INTERNATIONAL MULTI DISCIPLINARY JOURNAL FOR RESEARCH & DEVELOPMENT
eISSN 2394-6334 Impact factor: 8.854 Volume 13, issue 04 (2026)

UDC.615.276

STUDY OF SOME FEATURES OF THE ANTI-INFLAMMATORY PROCEDURE OF THE NEW DERIVATIVE THIOUREA

P.M.Madraximov
Asia international university.

Annotation: *on the instance of experiments on white rats and rabbits, the mechanisms of the anti-inflammatory action of the new derivative thiourea UB-423 are reflected in the article. The results indicated that the anti-phlogiston activity of UB-423 is superior to butadiene and indomethacin.*
Key words: *thiourea derivative, inflammation, anti-inflammatory effect, adrenalectomy, butadionum, indomethacin.*

Initially, we found that the new thiourea derivative (coded UB-423) clearly suppresses both exudative and proliferative phases of inflammation. Currently, non-steroidal anti-inflammatory drugs used do not always show a pronounced therapeutic effect and often cause erosion and ulcers of the stomach and duodenum and a number of other side effects. In this regard, the search and study of highly effective and low-toxic anti-phlogistics is an urgent problem of modern medicine.

According to the scientific sources, non-steroidal anti-inflammatory drugs have a complex mechanism of action. [1; 5-13, 2; 38-46, 3; 15-19]

The purpose of the research: to study some aspects of the anti-inflammatory action mechanism of the new derivative thiourea UB-423.

The Research Methods and Means: This compound is synthesized at the Department of Biological and Medical Chemistry at the Tashkent Medical Academy. The study was carried out on 72 white rats of both sexes of a mixed population weighing 150-170 g, 72 rabbits of both sexes of the chinchilla breed weighing 2.5-3 kg.

As a reference standard, the well-known anti-inflammatory drugs butadion at a dose of 100 mg / kg and indomethacin at a dose of 10 mg / kg 'were used.

The anti-inflammatory effect of the drug was studied on a widely used model of arthritis caused by a 1% formalin solution, which was injected in an amount of 0.2 ml into the back surface of rat ankle neurosis (intact and adrenalectomized). The anti-inflammatory activity of the drug was determined using a ple-thysmometer (oncometrically) by the difference in the volume of the paws of the under-control and experiment animals. The drug UB-423 was administered orally 72, 48, 24 and 2 hours before formalin injection at a dose of 100 mg / kg. To clarify some aspects of the antiphlogistic mechanism, the effect of the drug on inflammation in adrenalectomized rats was studied. [4]

Adrenalectomy was performed according to the method of Y.B. Kabaka. In white rats under hexenal anesthesia (90-100 mg / kg, into the abdominal cavity) the skin was cut 1.5-2 cm along the spine. Then, soft tissue was cut below the XII rib, 1.5-2 cm long from two sides of the spine. The connecting cord, on which the adrenal gland is suspended, was captured with anatomical forceps and the adrenal gland was removed along with this cord and the surrounding adipose tissue. Soft tissue and skin were sutured tightly. After the operation, the animals consumed 1% solution of sodium chloride instead of water, and were kept, as before the operation, on a mixed diet. Animals were taken to the experiment on the eighth day after surgery. The test drug was administered orally at a dose of 100 mg / kg 72, 48, 24 and 2 hours before formalin injection.

The effect of drugs on the reactivity of skin capillaries was studied according to the method of K.N. Monacov on rabbits. The animals were fixed to the loom with a back, and then a section of the skin of the abdomen measuring 10x15 cm2 was cleaned of fur. A 1% trypan blue solution was injected into the vein of the ear at the rate of 2 ml of solution per 1 kg of mass. It was applied 5, 30 and 60 minutes after the introduction of suspense into the skin of the abdomen in two symmetrical areas using a micropipette of 0.02 ml of xylene. The results were evaluated by the rate of blue spot rushing at the xylene application sites. The studied drug was administered orally at doses of 25, 50 and 100 mg / kg for 72, 48, 24 and 2 hours before the introduction of the standard agent.

The effect of drugs on the activity of the enzyme hyaluronidase was studied in rabbits according to the method of I.I. Matusis. Lidase was used as a hyaluronidase preparation. It was dissolved at the rate of 128 pieces / ml in an isotonic sodium chloride solution and added in an amount of 0.5 ml to 0.8 ml of a 0.75% trypan blue solution. The result mixture was injected in intradermal in an amount of 0.1 ml, after which the area of the rushed spots was determined. Three hyaluronidase were placed on each rabbit. The under research drug was administered orally at doses of 25, 50 and 100 mg / kg 72, 48, 24 and 2 hours before lidase injection.

The effect of drugs on the activity of the kinin system of the blood was determined according to G.S. Paskhina on white rats and rabbits. In rats under thiopental anesthesia (80 mg / kg, intra-peritoneal), blood was taken from the femoral vein into a silicon tube and centrifuged. To activate the kinin system, 0.1 ml of the resulting serum was placed in a clean silicon tube and 0.9 ml of an isotonic sodium chloride solution was added. In this case, a mixture was obtained in the ratio of parts 1.10, which had the highest kinin activity. Subsequently, adding physiological saline of sodium chloride to it, a dilution of 1:20, 1:60, 1.240, etc. was obtained.

Table 1: The Effect of Ub-423 And Butadione On Formalin Inflammation In Intact And Adrenalectomized Rats After Oral Admission

Drug	Number of animals in the group	Dose, mg / kg	Time of appearance of the "blue spot" after intravenous administration through:					
			In Norm	6 hours after injection of phormalyn	Ml	%		
In intact rats								
Control	6	-	0.54	1.14	0.60 ± 0.008	111.1	0	-
UB-423	6	100	0.56	0.80	0.24 ± 0.007	42.8	61.5	<0.001
Butadion	6	100	0.55	0.96	0.41 ± 0.013	74.5	33.0	<0.05
Of Adrenalectomized Rats								
Control	6	-	0.69	1.41	0.72 ± 0.026	104.3	0	-
UB-423	6	100	0.59	1.16	0.57 ± 0.03	96.6	7.4	<0.02
Butadion	6	100	0.72	1.24	0.52 ± 0.007	72.2	30.8	<0.001

About the activeness of kinin system blood was evaluated according to the higher level of dilution of serum, endemic injection of amount 0.1 ml which caused the red spots on skin of

rabbits in 20 minutes after the injection. The under research drug was injected in in a dose of 25, 50 and 100mg/kg for 72, 48, 24 and 2 hours before blood test.

Statistic treatment of data was carried out according to Student and Fisher methods

Research results and Discussion: In order to find out the degree of participation of the adrenal cortex in the anti-inflammatory effect of UB-423, experiments were performed on intact and adrenalectomized rats.

The results of the first series of experiments in intact animals showed that under the influence of UB-423 at a dose of 100 mg / kg, an inhibition of the inflammatory process by 61.5% is observed.

The second series of experiments was performed on adrenalectomized rats. The study drug was administered in the same doses. The data obtained (Table 1) showed that UB-423 in adrenalectomized rats also indicates a statistically significant anti-inflammatory effect. However, this effect of the drug in adrenalectomized rats is less distinct (7.4%) than in intact animals (61.5%).

There was no clear difference in the anti-inflammatory effect of butadion in intact (33%) and adrenalectomized (30.8%) animals. Therefore, in the anti-inflammatory effect of the drug UB-423, the adrenal glands play a significant role. In this regard, UB-423 is different from butadione.

The effect of UB-423 on capillary permeability was carried out on rabbits. In the control series of experiments when applying xylene and the appearance of blue sports was 5.03 + 0.12 min. When xylene was applied to the skin of the stomach of rabbits 30 minutes after intravenous administration of paint, spots appeared, on average, after 5.37 + 0.04 minutes. The application of the excitatory in 60 minutes after the introduction of trypan blue caused spots on average, after 5.52 + 0.23 min (table. 2).

In under experiment rabbits receiving UB-423 at a dose of 25 mg / kg, application of xylene 5 minutes after administration of trypan blue caused spots after 6.33 + 0.07 minutes. At doses of 50 and 100 mg / kg, this time was 6.94 + 0.24 minutes, 7.41 + 0.4 minutes, respectively. After 30 minutes, the time for the appearance of blue spots on the skin at the site of xylene application was 6.54 + 0.28; 7.5 + 0.29; 8.0 + 0.39 minutes, and after 60 minutes it was 7.12 + 0.36; 8.35 + 0.33; 9.16 + 0.38 minutes according to the doses.

In experimental rabbits treated with butadione, the time for the appearance of blue staining on the skin at the site of xylene application after 5 minutes was 6.2 ± 0.07 minutes, after 30 minutes it was 6.61 ± 0.41 minutes, 60 minutes after administration paint, it was 7.4 ± 0.35 minutes. .

From the above results it is seen that, on the background of UB-423, the period of time elapsing from the moment of application of the stimulus to the appearance of noticeable staining on the skin is significantly extended. Consequently, under the influence of UB-423, the reactivity of skin capillaries to the action of an inflammatory irritant is significantly reduced and is stronger than butadione in activity.

Table 2 The effect of UB-423 and butadion on the reactivity of skin capillaries to the action of an inflammatory stimulant.

Drug	Number of animals in the group	Dose, mg / kg	Time of appearance of the "blue spot" after intravenous administration through:					
			5 minutes	P	30 minutes	P	60 minutes	P
Control	6	_	5.03 ± 0.12	-	5.37 ±	-	5.52 ±	-

					0.04		0.23	
UB-423	6	25	6.33 ± 0.07	<0.01	6.54 ± 0.28	<0.01	7.12 ± 0.36	<0.02
UB-423	6	50	6.94 ± 0.24	<0.02	7.50 ± 0.29	<0.002	8.35 ± 0.33	<0.02
UB-423	6	100	7.41 ± 0.40	<0.02	'8.0 ± 0.39	<0.02	9.16 ± 0.38	<0.001
Butadion	6	100	6.20 ± 0.07	<0.001	6.61 ± 0.41	<0.02	7.40 ± 0.35	<0.01

A study of the influence of UB-423 on the activity of the kinin system of the blood indicated that in the control group of rabbits, color exit from capillaries and the appearance of blue spots on the skin was observed with intradermal admission of rat kinin-containing serum at a dilution of 1:50 000.

Under the influence of UB-423 at a dose of 50 mg / kg, spot was observed in under experiment animals at a dilution of serum of 1: 240, at a dose of 100 mg / kg at a dilution of 1: 120. In animals treated with butadione and indomethacin, the appearance of a blue spot was observed respectively in dilutions of 1: 320 and 1: 180.

Thus, UB-423 significantly inhibits the activity of kinin systems and, in this regard, is superior to butadiene and indomethacin.

A study of the influence of UB-423 on the activity of hyaluronidase showed that if in control animals, after intradermal administration of a solution of trypan blue with hyaluronidase (lidase), the area of paint distribution in the skin is on average 333 3 ± 9.74 mm2, then in animals treated with UB -423, this area decreases markedly at a dose of 25'mg / kg to 297.3 ± 1.45 mm2, at doses of 50 and 100 mg / kg to 232.3 ± 1.02 and 189.0 ± 1.05 mm doses correspondingly.

Under similar conditions, butadione and indomethacin reduced the spot area to 226.8 ± 1.85 and 211.0 ± 1.09 mm2 correspondingly. (Table 3)

Thus, UB-423 clearly suppresses the activity of hyaluronidase, which promotes an increase in the permeability of capillaries in the blood-tissue direction, and in this respect is stronger than butadione and indomethacin.

Therefore, the drug UB-423 has a rather complex mechanism of anti-inflammatory action.

Table 3: The effect of UB-423, butadione and indomethacin on the area of paint distribution in the skin during intradermal admission of lidase

Drug	Amount of animals in the group	Dose, mg / kg	Area of color distribution (trypan blue) on the skin, mm2	Decrease in the spotted area of the skin in relation to the control, %	P
Control	6	-	333.3 ± 9.74	0	-
UB-423	6	25	297.3 ± 1.45	10.9	<0.01
UB-423	6	100	189.0 ± 1.05	43.3	<0.002
UB-423	6	50	232.3 ± 1.02	30.4	<0.001
Butadion	6	100	226.8 ± 1.85	32.0	<0.05
Indomethacin	6	10	211.0 ± 1.09	36.7	<0.001

Conclusion:

1. The procedure of anti-inflammatory action of the new derivative of thiourea UB-423 is due to its effect on the adrenal cortex, inhibition of the activity of the hyaluronidase enzyme, suppression of the activity of kinin systems and a decrease in vascular permeability.

2. UB-423 has a pronounced anti-inflammatory effect and in this respect it is significantly superior to butadion and indomethacin and may be of some practical interest as a potential anti-inflammatory agent.

Reference:

1. Zverev Y. F. Flavonoids through the Eyes of a Pharmacologist. Antioxidant and Anti-Inflammatory Activity. Reviews of Clinical Pharmacology and Drug Therapy. 2017.-Vol. 15, No. 4. pp. 5-13
2. Kutyakov V.A., Shadrina LB, Trufanova LB and others. Non-steroidal anti-inflammatory drugs: Key Mechanisms of Action and Neuro-protective Potential. Experimental and Clinical Pharmacology. - 2019.-Volume 82, No. 2. pp. 38-46
3. Shukurlaev K.Sh., Bekova N.B. The Study of Thiourea outcomes against the inflammation. Urgench, "Ilm sarchashmalari." In Uzb. 2019, No. 2. Pp. 15-19
4. Kabak Y.M. Practical course on Endocrinology. M., “Medicine”, 1945, p. 146-152