Published: May 10, 2023 | Pages: 01-05

DETERMINATION OF ACUTE TOXICITY D-38, KS-39 AND R-37 POLYSACCHARIDES

Raimova G.M

Institute Of Biophysics And Biochemistry At The National University Of Uzbekistan Named After Mirzo Ulugbek, Tashkent, Uzbekistan

Ortikov M.M

Institute Of Biophysics And Biochemistry At The National University Of Uzbekistan Named After Mirzo Ulugbek, Tashkent, Uzbekistan

Nasirov K.E

Institute Of Biophysics And Biochemistry At The National University Of Uzbekistan Named After Mirzo Ulugbek, Tashkent, Uzbekistan

Khoshimov N.N

Institute Of Biophysics And Biochemistry At The National University Of Uzbekistan Named After Mirzo Ulugbek, Tashkent, Uzbekistan

Madaminova G.A

National University Of Uzbekistan, Tashkent, Uzbekistan

Abduraxmanov J.A

Institute Of Bioorganic Chemistry Named After Academician A.S.Sadikov, Tashkent, Uzbekistan.

Shodmonova D.Sh

University Of Science And Technologies, Tashkent, Uzbekistan

ABSTRACT: In experiments the acute toxicity of D-38, KS-39 and P-37 sulfated polysaccharides with anticoagulant and antiaggregant properties was studied. From the obtained results, it was known that when D-38, KS-39 and P-37 polysaccharides were injected into the abdomen of animals at doses of 1000 and 2000, no death of animals was recorded during the entire experiment. At 4000 doses, death was observed in 1 out of 6 animals, i.e. 16.6% of animals. 50% mortality was observed in all mice when 5000 mg/kg of the above polysaccharides were administered intraperitoneally.

KEYWORDS: polysaccharides, anticoagulant, thrombin time.

Published: May 10, 2023 | Pages: 01-05

INTRODUCTION

The pathogenesis of one of the main clinical forms of coronary heart disease is associated with a violation of the functional activity of platelets, which determines the relevance of studying the various mechanisms of their aggregation. Regulators of the functional state of platelets are adenosine diphosphate (ADP) and adrenaline, the effects of which are realized through specific receptors on the platelet membrane [1-3].

In the study of platelet aggregation induced by ADP, adrenaline in patients with various forms of coronary heart disease, it was found that in the blood plasma of patients with stable angina, the degree of adrenaline-induced aggregation exceeds that in patients with unstable angina and healthy people. In patients with stable and unstable angina, there were no differences in the maximum degree of platelet aggregation induced by ADP compared with healthy people [4-6].

Cardiovascular diseases are caused by a violation of the hemostasis system. Anticoagulant and antiaggregant drugs are widely used to influence and control the hemostasis process [7,8]. At the same time, it is necessary to study the acute toxicity of drugs with anticoagulant and antiaggregant properties [9]. The acute toxicity of D-38, KS-39 and P-37 sulfated polysaccharides with anticoagulant and antiaggregant properties was studied.

MATERIAL AND METHODS

In the experiments, general effect and acute toxicity of D-38, KS-39 and P-37 polysaccharides were determined in purebred, white mice by Litchfield and Wilcoxon method by intraperitoneal injection. Six animals of both sexes, their body weight 25±2.0 g, were included in the research groups. The experiments were carried out on healthy, sexed mice that had passed the quarantine period of at least 10-14 days in vivarium conditions. The drugs under study were injected into the stomach of mice through a special probe in doses ranging from 1000 to 8000 mg/kg. Each dose of polysaccharides studied in the experiment was studied in 6 animals of two different sexes. On the first day of the experiment, every hour, the general condition of the animals of the research and control groups, all possible conditions were observed in the laboratory. From the first day to the seventh week, in vivarium conditions, the general condition of the animals, activity, fur coat, condition of the skin and tail, behavior, rate and depth of respiration, amount and consistency of feces (soft or hard), urination rate, body changes in weight and other indicators were checked.

Published: May 10, 2023 | Pages: 01-05

The experiment was carried out in the conditions where the animals were fed a regular diet, water and food were not limited. At the end of the experiment, the average-lethal dose (LD50) of the investigated drugs and, accordingly, the toxicity class are determined.

RESEARCH RESULTS

In the experiments, D-38, KS-39 and P-37 polysaccharides were administered intraperitoneally to animals (mice) at a dose of 1000 mg/kg each. In the experiments, when 1000 mg/kg of D-38, KS-39 and P-37 polysaccharides were administered, tachycardia was observed after 10-15 minutes, tremors after 20 minutes, and relaxation after 60 minutes. No death was recorded when the animals were observed for 14 days. In our next experiment, when D-38, KS-39 and P-37 polysaccharides were administered at a dose of 2000 mg/kg, tachycardia was observed in animals after 5 minutes, restlessness increased after 10 minutes, their activity was normalized after 2 hours, and no death was observed for 14 days.

In the next experiment, when 4000 mg/kg of D-38, K-39 and P-37 polysaccharides were administered, tachycardia was observed in animals after 5 minutes, their general condition was moderately good, and 1 case of death was recorded in 8 days of the experiment. In a further experiment, when D-38, KS-39, and P-37 polysaccharides were injected intraperitoneally in both sexes at a dose of 5000 mg/kg, after 15-30 minutes, all male mice showed tremors, decreased activity, and respiratory failure, and after 1 hour, a prone position after emergence, mortality was observed in 17-23 hours, and in female mice, decreased activity, respiratory failure after 1 hour, flexcity state, 5 out of 6 died after 19-26 hours. 8000 mg/kg of D-38, KS-39 and P-37 polysaccharides showed tachycardia in animals after 5 minutes, their general condition worsened and 100% mortality was recorded.

Finally, the results of the study of the acute toxicity of D-38, KS-39 and P-37 polysaccharides are presented in Table 1.

Table 1. Results of acute toxicity of D-38, KS-39 and P-37 polysaccharides when administered intraperitoneally to animals (M±m; n=5)

The types of animal. Method of introduction into the body	Sex	Doses (mg/kg)	Number of animals in the experimental group/number of dead animals (units)	LD_{16} (–m+m mg/kg)	LD_{50} (–m+m mg/kg)	LD_{84} (–m+m mg/kg)
Mice. By oral	Ma	1000	6/0	4000	5000	8000

Published: May 10, 2023 | Pages: 01-05

		2000	6/0			
		4000	6/1			
		5000	6/3			
		7000	6/5			
		8000	6/6			

CONCLUSION

From the obtained results, it was known that when D-38, KS-39 and P-37 polysaccharides were injected into the abdomen of animals at doses of 1000 and 2000, no death of animals was recorded during the entire experiment. At 4000 doses, death was observed in 1 out of 6 animals, i.e. 16.6% of animals. 50% mortality was observed in all mice when 5000 mg/kg of the above polysaccharides were administered intraperitoneally. This dose killed 50% of animals of both sexes. When administered to animals at a dose of 7000 mg/kg, in the first 30 minutes, all male mice were found to have a whole body dysfunction. On average, 5 out of 6 males died after 12.5 hours, and 83.7% of females died after 16.5 hours. 100% mortality was observed when polysaccharides were administered at a dose of 8000 mg/kg. The results of the study of the acute toxicity of D-38, KS-39 and P-37 polysaccharides showed that this drug belongs to class V compounds of low toxicity.

REFERENCES

1. Nozim N. Khoshimov, Guli M. Raimova, Kabul E. Nasirov, Zulayho A. Mamatova, Nodira I. Mamadaliyeva, Abbaskhan S. Turaev. The effect of Sulphated cellulose on System of Haemostasis. Research Journal of Pharmacy and Technology. 2021; 14(6):3283-9. doi: 10.52711/0974-360X.2021.00571
2. Guli M. Raimova, Nozim N. Khoshimov, Kabil E. Nasirov, Abbaskhan S. Turaev, Malokhat E. Savutova. Anti-thrombotic action of sulfated polysaccharides on thrombosis caused by thromboplastin. Research Journal of Pharmacy and Technology. 2021; 14(11):6085-8. doi: 10.52711/0974-360X.2021.01057.
3. Antithrombotic Trialists' Collaboration. Collaborative meta–analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients / Antithrombotic Trialists' Collaboration // BMJ. – 2002. – Vol. 324. – P. 71–86
4. Nozim N. Khoshimov, Alisher A. Mukhtorov, Kabil E. Nasirov, Rakhmatillo N. Rakhimov, & Rahmatjon R. Mamadaminov. (2022). Effects of Polyphenols on Changes in the Transport

Published: May 10, 2023 | Pages: 01-05

of Ca2+ NMDA-receptors Under the Influence of L-glutamate against the Background of Alzheimer's Disease. Journal of Pharmaceutical Negative Results, 1322–1332. (Q4) CiteScore (1). Retrieved from https://www.pnrjournal.com/index.php/home/article/view/1203

5. Alisher A. Mukhtorov, Rahmatjon R. Mamadaminov, Nozim N. Khoshimov, Kabil E. Nasirov, Rakhmatilla N. Rakhimov, Lutpillaev X. Gaybullo. Regulation of transport of Ca2+ NMDA-receptors in rat brain synaptosomes under the influence of polyphenols. European Journal of Medicine. 2022. 10(1): 3-11.
6. Khoshimov N.N., Ortikov M.M., Dedaboev J.I., Nasirov K.E., Ashirmatova N.M., Khasanova Kh.I., Eshbakova K.A. Influence of emodin on plasma hemostasis. Инфекция иммунитет и фармакология. Спец. Вып. Ташкент. №3.2022.С.275-283.
7. Khoshimov N.N., Mamatova M.Sh., Ortiqov M. M., Mukhtorov A.A., Mamadaminov R.R., Eshonov M.A. Changes in thrombin time in the blood plasma of rats under the influence of Acuzun. XXV Anniversary International Biomedical Conference of Young Researchers «Fundamental Science and Clinical Medicine - Homo and Health». St. Petersburg State University. 2022. P.408-409.
8. Khoshimov N.N., Mamatova M.Sh., Ortiqov M. M., Eshonov M.A. Study of the effect of alkaloid acuzun on the platelet aggregation of the blood plasma of patients with coronary heart disease. XXV Anniversary International Biomedical Conference of Young Researchers «Fundamental Science and Clinical Medicine - Homo and Health». St. Petersburg State University. 2022. P.412-413.
9. Ortiqov M. M., Khoshimov N.N., Rakhmonova N. Sh., Musaeva M.K., Nasirov K.E. Study of the influence of biologically active compounds on the coagulation of the blood plasma of rats with the help of venom vipera lebetina. XXV Anniversary International Biomedical Conference of Young Researchers «Fundamental Science and Clinical