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ANTI-INFLAMMATORY EFFECT OF "TRIBULEPIL " COMPOUND

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ANNOTATION

In the article were studied the acute toxicity of the anti-inflammatory "Tribulepil" herbal preparation and the main effect oh the preparation is anti-inflammatory effect in the infusionof its components which is developed by the scientists of the Tashkent Pharmaceutical Institute,. "Tribulepil" medicine was compared with the "Verona" medicine produced in Pakistan with the narrow-leaved *Chamaenerionangustifolium*.

Key words: The narrow-leaved *Chamaenerionangustifolium*, anti-inflammatory compound, Tribulepil, rats,

Latent period classical model, androgen-hormonal status, testosterone propionate

It is known that among more than 4,500 plants growing on the territory of Uzbekistan, more than 500 plant species have been used in folk medicine for the treatment and prevention of various diseases since ancient times. Currently, more than 100 of them are widely used in modern medicine.

Plants are a great miracle of nature; they synthesize various substances and create more than 1000 biologically active substances.

It is known from the literature that during the whole 20th century, thousands of medicines that help people's ailments were developed by chemical synthesis.

These medicines are really very powerful and have been of great importance in the prevention and treatment of human pain, and they are still producing such effects today. Unfortunately, by the end of the 20th century, the indiscriminate use of these drugs with powerful effects derived from chemical synthesis, the self-medication process without realizing it, caused and continues to cause various side effects of the used drugs. According to A.N.Yunuskhujaev and B.Sh.Shoyslomov 1/3 of the world's population is currently suffering from side effects caused by drugs, along with the healing provided by these drugs.

That's why doctors pay special attention to treating patients with plants and biologically active substances extracted from them, i.e. phytotherapy. As a result, in-depth study of the plants used by IbnSina (Avicenna) and widely used in folk medicine, and the development of new bioactive drugs based on them, their application to scientific medicine is one of the topical issues of pharmacologists today. We set ourselves the goal of comprehensive study of the collection called.

The narrow-leaved *Chamaenerionangustifolium* and thorn plants growing on the ground contain biologically active substances, emulsifiers and mucilaginous substances, alkaloids, pectin, coumarins. At the same time, it was determined that there are macro- and microelements (Fe, Si, Mg, etc.), vitamins, flavonoids, a large amount of β-sitosterol, etc.

These plants are used in folk medicine for gastric and duodenal ulcers, gastritis, colitis, as a sedative and sedative in neurosis, lack of energy, headaches, insomnia, bleeding, anti-inflammatory, wounds and an injury, colds in female genital organs, treatment of prostate adenoma in men, etc. used in cases and is still used. One of the main effects of the "Tribulepil" compound and the plants included in its component is their anti-inflammatory effect.

Taking into account the above, the acute toxicity of "Tribulepil" plant extract infusion and its main effect, the anti-inflammatory effect, was studied. Experiments were studied in laboratory mice and rats.

Experiments 48 mass 18-21 gr. was conducted in infected laboratory mice. The status of white mice was monitored for 14 days after oral administration of the studied infusions. The main attention was paid to the general condition of the animals, the nature and intensity of the movement, the coordination of the movement, the tone of the skeletal muscles, the speed and depth of breathing, the condition of the fur of the mice and the desire for food, and the change in the mass of the animals. Each dose was given to 6 animals once orally using a special probe up to the maximum possible dose (1 ml/mass).

The studied infusions did not cause any negative reactions in animals at relatively small doses (0.25-0.5 mg/kg). At relatively large doses (in the amount of 0.75-1 mg/kg), the movement of animals slows down for a short time, they gather in one place. There were no significant changes in appetite, hair condition, respiration, and no death in any group during the 14-day follow-up period.

So, it was found that "Tribulepil" and its components are relatively non-toxic when administered once orally.

The effects of the studied plants and the infusions of the herbal composition "Tribulepil" developed on their basis on experimental inflammation were studied in 102 laboratory rats with a mass of 150-205 g. in models of ascetic arthritis, which were exposed to phlogogenic substances: formalin, histamine and serotonin. The effect of the studied infusions against experimental inflammation - arthritis was evaluated by comparing the swelling of the paws of rats in the control and experimental groups. 45 minutes before the administration of phlogogenic substances, the animals in the experimental group were orally injected with the infusion of the studied plants in the therapeutic dose determined in the screening experiments - 25 ml/kg. Under the same conditions, the animals in the control group were given distilled water in the amount of 25 ml/kg. Preparations taken for the comparative effect study: gliciram 75 mg/kg, and indomethacin 15 mg/kg were administered orally. These drugs produce a high therapeutic effect in the indicated doses according to the data presented in the literature.

The paw size of the rats was measured by the oncometric method before and after the introduction of phlogogenic substances at 2, 4, 6 and 24 hours of the experiment.

In the first series of experiments, the anti-inflammatory effect of the studied infusions released on the surface with formalin was studied. The obtained results are presented in Table 1. Based on the data presented in this table, it can be seen that the studied infusions have a high level of effectiveness against formalin inflammation. In particular, at the time of formalin-induced inflammation at a high level (at 4 hours of the experiment), the studied infusions reduced the level of inflammation in the paws of rats by 41.5%, 39.7% and 43.97%, respectively, compared to the results of the control group at doses of 25 ml/kg. (Table 1).

Table 1

Anti-inflammatory effect of the studied infusions released by formalin

(M±m; n=6; npu P=0.05)

№	Sentpreparations	Amount of sent infusions the	Foot paw size of experimental rats		Increased paw paws in rats compared to the norm		Anti-inflammatoryeffect
			Norm (ml)	Volume 4 hours after formalin injection	In ML	In %	
	the control group, in the group that received the infusion of narrow-leaved *Chamaenerionangustifolium* , in the group that received the infusion of St. John's wort, in the group that received the infusion of Tribulepil	25 ml/kg H_2O	0,71	1,40	0,69±0,038*	100	-
		25 ml/kg дамлама	0,72	1,12	0,40±0,066*	58,5	41,5
		25 мл/кг infusion	0,70	1,11	0,41±0,062*	60,3	39,7
		25 мл/кг infusion	0,71	1,0,96	0,38±0,031*	56,03	43,97

Note: * - the level of mathematical precision is equal to R<0.05 compared to the control.

In the second series of experiments, the anti-inflammatory effect of the infusions produced by histamine was studied. The anti-inflammatory effect of infusions was compared with glyciram and indomethacin preparations. The results obtained in the experiment are presented in Table 2.

From the data in Table 2, it can be seen that the studied infusions have an anti-inflammatory effect on the surface of the histamine. The anti-inflammatory effect of "Tribulepil" compound did not lag behind the anti-inflammatory effect of glyciram and indomethacin.

Table 2

Anti-inflammatory effect of the studied infusions with histamine (M±m; n=6; P<0.05)

№	**Sentpreparations**	**Amount of sent infusions the**	**Foot paw size of experimental rats**		**Increased paw paws in rats compared to the norm**		**Anti-inflammatoryeffect in %**
			Normally, (in ml)	**Foot size after histamine injection**	**In ML**	**In %**	
	In the control group	25 ml/kgH_2	0,72	1,45	0,72±0,095	100	-
	In the group that received the infusion of narrow-leaved cypress	0 25 ml/kg	0,75	1,15	0,40±0,067*	55,5	44,5
	In the group that received the infusion of thistle, the land grows wild	25 ml/kg	0,73	1,13	0,41±0,034*	56,4	43,6
	In the group that received Tribulepil compound infusion						
	In the group that received the drug Glitziram In the group that received the drug Indomethacin	25 ml/kg	0,72	1,08	0,36±0,025*	50,5	49,5
		75 ml/kg	0,72	1,00	0,37±0,053*	51,4	48,6
		15 мг/кг	0,74	1,09	0,35±0,045*	48,6	51,4

Note:* - the level of mathematical precision is equal to R<0.05 compared to the control.

Table 2 shows that the studied infusions have a high anti-inflammatory effect against histamine-induced inflammation, and this effect shows the effect of "Tribulepil" as well as glyciram and indomethacin drugs.

In the third series of experiments, the anti-inflammatory effect of the infusions produced by serotonin was studied. In this series of experiments, the anti-inflammatory effect of infusions was compared with glyciram and indomethacin drugs. The obtained results are presented in Table 3.

Table 3

Anti-inflammatory effect of studied infusions on serotonin (M±m; n=6; P<0.05)

№	**Sentpreparations**	**Amount of sent infusions the**	**Foot paw size of experimental rats**		**Increased paw paws in rats compared to the norm**		**Anti-inflammatoryeffect in %**
			Normally, (in ml)	**Foot size after serotonin administration**	**In ML**	**In %**	
1	In the control group, in the group that received the infusion of the	25 ml/kgH_20	0,72	1,44	0,72±0,095	100	-
2	narrow-leaved *Chamaenerionangustifolium*	25 ml/kg	0,70	1,12	0,42±0,061*	58,3	41,7
3	In the group that received the infusion of the thorn that grows on the ground	25 ml/kg	0,73	1,18	0,45±0,066*	62,7	37,3
4	In the group that received the infusion of Tribulepil In the group receiving the drug Glyciram, in the group receiving the drug Indometacin	25 ml/kg	0,71	1,12	0,41±0,043*	57,1 61,1	42,9
5		75 mg/kg	0,72	1,16	0,44±0,039*	59,1	38,9
6		15 mg/kg	0,72	1,14	0,42±0,044*		40,9

Note: * - level of mathematical accuracy is equal to R<0.05 compared to the control.

As shown in Table 3, the studied infusions have a positive effect on serotonin-induced inflammation and reduce serotonin-induced inflammation by 41.7%, 37.3%, and 42.9%, respectively, compared to the control, and this effect is similar to that of Tribulepil compound glyciram and indomethacin. did

It should also be noted that the studied infusions

In rats, the inflammatory process in the foot paw released by phlogogenic substances was relieved 2-3 days earlier compared to the control group, and 3-5 days earlier compared to the rats in the control group.

Among the studied infusions, "Tribulepil" infusion showed the same intensity and better anti-inflammatory effect compared to the "Tribulepil" herbal infusion in all three models of inflammation. The anti-inflammatory effect of "Tribulepil" infusion did not exceed the anti-inflammatory effect of certain drugs: glyciram and indomethacin.

In order to apply "Tribulepil" compound to medicine, its dry extract was isolated at the department of pharmacognosy and its tablet form was developed.

The pharmacological effect of the "Tribulepil" tablet produced in the next experiments was studied.

The acute toxicity of the drug "Tribulepil" was studied in 36 laboratory mice weighing 18-21 g. For this, a 1-3% solution of dry extract of "Tribulepil" was prepared and given to animals at 125mg/kg

Up to 1500 mg/kg was administered as a suspension. Each dose was administered orally to 6 mice, and the mice were monitored for 14 days. During this observation period, no drug-related changes and death were noted in the condition of mice (according to the indicators indicated above).

In the same conditions, the acute toxicity of "Tribulepil" dry extract in tablet form was studied. The tablet consists of 0.5 g, and 0.3 g of 1 tablet is dry extract. Therefore, 2 tablets of 20 ml. dissolved in distilled water. The resulting 3% tablet solution as a suspension was administered orally to mice (1 ml/mass) and their condition was monitored for 14 days. As a result, it was noted that there were no negative effects related to the "Tribulepil" tablet in the case of mice, and no deaths were recorded during the observation period.

Therefore, it was determined that the dry extract of "Tribulepil" and its tablet form are non-toxic, as well as its infusion.

In a separate group of rats, the specific effect of "Tribulepil" drug was compared with glyceram and indomethacin drugs. In particular, the effect of these drugs on the inflammatory process is formalin. was studied with an inflammation model. Experiments were conducted on 24 laboratory rats weighing 163-195 gr. The obtained results are presented in Table 4.

Table 4.

Anti-inflammation effect of tribulepil, gliciram and indomethacin drugs (M+t; p=6).

№	**Sentpreparations**	**Amount of sent infusions the**	**Foot paw size of experimental rats**		**Increased paw paws in rats compared to the norm**		**Anti-inflammatoryeffect in %**
			Normally, (ml)	Foot size after formalin injection	In ML	In %	
	e control group,	25 ml/kg H_2O	0,76	1,50	0,74±0,044	97,4/100	-
	the group that received Tribulepil pill	25 mg/kg	0,75	1,746	0,39±0,045*	52,2	45,2
	Glyciram-treated group						
	Indomethacin-treated group	75 mg/kg	0,75	1,25	0,50±0,042*	66,2	31,2
		15 mg/kg	0,74	1,12	0,37±0,040*	49,5	47,9

Note:* - the level of mathematical precision is equal to R<0.05 compared to the control.

As can be seen from Table 4, Tribulepil had a higher anti-inflammatory effect than glycyram and an equal anti-inflammatory effect compared to indomethacin.

Currently, among the population of the world, including in Uzbekistan, relatively safe hyperplasia of the prostate gland and dangerous prostate adenoma diseases are increasing. Because worldwide environmental degradation, increasing iodine deficiency, weakening of people's ability to fight against various influences, decrease of their immune system and physical weakness - cause diseases to appear. As a result, there is an increase in secondary immunodeficiency diseases among people. One of them is the hypertrophy of the prostate gland and the occurrence of impotence. The basis of the pathogenesis of prostate gland hypertrophy is inflammation, hormonal imbalance, environmental disturbance and weakening of the immune system. (G.G. Korik, N.M. Dementeva., 1976; D.A. Arustamov et al., 2001; A.E Vishnevsky., 2002, etc.) The basis of drugs used in the treatment of

prostate hyperplasia are herbal preparations in modern urological clinics.In particular, in Uzbekistan drugs imported from abroad: “PEPONENE” obtained from pumpkin seed oil, “TIKVEOL” preparation, consisting of durnishnik extract –“ADENOSTOP”, consisting of nettle extract –“URITRON” and a combination of plants – “PROSTAMOL UNO”preparations are used.

Therefore, the basis of the drugs used for the conservative treatment of prostatic hyperplasia and prostate adenoma is limited and imported drugs.
Taking into account the above, we found it necessary to study the effect of the drug "Tribulepil" on the androgen system of rats. The reason for this is: 1 high anti-inflammatory effect of "Tribulepil" drug;
2. The inclusion of the narrow-leaved tea plant, which is part of the "Tribulepil" drug, into the "Verona" drug produced in Pakistan;
3. *The**Chamaenerionangustifolium*contains a large amount of beta-sitosterol, which is of great importance in the treatment of prostate adenoma.

Don't forget that. It is necessary that "Tribulepil" drug also has a calming effect on neuroses similar to valerian. These reasons can be used to prevent and treat the physical weakness associated with hyperplasia of the prostate gland.
In separate experiments, the effect of the drug "Tribulepil" (powdered extract and its pill form) on the sexual state of rats was examined. For this, a female rat was placed in front of a male rat kept in separate devices, and for 20 minutes, the male rat's level of sexual physical activity was measured (the latency period or the time of starting the interaction with the female rat), the number of sniffing and licking of the female rat's genitals, and the number of times the female rat was thrown to the female rat. the conditions were controlled. The observation was carried out in a special room that was completely quiet and relatively dark. The number and intensity of symptoms and conditions in the specified control group were compared. Based on the obtained results, the overall sex status of the animals was assessed.
Experiments were conducted on 24 male and 24 female rats weighing 160-185 g. They were divided into 4 groups of 6:
The rats in group 1 were the control group, and the male rats in the group were given distilled water accordingly.
Group 2 is the experimental group, male rats in this group were administered Tribulepil powder extract at doses of 25mg/kg and 50mg/kg, 2 days before the start of the experiment and 45 minutes before the start of the experiment, respectively.
Group 4 was also an experimental group, and male rats in them were given Tribulepil tablets at doses of 50 mg/kg, as in groups 2-3.
The data obtained as a result of the experiment are presented in Table 5:

Table 5

Effect of tribulepil drug on sexual status of female rats when male rats were placed in front of them (M+sh; p=6).

№	Maleratgroup	Latencyperiod (minutes)	For 20 minutes, male rats were exposed to the penis		Number of sexual intercourses in 20 minutes	Generalsexualactivityindex
			Odorcount	Numberoflicks		
	Control-intact group	8,0±0,72	22,0±2,87	5,0±0,71	1,16±0,043	28,1
	Group receiving 25 mg/kg Tribulepil dry extract	6,5±0,014	27,0±3,13	8,16±0,78*	2,16±0,42*	37,3
	Group receiving 50 mg/kg Tribulepil dry extract	5,2±0,044*	30,0±0,75*	9,5±0,15*	2,33±0,54*	41,8
	50 mg/kg Tribulepil the group that received the pill	5,1±0,58*	31,6±2,57	9,0±0,87	2,33±0,54*	42,9

Note: * - level of mathematical accuracy is equal to R<0.05 compared to the control.

From the data presented in Table 5, it can be seen that male rats are more active in the "handling" behavior and situations of female rats than in the control group.

Male rats treated with tribulepil increased their physical activity levels by mathematical precision. After female rats were placed in front of them, their interaction with female rats ("interaction" state) decreased the onset time - latency period, the number of female rats sniffing, licking and sexual intercourse increased compared to the control group. due to the increase in the condition, the pointer will be broken.

In a separate experiment, we studied the effect of the drug Tribulepil on the androgenic activity of rats. Experiments were conducted on 18 male rats weighing 187-215 gr. After the rats were anesthetized (40-55 mg/kg, ethaminal sodium was injected into the cortical space), we performed orchiectomy. Orchiectomy is considered a classic model of androgen deficiency in laboratory animals. In this way, the rats' tusks were removed and the tusks were sewn up and burned. After surgery, after surgical wound healing, rats were injected with testosterone propionate at doses of 10 mg/kg once daily for 10 days to compensate for their androgenic hormonal status. During this period, Tribulepil preparation was given orally to experimental animals in doses of 25 mg/kg. The rats in the control group were given the comparative drug prostamoluno dose under the same conditions.

The condition of the androgen system of rats was evaluated according to the following indicators: the effect of drugs on protein metabolism was evaluated based on the mass of the prostate gland and the medulla that holds the sperm, the effect of drugs on protein metabolism was evaluated based on the amount of proteins in the liver and bone serum, and the effect of drugs on the immune system was evaluated based on the mass of the prostate gland and thymus gland. The results obtained in the experiment were calculated by the method of variational statistics.

The conducted analyzes showed that as a result of orchiectomy, the androgen system of rats was strongly weakened, as a result, the mass of the prostate gland decreased by 4 times compared to the norm, and the mass of

the seminal vesicles decreased by 72%. Liver mass also decreased significantly, thymus mass increased by 50%, cortical mass decreased by 31.3%, and adrenal gland mass increased by 30%.
Androgen-hormonal status of rats gradually recovered in animals receiving testosterone propionate. In particular, in the rats that received testosterone propionate, the oxygen synthesis process and the immune system were closer to normal. The internal genital organs were highly activated: the mass of the seminiferous tubule-cavity increased by 2 times, and the mass of the prostate gland by 1.4 times.
The effects of testosterone propionate were enhanced in rats receiving tribulepil. So, Tribulepil potentiates the effect of testosterone propionate in the preparation. As a result, the effect of testosterone propionate on the seminal duct increased by 10%, and the effect on the mass of the prostate gland increased by 43.6%. In the same conditions, Prostamol-uno significantly enhances the effect of testosterone propionate. The seminiferous tubule mass increased by 39%, and the prostate gland mass increased by 22.5%.
So, Tribulepil has the ability to stimulate the function of internal genital organs like Prostamol-uno. But Tribulepil has a closer effect on the function of internal genital organs than Prostamol-uno to the effect of the "Verona" drug and significantly increases the amount of sperm in the seminiferous tubule.
Nonsteroidal anti-inflammatory drugs inhibit the release of prostaglandins, one of the biologically active substances that control persistent symptoms of most diseases: pain, inflammation, and fever. As a result, the pain, inflammation and high temperature noted due to the disease will return to normal. Due to these effects, the analgesic, antipyretic and anti-inflammatory effects of nonsteroidal anti-inflammatory drugs appear.
At the same time, when non-steroidal anti-inflammatory drugs are used, in addition to their therapeutic effects, extremely dangerous side effects related to the irritating effect on the tissues of the generative organs and the mucous membrane of the stomach occur. The reason for this is that nonsteroidal anti-inflammatory drugs block not only prostaglandins released from inflammatory sites, but also prostaglandins released from healthy organs and blood tissues. We know that prostaglandins released from healthy organs and tissues protect these organs and tissues from various aggressive effects.
For example, prostaglandins released from a healthy gastric mucosa protect the gastric mucosa from the effects of gastric juices with an acidic environment, while prostaglandins released from blood tissues slow down the process of blood clotting and protect the body from the risk of excessive bleeding. Therefore, when nonsteroidal anti-inflammatory drugs are used, along with their therapeutic effects, side effects related to irritation of the mucous membrane (gastropathy, stomach and duodenal ulcers) also occur. Due to the slowing down of blood clotting, patients with ulcers (patients with ulcers are given non-steroidal anti-inflammatory drugs) may have open wounds and a lot of bleeding.
The side effects mentioned above are relatively rare in anti-inflammatory drugs derived from natural anti-inflammatory medicinal plants. Taking this into account, we studied the effect of the drug Tribulepil against experimental gastric ulcers.
Experiments were conducted on 30 laboratory mice weighing 22-24 grams and 64 laboratory rats weighing 183-210 grams. Experimental gastric ulcers S.V. Anichkov et al. According to (1969) method, it was caused by neurogenic injury of gastric mucosa and injury of gastric mucosa with indomethacin and histamine (S.G. Krylov et al., 2007; L.A. Efimova, 2008).
Tribulepil was administered to mice at doses of 10 and 50 mg/kg and to rats at doses of 50 and 100 mg/kg as a preventive treatment course. In this experiment, oblepixa oil was taken as a comparative drug in doses of 2.5 ml/kg and glyciram in doses of 75 mg/kg. The drugs were administered orally 1 time for 5 days and 1 hour before the start of the experiment. Animals in the control group received distilled water, respectively.
At the end of the experiment, the animals were euthanized, and the number of ulcers in the gastric mucosa and their size, degree of injury, macroscopic analysis was performed based on the requirements of the used method, and the Pauls index (IP) and anti-wound activity (AQA) of the tested preparations were determined. The results obtained in the experiment are presented in Table 6.

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