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Study of the Skin-Resorptive Properties of Chitosan

Azim Kenjayevich Baykulov

Department of Pharmaceutical and Toxicological Chemistry Samakand State Medical University, Samakand, Uzbekistan

ABSTRACT

The Aim of the Work: study of the skin-resorptive and sensitizing effects of various chitosan de-rivatives.

Material and Methods: To study the skin-resorptive and allegnizing effects of chitosan sulfate and chitosan with furacilin according to the recommendations for the study of the toxicological proper-ties of drugs.

Results: For the first time, a complex of preclinical experimental studies of various chitosan deriva-tives developed at the nstitute of Polymer Chemistry and Physics of the Academy of Sciences of the Republic of Uzbekistan was carried out. It was revealed that they do not have a resorptive and irritating effect on the skin and mucous membranes of the eyes, does not cause sensitization of the body of guinea pigs. The drugs do not have a cumulative effect and sensitizing effect.

Conclusions:

- Chitosan sulfate and chitosan preparations with furacilin do not have a skin-resorptive effect and a locally irritating effect.
- Chitosan sulfate and chitosan preparations with furacilin do not have an allergenic effect.

Corresponding author

Azim Kenjayevich Baykulov, Department of Pharmaceutical and Toxicological Chemistry Sa-makand State Medical University, Samakand, Uzbekistan.

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Introduction

The problem of creating domestic highly effective medicines is very relevant today. One of the objects for obtaining dosage forms are biopolymers chitin and chitosan (ChS) obtained from Bombyx mori [1]. By changing the functional groups or including additionally biologically active compounds, various dosage forms with certain properties can be created [2]. Thus, at the Institute of Polymer Chemistry and Physics of the Academy of Sciences of the Republic of Uzbekistan, including a sulfogroup in the chitosan molecule, which plays an exceptional role in the vital processes of a living organism, the drug chitosan sulfate has been developed, which has anti-sclerotic and hypocoagulant properties [1, 3-5]. One of the modern approaches to increasing the regenerative potential of the skin and mucous membranes is the combination of antiseptics with polymers with biological activity. These medicines have a number of advantages over traditionally used antibacterial drugs. By providing a prolonged effect, they allow long-term maintenance of therapeutic concentration on the wound surface, which reduces the possibility of resistance and sensitization [2, 6]. Therefore, the staff of the IPChaPh of the Academy of Sciences of the Repub-lic of Uzbekistan created complex preparations of ChS with furacilin, which has a regenerative ef-fect [1, 7-9]. In this work, Bombyx mori chitosan-based gels were used, cross-linked by glutaralde-hyde (GA) and filled with biologically active elements. Furacilin was used as biologically active elements, an aqueous solution of which was prepared for experiments by dissolving furacilin pow-der [1, 10]. The gelation process is accompanied by the formation of a mesh supramolecular struc-ture, which, depending on the conformational state and the laying of chains, is characterized by different porosity. The results of lyophilic drying of the swollen sample showed that the cross-linked chitosan contains about 0.5% furacilin in its composition. The latter opens up new opportu-nities 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 de-termines the widest possibilities of its application in human life [2, 6, 10, 11]. It, soluble in acidic solutions, has wide possibilities for use in various branches of national economy and, in particular, in medicine. There are isolated reports in the literature about the low toxicity of chitosan and its use in medicine.

The Aim of this Work

study of the skin-resorptive and sensitizing effects of various chitosan derivatives.

Material and Methods of Research

The study of the skin-resorptive effect of the preparation's chitosan sulfate and chitosan with fura-cilin was carried out on 12 white rats with a body weight of 140-160 g, which were fixed in special machines, the tails of the animals were immersed in test tubes with the studied drugs for 2/3 of the tail length [12-14]. The samples were placed in a water bath with a temperature of 28-30 ° C. The exposure time is 4 hours. After the end of the experiment, the skin of the tails was washed with warm water and soap. The animals

were monitored for 3 weeks. Studies of a single local irritant effect of these drugs were carried out on 12 white rats with a body weight of 130-145g, which were applied to a 2x2cm-sized area of the skin in the form of a solution. The animals were fixed for 4 hours. The skin reaction was recorded at the end of the exposure 1 and 16 hours after application. Studies of multiple local irritant effects of drugs on the skin were carried out on 20 white rats with a body weight of 130-140g, which were applied to a 2x2cm-sized area of the skin in the form of a solution daily 1 time 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 pro-cessed by the method of variational statistics.

Results and their Discussion

When applying chitosan sulfate and chitosan with furacilin to the skin, the goal was to find out whether these substances have a skin-resorptive, locally irritating effect with single and multiple exposures. The results of the evaluation of the skin-resorptive effect of the drugs showed that dur-ing the observation period of 3 weeks, symptoms of intoxication in experimental animals and their death were not detected. The animals remained active, willingly ate food, adequately reacted to ex-ternal stimuli. Consequently, the preparations chitosan sulfate and chitosan with furacilin do not have a toxic skin-resorptive effect.

With single and multiple application of chitosan sulfate or chitosan with furacilin to the skin of white rats on the exposed area, it was found that the tested substances did not cause irritation of the skin, symptoms of intoxication and death of animals were not noted. Thus, it was determined that these drugs do not have a locally irritating effect.

To assess the single local irritant effect of the drugs chitosan sulfate and chitosan with furacilin on the mucous membranes of the eyes, 2 drops of a solution of these drugs were once injected into the conjunctival sac of the left eye of 12 rabbits. The right eye served as a control. During insertion, the inner corner of the conjunctival sac of the eye was pulled back, preparations were instilled, and then the lacrimal-nasal canal was pressed for 1 minute.

The observation was carried out for 7 days. No irritation was detected during the entire observation period when using both drugs. The condition of the eyelids, sclera, cornea and pupil width of the experimental left eye did not differ from the right control. Consequently, the drugs do not have an irritating effect on the mucous membranes of the eyes.

The study of the sensitizing properties of the drugs was carried out by a conjunctival test. The con-junctival test is a very sensitive test and, in some cases, even makes it possible to detect the reaction of animals to an allergen with weak allergization and negative skin tests [13, 14]. Experiments were conducted on 20 rabbits weighing 2.5-3.0 kg, in which 0.01 and 0.1% solution of chitosan sulfate or chitosan with furacilin was instilled into the left eye, 1 drop of saline solution was injected into the second eye (control). The reaction was taken into account after 15 minutes (rapid reaction) and after 24-48 hours (delayed hypersensitivity) and evaluated on the following scale (in points): 1 - slight redness of the lacrimal duct; 2 - redness of the lacrimal duct and sclera in the direction of the cornea; 3 - redness of the entire conjunctiva and sclera. In addition, the degree of hyperemia, swell-ing, lacrimation was taken into account.

The results of observations showed that the preparations chitosan sulfate and chitosan with furacil-in did not cause even slight redness after 15 minutes, 24 and 48 hours. Based on this, it can be con-cluded that the studied drugs in 0.1% and 0.01% concentrations do not have an irritating effect.

The study of the effect of these drugs on the development of anaphylactic shock was carried out on 54 guinea pigs weighing 220±20g [13, 14]. 6 in each group (9 groups). The guinea pigs of the 1st and 2nd groups were injected with chitosan sulfate, the 3rd and 4th groups - chitosan with fura-cilin intramuscularly in doses of 1 mg/kg and 10 mg/kg. Sensitization was carried out according to the following scheme: the first injection subcutaneously; the next two intramuscularly, every other day in the thigh area. Permissive injection intravenously on the 21-st day after sensitizing injection (2mcg/kg and 20mcg/kg). After the permissive injection, the observation was carried out for 30 minutes. Its severity was assessed in indices on the W.O. Weigll scale. The severity of anaphylaxis after intravenous administration of drugs correlated with the results recorded in the group of guinea pigs prepared for shock (group 5). 100% death of animals in this group occurred as a result of sub-cutaneous administration of 0.1 ml of horse serum 3 weeks before the permissive dose of 0.3 ml (positive control, group 5). At the same time, a permissive dose of the test substance was adminis-tered to animals who, instead of sensitizing injections of drugs, were injected with an appropriate volume of saline solution negative control (groups 6 and 7 for chitosan sulfate and groups 8 and 9 for chitosan with furacilin). During the experimental period and after the introduction of the per-missive dose, no changes in weight, temperature, and behavior were detected in the experimental groups and groups of "negative" control. Preparations of chitosan sulfate and chitosan with furacil-in in doses of 1 mg / kg and 10 mg / kg do not cause anaphylactic shock.

To study the effect of sulfaporin and chitosan with furaciline on the course of delayed-type hyper-sensitivity reactions, 48 guinea pigs weighing 220±10 g, 6 in each group (group 8) were used [13, 14]. Animals of the 1st and 2nd experimental groups were sensitized once by the introduction of chitosan sulfate into the pads of 4 paws, of the 3rd and 4th groups - chitosan with furacilin mixed with a full Freud adjuvant (PFA) in a volume of 0.5ml in a ratio of 1:1. The drug was injected into doses of 1 (1st and 3rd groups) and 10 mcg / kg (2nd and 4th groups). Control animals were inject-ed with PFA in a similar way (groups 5 and 6 for chitosan sulfate, groups 7 and 8 for chitosan with furacilin). On the 21st day of the experiment, animals were intradermally injected with a permissive dose of drugs (2 and 20 mcg/kg) in the volume of 0.05ml on the trimmed area of the skin of the back. After 1, 6, 24 and 48 hours, skin reactions were determined. The skin reaction was visually assessed in points according to the following scheme: 0 - there is no visible reaction; 1- pale pink erythema throughout the site or its periphery, 2 - bright pink erythema throughout the site or its pe-riphery; 3- red erythema throughout the site; 4 - infiltration and swelling of the skin; 5 - erythema, pronounced infiltration, focal ulceration. The studied drugs in doses of 1 and 10 mg/kg did not cause any reactions on the trimmed area of the skin surface of guinea pigs, which will allow us to conclude that chitosan sulfate and chitosan with furacilin do not cause delayed hypersensitivity.

To study the effect of sulfaporin and chitosan with furacilin on skin applications, experiments were conducted on 20 guinea pigs weighing 220±10 g, 5 in each group. 3 drops of 0.1 and 1% (groups 1 and 2) chitosan sulfate solution and 0.1 and 1% (groups 3 and 4)

chitosan solution with furacilin, prepared in saline solution, were applied to the trimmed skin area of the lateral surface closer to the middle of the trunk. The drugs were applied for 4 weeks 5 times a week. The skin reaction was tak-en into account daily according to the scale of skin tests given above. This experiment allows us to identify the danger of developing non-allergic contact dermatitis depending on the dose of drugs. The study of the sensitizing effect of chitosan sulfate and chitosan with furacilin was carried out by 20 repeated applications. The first test was carried out after 10 applications and with a negative re-sult, the number of applications was brought to 20. Preparations in 0.1% and 1% concentrations did not cause any reactions on the trimmed area of the skin surface of guinea pigs throughout the ex-periment (20 applications). Thus, it can be concluded that the substances used do not have the abil-ity to cause non-allergic contact dermatitis.

Conclusions

- The preparations chitosan sulfate and chitosan with furacilin do not have a skin-resorptive effect and a locally irritating effect.
- The preparations chitosan sulfate and chitosan with furacilin do not have an aller-genic ef-fect.

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