DETERMINATION OF THE PARAMETERS OF ACUTE AND SUBACUTE TOXICITY OF DRUG BASED ON TILMICOSIN

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The article presents the results of the determination of acute and subacute toxicity of the drug "TILMOZIN 25", which was made on the basis of tilmicosin. In result of the conducted researches, it was found out, that a single administration of the drug according to the classification of substances for toxicity (according to the SOU 85.2-37-736: 2011) belongs to the fourth grade of toxicity - less toxicity substances. LD_{50} by the intragastrical administration to white mice (calculations by G. Kerber's method) is 14167 mg/kg, and for white rats is greater than 25000 mg/kg. The use of the drug for 14 days caused functional changes in the liver, spleen and immune system, increased of catabolic processes, which led to the decrease in immunity and body weight of animals.

Determination of the parameters of acute toxicity of the drug TILMOZIN 25 (solutions for oral administration) were conducted on 42 white mice 2-3 months old, weighing 19-22 g and 12 white rats, 2-3 months old, weighing 180-200 g. Preparation was entered intra-gastric, non-permanent.

In the study of acute toxicity on white rats for intra-gastric administration, in an indicative experiment, the medicinal product was administered in the doses of 1.0 (5000 mg/kg), 3.0 (15000 mg/kg) and 5.0 (25000 mg/kg) ml per animal. A dose of 25,000 mg/kg body weight was re-administered on a double amount of animals.

Subacute toxicity of TYLMOZYN 25 was studied on white rats 3-4 months old, weighing 180-200 g. For the experiment were formed on the principle of analogues, two experimental and control groups, 6 animals in each. The tested drug was entered intra-gastric daily for 14 days. Animals of the control group were administered water. Animals of the I experimental group, the drug was administered in therapeutic dose of 80 mg/kg body weight, animals of the II group - ten times the therapeutic dose - 800 mg/kg body weight.

In determining the acute toxicity of TILMOZIN 25, it was found out that its administration to white mice in dose of 25,000 mg/kg caused 100% death of animals

and partly in dose of 15,000 mg/kg. The DL_{50} of the drug for white mice was determined by G. Kerber's method.

In determining the acute toxicity of the drug TILMOZIN 25 on a white rats, it was established that the maximum dose of the drug (25000 mg/kg) did not cause death of animals.

It was found out that the drug "TILMOZIN 25" (solutions for oral administration) according to the SOU 85.2-37-736: 2011 belong to the less-toxic substance - 4^{th} class. DL_{50} by the intragastrical administration to white mice (calculations by G. Kerber's method) is 14167 mg/kg, and for white rats is greater than 25000 mg/kg.

The next stage was to study the effects of the drug on the organism of animals for long-term use. During the all period of the experiment, was not found the death of laboratory animals. At the same time, it should be noted, that the animals were active, eat well fed, fur was thick, shiny.

In studying the effect of the tested drug on hematological parameters, it was established that the use of the drug in therapeutic and 10-fold therapeutic doses (I, II experimental groups) did not cause significant changes in hemoglobin concentration, the number of erythrocytes, hematocrit, the mean corpuscular hemoglobin (MCH) and the mean corpuscular hemoglobin concentration (MCHC). At the same time, in animals of the 2nd experimental group, there was a significant decrease in the number of leukocytes and the mean corpuscular volume (MCV). It was found out that, 14 days of administration of the drug caused decrese in body weight in white rats. The therapeutic dose of the drug led to the reliable reduction in the weight of the liver and spleen in animals; also, there is a tendency to decrease the number of leukocytes, statistically decreases mean corpuscular volume (MCV). The use of therapeutic doses of the drug in serum, there is a tendency to an increase in total protein, decrease in α and β-globulins. The 14-day use of experimental doses of the drug led to the decrese in serum urea concentration and an increase in albumin, total protein, activity of lactate dehydrogenase.

In general, the administration of the drug in the body of rats, the catabolic processes are intensified, decrese the weight of the liver and spleen (the reserves of red and white blood are spent).

Keywords: ACUTE TOXICITY, SUB-ACUTE TOXICITY, LABORATORY RATS, "TILMOZIN-25", HEMATOLOGICAL AND BIOCHEMICAL PARAMETERS.