

# Study Of Anti-Inflammatory Properties Of Paranitrophenylglyoxilic Acid Thyosemicarbase

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**Abstract:** *Anti-inflammatory drugs are widely used in medical practice for the treatment of diseases associated with the inflammatory process. However, despite this, many of these medications have the property of causing a variety of side effects and serious conditions. Therefore, the anti-inflammatory activity and toxicity of the new product of phenylglyoxyl acid was studied in rats. Paranitrophenylglyoxyl acid thiosemicarbazone, which has shown high activity and low toxicity, can be used as an anti-inflammatory drug.*

**Keywords:** *aseptic inflammation, flagogenic agents, exudation, proliferation, paranitrophenylglyoxyl acid thiosemicarbazone.*

## 1. INTRODUCTION

Many diseases and pathological conditions are accompanied by an inflammatory process. It is known that the pathogenesis of inflammation itself is a complex, multifaceted process [4]. Strong and persistent inflammation negatively affects the activity of organs and tissues. For this reason, a large group of anti-inflammatory drugs is currently used in the treatment of many diseases and pathological conditions, and their range is expanding. However, most of them are not always used successfully due to their toxicity, side effects, invasive complications, or low therapeutic efficacy [1,3]. Therefore, it is important to search for, study and apply in practice new drugs that have high anti-inflammatory activity and are less toxic, among the compounds with a nonsteroidal structure [2].

## 2. MATERIALS AND RESEARCH METHODS

In the scientific study, the yield of phenylglyoxyl acid was obtained by synthesis of paranitrophenylglyoxyl acid thiosemicarbazone. This compound is in powder form and is soluble in alcohol and poorly soluble in water. Therefore, it was sent to the animals in the form of a suspension in a 3% starch paste. The experiments were performed on white rats of different breeds, weighing 170-220 g. Its anti-inflammatory effects have been studied in aseptic models of inflammation induced using various flagogenic agents.

Formalin, histamine, serotonin, carrageenan solutions were used as flagogenic agents. For this purpose, solutions of these agents were administered in an amount of 0.1-0.2 ml under the aponeurosis of the foot claws of experimental animals. The anti-inflammatory activity of the compound was determined based on the difference between the size of the foot claws of the comparison group and the experimental animals. It has been studied in comparison with butadione and voltaren drugs, which are widely used in medical practice. According to the literature, these drugs had the strongest anti-inflammatory effect in white mice and rats when administered orally at doses of 100 and 10 mg / kg, respectively [5]. The animals in the comparison group were given an equal amount of starch paste during this period. In the formalin-induced type of inflammation, rat paw volumes were measured 30 minutes before the start of the experiment with plethysmometry, 3, 6, 24 hours after formalin delivery, and daily for the last 7 days. Paranitrophenylglyoxyl acid thiosemicarbazone was administered orally to experimental animals 30 minutes before and 7 days after administration of formalin at 50, 100, and 200 mg per kg. In inflammation caused by histamine and serotonin, the paw volumes of the animals were measured with a plethysmometer every 1 hour for 30 minutes before and after the delivery of flagogenic agents every 6 hours for the last 1 day. The compound was administered orally at 50, 100, and 200 mg per kg 72, 48, 24, and 2 hours before the inflammation caused by histamine and serotonin. Using the carrageenan model, the rat claw size was measured using a plethysmometer 30 minutes before the start of the experiment and at 3, 6, and 24 hours after carrageenan delivery. Dosage and administration of the drug were maintained.

The effect of the compound on the exudative phase of inflammation was studied by inducing aseptic peritonitis by injecting animals into the abdominal cavity using a silver nitrate solution. 30 white rats were injected intraperitoneally with 0.5% solution in 1 ml. Six hours later, the rats were decapitated and killed, and the exudate collected in the abdominal cavity was injected through a syringe. The effect of the drug on the exudative stage of inflammation was determined by comparison and the difference between the amount of exudate absorbed from the abdominal cavity of the experimental group of animals. The drug was administered orally to animals 30 minutes before peritonitis was called.

To study the effect of the drug on the proliferative stage of inflammation, we used the method of "cotton pellet" proposed by Mejer and co-authors (1950). To complete this section, sterilized cotton balls weighing 7 mg were implanted under the skin of the shoulder blades of 30 white rats. The drug was administered orally once a day, 30 minutes before implantation of "cotton swabs" and for 7 days after surgery. On the eighth day of the experiment, cotton swabs were isolated and first weighed, then dried in a thermostat at a temperature of 700 C until constant weight, and the weight was re-measured. The antiproliferative activity of the drugs was determined based on the difference between the weights of the cotton swabs belonging to the control and experimental groups. We studied the acute toxicity of the drug by oral administration to mice for 1 day. We determined its chronic toxicity by injecting it into the stomach daily in rats for 6 months. The main focus was on the condition of the gastrointestinal mucosa and peripheral blood, and some animals were decapitated and pathomorphological examinations of their internal organs and brain sections were performed. The results obtained were statistically processed.

### 3. ANALYSIS AND RESULTS

The study showed that 3 hours after the administration of formalin, the mean increase in paw volume of comparative animals was  $0.74 \pm 0.02$  ml, while in experimental group heifers receiving thiosemicarbazone of paranitrophenylglyoxyl acid at 50, 100 and 200 mg per kg,

this figure was 0, respectively. ,  $51 \pm 0.05$ ;  $0.44 \pm 0.04$  and  $0.41 \pm 0.03$  ml, respectively, the anti-inflammatory activity of the drug was 32.2 according to the dose; 44.9 and 47.1%, respectively. In the group of experimental animals receiving butadione and diclofenac sodium, the mean increase in paw volume was 84.5 and 55.9%, and the anti-inflammatory activity was 28.1 and 52.4%, respectively. Thus, the anti-inflammatory activity of the drug caused by formalin was 1.7 times stronger than that of butadione.

As shown in Table 1, the anti-inflammatory activity of paranitrophenylglyoxyl acid thiosemicarbazone induced in rats by induction of various phlogogenic agents (carrageenin, histamine, and serotonin) was also observed. Comparing the results obtained, it was found that its anti-inflammatory activity caused by phlogogenic agents is 1.7 times higher than that of butadione and equal to voltaren.

Table 1

Anti-inflammatory effect of paranitrophenylglyoxyl acid thiosemicarbazone (PTK) induced by various agents

(n = 6; p < 0.05)

Preparation	Dose mg / kg	Anti-inflammatory effect, %		
		Carrageenan	Histamine	Serotonin
Comparison group	-	-	-	-
PTK	50	30,0	38,1	38,6
PTK	100	42,2	45,3	46,3
PTK	200	50,1	51,5	56,9
Butadione	100	27,0	30,0	31,9
Voltaren	10	50,9	47,9	54,8

We studied the effect of thiosemicarbazone of paranitrophenylglyoxyl acid by inducing aseptic peritonitis by injecting a solution of silver nitrate into the abdominal cavity. The mean amount of exudative fluid formed in the abdomen of the animals in the comparison group and absorbed by syringe was  $1.80 \pm 0.09$  ml, while the amount of fluid in the abdomen of the animals in the experimental group was 50, 100 and 200 mg per kg of paranitrophenylglyoxyl acid thiosemicarbazone. while  $1.45 \pm 0.11$  according to the above doses;  $1.05 \pm 0.09$  and  $0.60 \pm 0.05$  ml, respectively, and the antiexudative activity of the drug under study was 19.5 according to the doses; 41.7 and 66.7%, respectively. Under these conditions, the antiexudative activity of butadione and diclofenac sodium was found to be 38.9 and 72.2%, respectively. This indicates that the new drug is 1.7 times stronger than butadione.

When studying the effect of inflammation on the proliferative stage by the method of implantation of "cotton swabs", paranitrophenylglyoxyl acid thiosemicarbazone showed its high antiproliferative properties. According to the results, the wet weight of the "cotton swabs" isolated from the comparison group of animals was  $420.5 \pm 4.4$  mg. In experimental group animals receiving paranitrophenylglyoxyl acid thiosemicarbazone at 50, 100 and 200 mg per kg, the weight of "cotton swabs" was  $305.5 \pm 3.1$  in accordance with the above doses;  $266.1 \pm 6.2$  and  $240.2 \pm 3.0$  mg, respectively, and the activity of the drug against the proliferative stage of inflammation is 27.3; 36.7 and 42.9% respectively. In the same case, the antiproliferative activity of butadione and voltaren was 27.2% and 36.9%, respectively. When the granulema tissue is dried to a constant weight, this value is 24.2 in accordance with the above doses of the new drug than in the wet state; Decreased by 28.8 and 38.3%, in butadione by 27.7% and in voltaren by 33.1%. That is, it has 1.6 and 1.4 times higher activity than

butadione obtained for comparison in terms of antiproliferative properties and is approximately equal to voltaren.

To determine the acute toxicity of paranytrophenylglyoxyl acid thiosemicarbazone, it was found that the mean lethal dose (LD50) when administered orally to mice was 2123 mg / kg. Given that the mean lethal doses of butadione, voltaren, and indomethacin given orally to mice in the literature [5] were 430, 370, and 47 mg / kg, the compound studied was 4.9, respectively; 5.7 and 45 times lower toxicity. This indicates that the new drug has little concern for the body. The chronic toxicity of this drug was studied in rats by oral administration of 200 m / gkg daily for 6 months. It was found to have no adverse effects on rat growth, weight, internal organs, brain morphological structure, and peripheral blood composition. This indicates its low toxicity when used for a long time.

#### 4. CONCLUSION AND RECOMMENDATION

1. Paranitrophenylglyoxyl acid thiosemicarbazone reduces aseptic inflammation caused by various flagogenic agents, and in this respect is on average 1.7 times superior to butadione, slightly weaker than or equal to voltaren.
2. Paranitrophenylglyoxyl acid thiosemicarbazone is much higher than butadione and equivalent to voltaren in its inhibitory properties on exudative and proliferative stages of inflammation.
3. Paranitrophenylglyoxyl acid thiosemicarbazone is less toxic and therefore of practical importance.

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