cause non-allergic contact dermatitis.

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CONCLUSIONS:

1.The drug Sulfoparin has no skin-resorptive or a local irritant effect.

2.The drug Sulfoparin does not have an allergenic effect.

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