



STUDY OF THE THERAPEUTIC ACTIVITY OF COMBINED ACTION OF "FENZIN" GEL

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ANNOTATION

Conducted's scientific research work developed drug "Fenzin" (fensulkal, tsetirezin) - gel combinations Rowan action. The studies were carried out in order to study the safety and specific activity in comparison with the drug "CINEPAR® ACTIVE" - a gel for external use manufactured by Marion Biotech® Pvt. Ltd, India in an experiment on white rats. Acute toxicity assessment and va whether the change in body weight and neuro-somatic indices. P Acquiring data indicating whether that LD₅₀ preparation and "Fenzin" - a combined gel, was more than 10 g / kg and belongs to practically non-toxic substances. Results and Learn the specific action and therapeutic activity of the drug - a combined gel "Dryer zin" for external application until Zali, that by prep atm removes aseptic edema, have anti-inflammatory action with desinsibiliziruyuschim effect. The studies were carried out in accordance with the requirements of GOST a O'zDSt 276: 2013 "Good Laboratory Practice", Tashkent 2013/

KEYWORDS: Fensulcal, Cetirizine, Therapeutic Activity, Safety, gel.

A number of works are known on the synthesis of new biologically active compounds based on aromatic α -keto acids and on the study of their pharmacological activity.

α -keto acids, due to their high reactivity, are the starting compounds in the synthesis of biologically active compounds. Thus, phenylglyoxylic acid is widely used for the synthesis of drugs. Protecting from radiation, in the production of antibiotics, cephalosporins and drugs used in oncology. On the basis of α -phenyl-glyoxylic acid and its ethyl ester developed anti during cn alitely formulation F ensulkal.^[1,2]

Ismatov D.N. and others.^[3] studied the anti-inflammatory activity of derivatives of phenylglyoxylic and para-nitrophenylglyoxylic acids obtained by interaction of α -keto acids. Based on the studies carried out, it was found that all tests give an anti-inflammatory effect at a dose of 50 mg / kg (P <0.05). The study of toxicity showed that the picture of poisoning in mice after the introduction of the test substances was approximately the same and was characterized mainly by the inhibition of their motor activity. The LD₅₀ of phenylglyoxylic acid derivatives is in the range 1756-2131 mg / kg. According to the literature, the (L) LD₅₀ of butadione when administered orally to white mice is 430 mg / kg. The comparison shows that the tested compounds are several times less toxic than butadione.

Studies of medical and biological properties of synthesized to mpleksnyh biometals compounds with derivatives of phenyl-ki with the items carried out at the Department of Pharmacology of the Samarkand State Medical Institute under the direction of k.med.n. D.N. Karshieva. Preclinical studies have shown that the synthesized phenylglyoxylic acid compounds are 1.5-2.5 times superior in anti-inflammatory effect to the butadione drug.

In known a priori, that the importance of the development and use and medicament has important pharmaceutical form. Also, therapeutic activity is achieved by choosing a rational light form and or combinations of drugs, or by combining to obtain synergism of action or adjusting to reduce side effects.^[4,5,6]

In view of the fact that AGLs occupy an important place in medical practice, it is necessary to study the pharmaceutical market in order to assess and prospects for the creation and introduction of active medicines (MPs) in domestic pharmacy. Currently, an increase in the frequency of allergic diseases - (AD), which is a serious problem for public health, is noted all over the world. A3 occupies the third place after cardiovascular and oncological diseases (in some ecologically unfavorable regions A3 take the first place.^[7]

It is known that cetirizine hydrochloride is a competitive antagonist of histamine metabolite of hydroxyzine and blocking the H1-histamine receptors. Prevents the development and facilitates the course of allergic reactions, has antipruritic and antiexudative action. Influences the early stage of allergic reactions, limits the release of inflammatory mediators at the late stage of the allergic reaction, reduces the migration of eosinophils, neutrophils and basophils. Reduces capillary permeability, prevents the development of tissue edema, relieves smooth muscle spasm.

Eliminates skin reaction to the introduction of histamine, specific allergens, as well as to cooling (with cold urticaria).

In therapeutic doses, it practically does not cause a sedative effect. Refers to antihistamines of the 11th generation. The onset of action after a single dose of 10 mg of cetirizine - after 20 minutes (in 50% of patients) and after 60 minutes (in 95% of patients), lasts more than 24 hours. After stopping treatment, the effect lasts up to 3 days.

Objective of the study: and study of the therapeutic activity and safety of the drug "Fensin" - a gel of combined action consisting of Fensulcal and Cetirizine.

"Fensin" - a combined gel developed at the Department of Pharmaceutical Chemistry Tashfarmi. Tests were conducted in test Nauchn ohm Centere standardization I le a medicament

The drug comparison is a gel - "TSINEPAR® ACTIVE" for outdoor use, production Marion Biotech® Pvt. Ltd, India.

It is used as a local symptomatic remedy for the treatment of pain, inflammation and swelling in: - injuries of tendons, ligaments, muscles and joints, for example, due to sprains, back pain after overexertion, injury x ; - localized forms of rheumatic diseases of soft tissues, such as tendonitis, shoulder-arm syndrome, bursitis, periarthropathy; - osteoarthritis of small to medium-sized joints and superficial joints such as the finger joints or the knee joint .

Dosage regimen: Outwardly, 2-4 g of gels (which is comparable in volume to the size of a cherry or a walnut, respectively, and is sufficient to treat a body surface area of 400-800 cm²) is applied in a thin layer, lightly rubbing into the skin over the inflammation focus, 2-3 times but a day.

Research objectives: Gel Fensin consists of:
Active substances - fensulcal - 2 g, cetirizine hydrochloride - 0.01 g;
Auxiliary substances: carbopol, glycerin, sodium hydroxide q s, purified water.

1. Study of the acute toxicity of the drug "Fenzin" - a combined gel developed at the Department of Pharmaceutical Chemistry TashFarmi in an experiment on white rats.
2. Study of the specific activity of the drug "Fenzin" - a combined gel developed at the Department of Pharmaceutical Chemistry TashFarm in comparison with the drug "CINEPAR® ACTIVE" - a gel manufactured by Marion Biotech® Pvt. Ltd, India in experiments on white rats.
3. Statistical processing of the results obtained.^[8]

Acute Toxicity Study

Material and Methods: The acute toxicity of the preparations was studied compared white rats, body weight 180 - 200 g, of both sexes by the method, but rather Kees and Sanderson (Noakes, Sanderson 1969). The rats were divided into 2 groups of 6 animals each. The animals are kept in a separate room in standard plastic cages on sawdust bedding. The air temperature is maintained within 20-25 ° C, relative humidity - 40-70%. Access to water and feed is free. All involved in the experience of the animals must be healthy, without any - any physiological off on neny.

One day prior to experimental research on the skin of the back rds and gayut wool, on a plot size of 7.5 x 4 cm. In a ystrizheny skin rat experimental groups applied drug "Dryer zin", Uzbekistan at a dose of 10 g / kg. The animals are observed hourly during the first day of the experiment. Then, every day, for 2 weeks, in animals of both groups, the general condition and activity are monitored, and behavioral reactions are taken into account. All e experimental animals are kept under the same conditions and at the general diet with free access to food and water. Acute toxicity estimates and are specified with the change in body weight and neuro-somatic indices:

1. The general condition of the animal,
2. Features of behavior,
3. The intensity and nature of physical activity,
4. The presence and nature of seizures,
5. Coordination of movement,
6. Reaction to tactile, painful, sound and light stimuli,
7. Frequency and depth of respiratory movements,
8. The condition of the scalp and skin, as well as the macroscopic changes in the skin.^[9]

The experiments showed that after a single cutaneous application of the test drug a at a dose of 10 g / kg, no visible changes were observed in the behavior and functional state of the animals, and the consumption of food and water was normal. All rats were active and there were no signs of intoxication. The rats responded adequately to tactile, painful, sound and light stimuli. The frequency and depth of respiratory movements were normal. Macroscopic changes in the skin and pathological changes in the hair of the animals were not observed. There was no death of rats within 2

weeks. The results of the experiment are shown in Table 1.

Table 1: Determination of acute toxicity drug a "Fenzin".

No. alive	"Feng Zin "			Result
	Weight, g	dose g / kg	P The path is In reference	
one	185	10 g / kg	N a short	No death
2	200			No death
3	188			No death
4	195			No death
five	192			No death
6	180			No death
LD₅₀	> 10 g / kg			

1.3 CONCLUSION

Thus, these data show that the LD₅₀ drug and "Dryer zin" - the combined gel elaborate th at the Department of Pharmaceutical Chemistry TashFarmI, it was more than 10g / kg, and relates to a substantially non-toxic substances.

Study specific IC TH Activity

Specific Single Activity: effect of drugs on acute aseptic inflammation studied ali 18 albino rats of both sexes, 180-200 g body weight. Rats pre measure whether the initial paw volume (mL) of normal.^[5]

For the experiment, the rats were divided or into groups of 6 individuals in each

Group 1 - control - skin gel base + 0.1 ml of 6 % dextran solution;

Group 2 - Experimental dermally drug "Dryer zin" + 0.1 ml of 6 % solution and dextran;

Group 3 - experimental - skin preparation "Fensulkal" + 0.1 ml of 6 % dextran solution;

Group 4 - experimental - skin preparation "CINEPAR® ACTIVE" manufactured by Marion Biotech® Pvt. Ltd, India at a dose of 10 g / kg + 0.1 ml of 6 % solution of a dextran.

Acute inflammatory reaction (edema) is reproduced or by subplantar (between 1 and 2 fingers of the left hind foot) administration of 0.1 ml of 6 % solution of a dextran. The compared preparations are applied in a thin layer or applied to the skin before the administration of dextran and after the administration every hour for 3 hours. Intensity of the inflammatory response by evaluating whether after 1 hour, 2 hours, 3 hours and 4 hour and after induction of inflammation paw volume change using a plethysmometer.

Anti-inflammatory activity (PV A) is calculated by the formula:

$$PVA = \frac{Po - PC}{PC} * 100, \text{ where}$$

Po - an increase in the volume of the paws in the experimental group;

Pc - increase in paw volume in the control group.

The data obtained were statistically processed using the STATISTICA program for Windows 95.

Studies have shown that the intact animal under the influence of dextran increased volume tabs hour at 165.8%, after 2 hours by 130, 4 %, after 3 hours by 104.8% and after 4 hours by 95% in comparison with the initial indicator (table 2). At the same time, the greatest increase in the volume of the paws was noted after 1 hour from the beginning of the experiment, which was statically significantly preserved for the next four hours. In contrast, the animals of experimental group, which Fenzin gel was applied, the maximum volume increase tabs composition PLD 113.4 % after 1 hour after administration of dextran, 2, 3 and 4 hours This figure was 84%, 73.2% and 47, 6 %, respectively, i.e., these indicators significantly less by 19.7%, 20.1%, 15.4%, 24.4% in comparison th data control animals at 1, 2, 3 and 4 chasa. MF A formulation made as 31, 7-49, 9%.

And Learn the e specific activity of the preparation Fenzin showed that after 1 hour the inflamed paw edema Expand I to 101.2 %, after 2 hours - 8 4.8 %, through 3 chasa - at 8 0.2 %, and after 4 hour a - by 56.9 % compared to the initial volume of the paw . During the experiment, when applying and Fensin gel, the severity of paw edema was statistically significantly less by 2 0.6 %, 1 5.8 %, 7.7 %, 15.6 % compared with the data of control animals. MF A formulation made as 36,9-37 %.

And Learn the e-specific activity of the drug "TSINEPAR® ACTIVE" produced by Marion Biotech® Pvt. Ltd, India showed that after 1 hour the swelling of the inflamed paw increased by 125%, after 2 hours - by 96.4 %, after 3 hours - by 71.4 %, and after 4 hours - by 70.2 % compared to with the original volume of the foot. During the application experience, the preparation "CINEPAR® ACTIVE" manufactured by Marion Biotech® Pvt. Ltd, India, the severity of paw edema is statistically significantly less by 13.3%, 12, 3 %, 14.2%, 10.6% compared with the data of control animals.

MF A formulation made as 23,1-40%. The experimental results presented in TABLE 2.

Table 2: Study of specific activity and preparations "Fenzin", Uzbekistan and "CINEPAR® ACTIVE" manufactured by Marion Biotech® Pvt. Ltd, India (M ± m, n = 6).

Groups	Paw volume, ml / PVA				
	Exodus	1 hour	2 hours	3 hours	4 hours
Control naya (gel base + 6% solution of dextran)	0.82 ± 0.02	2.18 ± 0.06 *	1.89 ± 0.05 *	1.68 ± 0.02 *	1.60 ± 0.04 *
" Fenzine " + 6% dextran solution	0.82 ± 0.02	1.75 ± 0.02 * #31.7	1.51 ± 0.03 * #35,7	1.42 ± 0.03 * #30.6	1.21 ± 0.04 * #49.9
"Fensulkal" + 6% dextran solution	0.86 ± 0.03	1.73 ± 0.05 *# 36.9	1.59 ± 0.07 * #31.8	1.55 ± 0.08 *# 19.3	1.35 ± 0.04 *# 37.0
CINEPAR® ACTIVE + 6% dextran solution	0.84 ± 0.04	1.89 ± 0.09 * #23.1	1.65 ± 0.07 *# 24.6	1.44 ± 0.07 *# 23.9	1.431 ± 0.08 * #40.0

Note: * - reliably in relation to the initial indices I m at P <0.0 5;

- significant in relation to control at P <0.0 5.

Consequently, we examine the first gel Fenzin has distinct antiedematous effect pointing in the presence of anti-inflammatory activity and By PVA gel formulation was more active Fenzin through 2 hours a 0.95 times over 3 hours 0.92 times as and after 4 hours a 0.89 times as compared with the gel eat "Fensulkal".

CONCLUSION

Thus, study the specific effect of the drug, "Dryer zine" - someone used inirovanny gel, developed at the Department of Pharmaceutical Chemistry TashFarmI, production IP LLC «Well Med Pharm», Uzbekistan in comparison with the preparation "TSINEPAR® ACTIVE" - Gel external use (p. 2027 year 02/2023, the register number and the date. DV / X 00600/07/15 17/07/15 B-250-95 15/09/05 33705 RU edited. 27/04 / 18) by Marion Biotech® Pvt. Ltd, India showed that the drug relates to a substantially non-toxic substances takes aseptic edema, possesses tave otivovospalite l nym action with desinsibiliziruyuschim effect.

The research results are presented in the form of a scientific report on research work in accordance with the requirements of GOST a O ´ zDSt 276: 2013 "Good Laboratory Practice", Tashkent 2013.

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