Experimental studies of information drugs

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Inflammation is the underlying pathogenic process of many diseases. Currently used in medical practice, anti-inflammatory drugs, mainly from the group of non-steroidal anti-inflammatory drugs and glucocorticoids, demonstrating sufficient clinical efficacy, have a number of significant adverse reactions, which stimulates the search for new, fairly safe, anti-inflammatory drugs. Over the past decades, physiologists have become interested in element 32 of the periodic system of DI Mendeleev - Germany (Ge). Organogermanium compounds have antioxidant activity, analgesic and antihypertensive effects, induce the production of interferon, and exhibit protective properties against radiation exposure.

The purpose of this study was a comparative study of the anti-inflammatory activity of the certified drug "Aqueous solution of germanium citrate, TU U 15.8- 35291116-008: 2009" produced by "Nanomaterials and Nanotechnologies LLC" and an informational drug (IP) obtained by transferring the informational properties of the original drug to the secondary carrier - for water for injection [1].

Study design

The study was pilot and was carried out on a small number of white outbred rats (15 males), weighing 150-170 grams, kept under standard conditions of a certified vivarium of the FBUZ "Center for Hygiene and Epidemiology in the Rostov Region" (certificate of accreditation of the testing laboratory center No. GSEN.RU .TSOA.060)

The study of the anti-inflammatory activity of the drug and its analog was carried out on a model of subacute formalin inflammation [2] caused by the introduction under the aponeurosis of the ankle joint of the hind right paw of a rat 0.1 ml of a 2% aqueous solution of formalin in animals of three groups (5 animals in each group): 1 - control animals; 2 - animals exposed to the “Ge” preparation; 3- animals exposed to the information drug. The information drug (IPGe) was obtained by transferring the informational properties of the original drug to a secondary carrier - an ampoule of water for injection (2 ml) using the information transfer generator "Golden Section" developed by ARTEMIDA LLC [3]. The severity of edema was assessed by measuring the thickness of the paw with a caliper 1, 3, 6, 24, 48 hours after the first injection of formalin. In 48 hours after the first, the second injection of formalin was carried out and measurements of the thickness of the paws of rats were carried out after 49, 51, 54, 72, 96, 120, 196 hours from the beginning of the experiment. The investigated substances (as well as water for injection to control animals) were administered by a tube intragastrically (0.5 ml) 1 hour after the first injection of formalin, then after 24, 48, and 72 hours (a total of 4 drinks). To assess the effect of anti-inflammatory effects on the functional state of the animal organism, the leukocyte formulas of rat blood were tested. The functional state of the body is associated with the development of general nonspecific adaptive reactions: stress reaction (Str) G. Selye [4] and anti-stress reactions [5] training (Tr) and activation. Based on the indicators of the leukocyte formula, the level of intoxication was assessed (6), tested adaptive reactions [5] corresponding to the functioning of each animal. Blood samples were taken for analysis: 1 - before the introduction of formalin (background); 2 - one day (24 hours) after the first injection of formalin; 3 - two days after the second injection of formalin (96 hours from the beginning of the experiment), 4 - the end of the experiment (196 hours from the beginning of the experiment and 120 hours after the end of the anti-inflammatory effects). All blood smears were recorded and stained as standard.

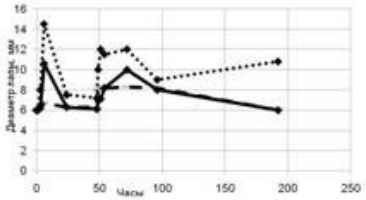
Results and discussion

The greatest severity of edema was observed 6 hours after the first injection

formalin and 24 hours after the second administration, i.e. after 72 hours from the start of the study. In addition, by this time (72 hours), only the rats of the control group had significant edema of the foot, which persisted and increased until the end of observations (Table 1, Fig. 1)

The increase in ankle swelling was calculated using the formula [5]: P = O - I x 100%,

where: P - increase in edema; O- the amount of edema after the introduction of formalin; AND- the size of the paw before the introduction of formalin.



Rice. 1. Change in the diameter of the paws in the control group (dotted line), in the group usingpreparation "Ge" (solid line) and in the group with the use of information preparation (dashed line).

The anti-inflammatory efficacy of the effects was assessed by the degree of inhibition of the edematous reaction in comparison with the control (Tables 1, 2) according to the formula [5]:

100 % - (O - AND (O) : (O - I (k)) NS 100%,
(AND AND)

where k is the control group; o - an experienced group.

Table 1

The effect of the drug "Ge" and the information drug ("IPGe") on the severity edema of the ankle joint of rats with the development of formalin inflammation

Group	Expressiveness edema (6 hours), %	Decongestant efficiency, %	Expressiveness edema (72 hours), %	Decongestant efficiency, %
Control	138.3	-	100 + 46.6 *	-
"Ge"	66.7	51.5	66.7 + 0 *	33.3
"IPGe "	33.3	75.1	43.3 + 0 *	56.7

* - severity of secondary edema of the foot.

As you can see from the table. 1, the anti-edematous efficacy exceeded 30% [6] in both study groups both after the first and after the second administration of formalin.

By the end of the experiment, 196 hours after the start of the experiment and 120 hours after the last administration of the studied anti-inflammatory drugs, no edema was observed in either the Ge-treated group or the IPGe-treated group (Table 2.).

table 2

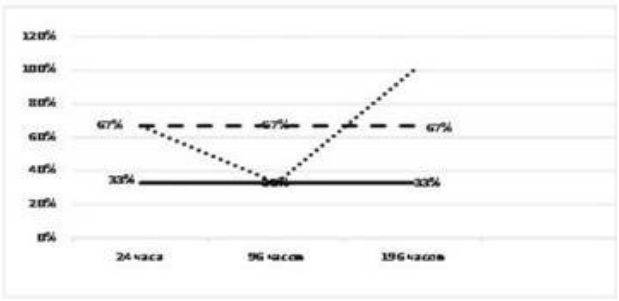
The effect of the drug "Ge" and the information drug ("IPGe") on the severity of edema ankle joint of rats with the development of formalin inflammation after 196 hours

Group	The severity of edema (196 hours), A	nti-edema efficiency,%%
Control	83.3 + 114 *	-
"Ge"	0 + 0 *	100
"IPGe"	0 + 0 *	100

* - severity of secondary edema of the foot

Thus, on the model of subacute formalin inflammation, the unidirectional action of the drug "Ge" and the informational drug "SPGe "with a more indicative anti-edematous effect of the informational preparation.

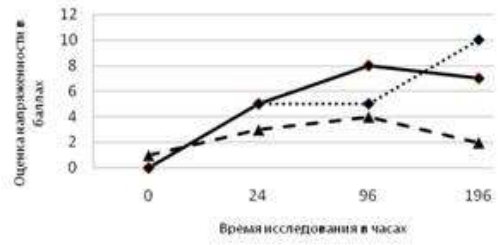
According to the leukocyte formulas of the blood of animals, intoxication was assessed in experimental animals in the process of developing inflammation. Cellular tests of reactivity and intoxication were used [6]. The results of counting the blood of animals from each of the groups for all three tests that were not included in the normal zone (intoxication) were estimated as a percentage and presented graphically (Fig. 2). As can be seen from the figure, by the end of the study, intoxication increased in all animals of the control group - 100%. In the "Ge" group, intoxication was 33% throughout the study. In the group with the use of PIGe intoxication was 66% throughout the study. Intoxication in the experimental groups did not increase even after the end of the exposure.



Rice. 2.The severity of intoxication (%) in the control group (dotted line), in the group withthe introduction of "Ge" (solid line) and in the group with the introduction of "IPGe " (dotted line).

According to the leukocyte blood formulas for each animal, the adaptive reactions developing during the study were determined. Before the start of the experiment (background), most of the animals demonstrated physiological adaptive responses without tension elements: training response (Tr), activation response (Act), and increased activation response (PAD). Only one animal was tested for overactivation (PeA) - the voltage on lymphocytes (above normal). During the experiment, adaptive reactions were maintained mainly in the physiological norm zone with an increase in stress elements. A day after the start of the experiment, the stress reaction (G. Selye) was tested only in one animal from the group with the effect of the drug "Ge". This reaction persisted until the end of observations. At the end of the experiment, stress was tested in the control as well.Ge " by the end of the experiment, the energetically most favorable adaptive reactions were tested in all rats: the activation reaction and the increased activation reaction.

The harmony of developing adaptive reactions was assessed in points according to the number of stress elements in each of the groups according to the timing of blood testing. The point assessment (Fig. 3) of developing adaptive reactions clearly demonstrates: an increase in the tension of adaptation in control; the rise and fall of tension in the group with the introduction of the drug "Ge"; and, in practice, the normalization of adaptation in the group with the introduction of the informational drug "IPGe "...



Rice. 3. Assessment of the tension of adaptive reactions in the control group (dotted line), inthe group using the "Ge" drug (solid line) and the group using the information drug "IPGe "(dashed line) by testing time.

Testing of adaptive reactions and assessment of their harmony showed that inflammation developing in the control group is accompanied by an increase in tension, a decrease in the percentage of lymphocytes, transition of adaptation states to the lower limits of the training reaction and into the stress reaction. Inflammation in this group does not stop, which is demonstrated by the developing secondary edema of the foot. In the group with the introduction of the drug "Ge", the increase in the tension of adaptive reactions after the first injection of formalin was similar to the control. On the first day of the experiment, the animals increased in excitement, they did not eat. Subsequently, the excitement decreased, to some extent persisting until the end of the observations. But, although one animal from this group developed a stress reaction, by the end of observations, the intensity of reactions in this group decreased and secondary edema was not observed. In the group with the introduction of the informational drug "IPGe " the tension of adaptive reactions was expressed to a much lesser extent. By the end of the observations, anti-stress adaptive responses were tested: activation (Act) and increased activation (PAD). Secondary (foot) edema was also not observed.

Evaluation of the adaptive reactions of animals in the control and experimental groups allows us to conclude that the anti-inflammatory effect of the "Ge" preparation is achieved by a greater tension of adaptation mechanisms than with the use of an information preparation.

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