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Pharmacological effect of Trinatrium salt of Glycyrrhizic acid

Abstract: Trinatrium salt of glycyrrhizic acid (Glycytrinate) with strong anti-ulcerous activity combined with anti-inflammatory effect was synthesized on the basis of glycyrrhizic acid. According to the parameters of acute toxicity in experiments on white mice and rats with per oral administration Glycytrinate was included to the group of little toxic substances. And according to the assessment of anti-ulcerous activity on the models of rats' gastric mucous membrane destruction caused by indo metasin, ortophen, and reserpin glycytrinate has an expressed antiulcer effect. The mechanism of glycytrinate's antiulcer effect is linked with its antioxidant property and suppression of the secretory function of gastric glands.

Keywords: extract Radix glycyrrhizae, glycyrrhizic acid, antiulcer activity.

The search of new sources of very active medical agent based on local raw materials is a topical problem of the modern science.

It is known that, Radix glycyrrhizae is widely used in various fields of national economy. Its basic component is glycyrrhizic acid. The presence of anti-inflammatory activity, low toxicity, and absence of severe side-effect make the new synthetic derivatives of glycyrrhizic acid compounds perspective for medicine [6].

Glycyrrhizic acid (GA) and its derivatives have strong antiulcer, anti-inflammatory, antiviral, antitumor and other pharmacological activity. The modern antiulcer agents in the modern time do not completely meet the requirements of clinical practitioners, as these agents often cause side-effects, and sometimes even severe complications. Some of these agents have insufficient therapeutic effect (5). While continuing the search of new biological active derivatives of glycyrrhizic acid we studied its trinatrium salt.

The objective. To study antiulcer activity of glycytrinate on an experimental model of ulcer caused by 24-hour immobilization of animals and to reveal the mechanism of antiulcer activity.

Materials and methods.

Experimental model of ulcer caused by 24-hour immobilization of animals was performed on rats with body mass equal to 160-200g [1]. Animals were divided to three groups, with 6 rats in every group. Glycytrinate 100mg/kg was introduced per orally in experimental groups every day for a week prior to stress. And in the control group the same volume of distillated water was given to the rats. The effect of the agent was compared with cymetidine, which was introduced in the dose 400mg/kg. at the seventh day all animals were fixed on a desk belly up. In 24 hours all animals were decapitated, gastric mucous membrane was examined macroscopically and antiulcer effect of the agents was evaluated. We studied the impact of glycytrinate on secretory function of stomach and acidity of gastric juice on rats. The agent was introduced per orally for a week; in 20 minutes after the last administration of the agent the ligature of pylorus was performed under narcosis. After that in 2-3 hours the animals were killed with further measurement of the volume of gastric juice and titration with 0.1 H of NaOH solution till appearance of pink color. In blood serum of rats we determined the activity of super oxide dismutase (SOD) [4] and catalase [7].

The obtained results were processed with the help of R. V. Strelkov s variation statistic method [9].

The results of the research. The performed experiments showed that, in the control group of rats the average number of ulcers was 5.66±0.54, and the average summary square area of ulcers was equal to 6.33+0.54 mm^2. Under the influence of glycytrinate the average number ofulcers and average summary square area of ulcers was diminished to 2.33±0.18 and 2.0±0.18 (58% and 68%). Under the influence of cymetidine the average number ofulcers and average summary square area diminished to *4.66+036* and 3.33±0.54 (18% and 48%), respectively, in comparison with the control group.

It is known that, an important role in the development of gastric and duodenal ulcer is played by hyper secretion of hydrochloric acid,

decrease of protective functions of gastric and duodenal mucous membrane, and its blood supply.

For the detection of the mechanism of antiulcer effect we studied the influence ofglycytrinate on secretory function of stomach and acidity of gastric juice on rats. Results of the experiment showed that, in the control group of rats the volume of gastric juice was 2.05 ml, pH = 1.33, total acidity 0.5 ml, titrated unit was 100 TU. Under the influence of the agent the volume of gastric juice decreased to 39%, pH = 3.25, total acidity 0.37, titrated unit 74 TU.

Development of ulcerous process proceeded together with background decrease of SOD antioxidant system enzyme activity [1.07 (1.0±1.14)] and catalase [1.41 (0.94±1.88)]. Glycytrinate
3.3 folds increased the activity of catalase in comparison with the control [4.76 (1.96±7.6)], and activity of super oxide dismutase [1.24 (1.14±1.34)J.

Thus, under the influence of the agent pH shifted to alkali side
1.4 folds; total acidity decreased to 26%. The agent decreased the speed of mucocytes exfoliation, and by these means increased formation of mucin and bicarbonates, which neutralize hydrogen ion, increasing mucous viscosity in stomach. Development of ulcerous process in animals was accompanied by significant decrease of enzyme activity of antioxidant protection. So we can state that, expressed antiulcer effect of glycytrinate is conditioned by its antioxidant properties.

We performed clinical testing of glycytrinate on patients with gastric and duodenal ulcers in the gastroenterology unit of Tashkent Medical Academy.

It was revealed that glycytrinate has antiulcer and anti-inflammatory effect. It is sufficiently effective and has no side-effects. Its efficiency and tolerance is similar to the agent for comparison De-nol.

Earlier we determined that, trinatrium salt of glycyrrhizic acid — “Glycytrinate” was little toxic, even in doses over 40005000 mg/kg, in case of per oral administration on rats it had no toxic effect, as it did not cause lethal outcome [3]. According to antiulcer activity on the models of rats’ gastric mucous membrane destruction caused by indometacin, ortophen, and reserpin, it was determined that, glycytrinate had expressed antiulcer effect [2].

On formalin model the agent was characterized by anti-inflammatory effect [8]. In experiments on various animals the agent doses with antiulcer effect did not have a significant influence on CNS, vegetative innervations, breathing, and arterial pressure. The study of chronic toxicity revealed that the agent had no local irritating, accumulative, or embryonic toxic effect [3].

Thus, it was determined that “Glycytrinate” agent was little toxic and had expressed antiulcer activity. The mechanism of antiulcer effect of glycytrinate is linked with its antioxidant property and suppression of the secretory function of gastric glands.

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