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DETERMINATION OF ACUTE TOXICITY AND INFLAMMATORY ACTIVITY OF 1,3,4-THIADIAZOLE

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Abstract: Objective: The aim of this study was to determine the acute toxicity and anti-inflammatory activity of new 1,3,4-thiadiazole derivatives to assess their potential as pharmacological agents. Methods: Acute toxicity was evaluated in outbred white male mice using the fixed-dose procedure according to OECD Guideline No. 420. The substances were administered orally at a dose of 2000 mg/kg. The anti-inflammatory potential was assessed using a carrageenan-induced paw edema model in rats. The animals were treated with the test substances at doses of 50 mg/kg and 100 mg/kg prior to carrageenan injection. Results: In the acute toxicity test, no mortality or significant changes in body weight were observed. The average lethal dose (LD50) was determined to be greater than 2000 mg/kg, classifying the substances as Class V (practically non-toxic) according to the OECD classification. In the anti-inflammatory assay, the derivatives demonstrated significant activity. Specifically, substances administered at a dose of 50 mg/kg showed the most pronounced inhibition of paw edema compared to the control group. Conclusion: The studied 1,3,4-thiadiazole derivatives exhibit a high safety profile with low toxicity and possess significant anti-inflammatory properties, particularly at lower doses, suggesting their potential for further pharmaceutical development.

Keywords: 1,3,4-thiadiazole derivatives, acute toxicity, anti-inflammatory activity, carrageenan-induced edema, LD50, OECD guidelines.

Relevance. Chemical, physical, and pharmacokinetic properties make it possible to recommend the 1,3,4-thiadiazole ring in the structure of thiadiazole derivatives as a target for the development of new drugs, which contributes to their wide study for use in medicine.
Objective: To determine the toxicity and inflammatory activity of 1,3,4-thiadiazole derivatives.

1) 2-2'((1,3,4-thiadiazol-2,5 diyl), bis-(sulfanediyl)) di (acetohydrazine);

2) diethyl-2-2'((1,3,4-thiadiazol-2,5 diyl), bis-(sulfanediyl)) diacetate;

3) 2-amino-5-ethyl-(1,3,4-thiadiazole); 4) 2-amino-5(4-tert-butyl - (1,3,4-thiadiazole);

Materials and methods: For toxicity determination. The experiments used a test to assess the acute toxicity of chemicals administered orally at a strict fixed dose, " recommended by the OECD (2002). Test No. 420. Acute Oral Toxicity - Fixed Dose Procedure (OECD Guidelines for the Testing of Chemicals, Section 4, OECD Publishing, Paris, https://doi.org/10.1787/9789264070943-enra). In this test, this is done by gradually administering a strictly defined dose of 2000 mg/kg to a group of animals of the same sex. The determination of the acute toxicity of 1,3,4-thiadiazole derivatives was studied. Experiments were performed on outbred white male laboratory mice with a body weight of 22±2.0 g. 5 heads of mice were taken for each group. Pharmacological experiments were performed on healthy

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individuals who had passed the quarantine period of 10-14 days. The experiment was carried out in two stages. At stage I: 2, mice in the group were injected into the stomach with 2000 mg/kg of each substance received once, in a volume of 0.4 ml using a special probe, and when they were observed for 2-3 days, no fatal outcome was recorded. At the second stage of the experiment, the remaining 3 heads of this group of animals were administered at a dose of 2000 mg/kg of each substance. At the same time, the animals in the control group were also given equal amounts of distilled water. On the first day of phases I and II of experiments, the general condition of the studied animals was monitored every hour, as well as possible cases of tremor and death. Every day for up to 2 weeks, the general condition of animals in all groups, motor activity, skin and hair condition, respiratory rate and depth, urinary excretion, changes in body weight, and other indicators were checked. Experimental animals were kept in a normal feeding regime, without restrictions on water and food. According to the results of the experiment, the average lethal dose of the substance - LD50, and the toxicity class were determined [1,2]. The obtained data were calculated on the basis of the arithmetic mean (M), arithmetic mean error (m), and subjected to statistical processing. A significance level of $p<0.05$ was recognized as a statistically significant change. Substance toxicity classes according to the modified classification Organization for Economic Cooperation and Development (OECD)

Results: 15 minutes after the introduction of the chemical at a dose of 2000 mg/kg, the animals showed increased respiration, concentration in one place, and squinting and narrowing of the eyes. After this process took 20-25 minutes, the mice started to return to normal. During the entire experiment, animals of all groups treated with a chemical substance at a dose of 2000 mg/kg did not have a fatal outcome (5/0). When comparing animals in the experimental groups with the control group at the administered dose, there was no decrease in body weight of mice during the experiment (days 7 and 14) ($p>0.05$). It was found that the average lethal dose of the substance, with a single injection into the stomach of mice at a dose of 2000 mg/kg is LD50>2000 mg/kg.

Conclusions: The results obtained with a single injection of the substance into the stomach of mice at a dose of 2000 mg/kg were classified by the OECD, and it was found that these samples belong to the almost non-toxic V-class of chemicals (LD50> 2000 mg/kg).

Material and methods. To determine the anti-inflammatory potential *in vivo*, before starting experimental work, animals were kept indoors for 10 days under quarantine conditions for acclimatization. In the animal room, all standard requirements were met, such as the ambient temperature (25±3°C), the 12-hour dark/light cycle, and the humidity range (30-70%), which were necessary for the survival of rats. The rats were fed regular food and given unlimited amounts of water. After acclimatization, the rats were randomly assigned to six rats per group/cage.

A model of acute inflammation, carrageenan-induced paw edema in rats. To assess the anti-inflammatory potential of 1,3,4-thiadiazole derivatives at doses of 50/100 mg/kg, animals were divided into 2 groups: the normal control group (NC) (received only food, drink and normal saline solution orally), the 2nd group received chemicals (50/100 mg/kg) and food, drink, For the study of acute inflammation A carrageenan-induced paw edema model was performed carrageenan using the described method [3]. A swab containing 0.05 ml of 1% carrageenan sodium salt was inserted into the right hind leg of each rat under the plantar aponeurosis carrageenan. The experimental group of rats was orally administered the test drugs 1 hour before

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the injection of carrageenan. At the same time, the control group was given 5 ml/kg of saline solution. The experimental group received 1,3,4-thiadiazole derivatives in doses of 50/100 mg/kg. The percentage of inhibition was calculated by taking the values in the control group as 0% of inhibition.

Research results. The effect of substances at doses of 50 and 100 mg /kg on induced carrageenan paw edema is presented in Table 2. In the study, the maximum reduction in paw diameter was observed 3 hours after carrageenan injection. During the fourth and fifth hours of follow-up (h), rats treated with the test substances showed more significant inhibition compared to the normal control. Substances 2-2'((1,3,4-thiadiazol-2,5 diyl), bis-(sulfanediyl)) di (acetohydrazine) and diethyl-2-2'((1,3,4-thiadiazol-2,5 diyl), bis - (sulfanediyl)) diacetate at a dose of 50 mg/kg significantly reduced carrageenan-induced inflammation by reducing the paw diameter of rats after 24 hours. [4,5]

Conclusion: substances 2-2'((1,3,4-thiadiazol-2,5 diyl), bis-(sulfanediyl)) di (acetohydrazine) and diethyl-2-2'((1,3,4-thiadiazol-2,5 diyl), bis-(sulfanediyl)) diacetate at a dose of 50 mg / kg showed the most pronounced anti-inflammatory activity.

References:

1. OECD (2001) Guideline for testing of chemicals. Acute Oral Toxicity – Fixed Dose Procedure No 420.

2. Guidelines for conducting preclinical studies of medicinal products. Part One / Edited by A. N. Mironov, Moscow: Grif and K Publ., 2012, 944 p.

3. Preclinical studies of medicines: rec. Ed. by O. V. Stefanov, Moscow: Avicenna Publ., 2001, 528 p.

4. Kumar H., Javed S.A., Khan S.A., Amir M. 1.3.4-Oxadiazole/thiadiazole and triazole derivatives of biphenyl-4-yloxy acetic acid: synthesis and preliminary evaluation of biological properties // Eur. J. Med. Chem. 2008. Vol.43. - P. 2688-2698.

5. Hafez H.N., Hegab M., Ahmed-Farag L.S., El-Gazzar A.B.A., A facile regioselective synthesis of novel spiro-thioxanthene and spiro-xanthene-90,2-1,3,4] thiadiazole derivatives as potential analgesic and antiinflammatory agents // Bioorg Med Chem Lett. 2008. Vol. 18. - P. 4538-4543.