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# FREE RADICAL REACTIONS IN GASTRIC ULCER



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The study investigated the effects of benzketozone, methyluracil, and glycyram on lipid peroxidation parameters (diene conjugates, malondialdehyde) and antioxidant defense systems (superoxide dismutase, catalase enzymes) in rats with immobilization stress-induced gastric ulcers. The results demonstrated that benzketozone reduces the elevated levels of lipid peroxidation products in the blood serum, which play a crucial role in ulcer pathogenesis. Furthermore, it enhances the diminished activity of antioxidant enzymes and accelerates the reparative regeneration of gastric ulcers.

**Keywords:** Benzketozone, gastric ulcer, peroxide oxidation, conjugated dienes, catalase.

## СВОБОДНОРАДИКАЛЬНЫЕ РЕАКЦИИ ПРИ ЯЗВЕННОЙ БОЛЕЗНИ ЖЕЛУДКА

**Аннотация**

В исследовании изучено влияние бензкетозона, метилурацила и глицирама на показатели перекисного окисления липидов (диеновые конъюгаты, малоновый диальдегид) и системы антиоксидантной защиты (ферменты супероксиддисмутаза, каталаза) у крыс с язвой желудка, индуцированной иммобилизационным стрессом.

Результаты продемонстрировали, что бензкетозон снижает повышенный уровень продуктов перекисного окисления липидов в сыворотке крови, играющих ключевую роль в патогенезе язвообразования. Кроме того, препарат повышает сниженную активность антиоксидантных ферментов и ускоряет репаративную регенерацию язвенных дефектов желудка.

**Ключевые слова:** Бензкетозон, язва желудка, перекисное окисление, диеновые конъюгаты, каталаза.

# ME’DA YARA KASALLIGIDA ERKIN RADIKALLI REAKSIYALAR

**Annotatsiya**

Tadqiqotda immobilizatsion stress orqali chaqirilgan me’da yarasi bo‘lgan kalamushlarda benzketozon, metiluratsil va glitsiramning lipidlarning peroksidli ochilishi ko‘rsatkichlari (diyen konyugatlari, malon dialdegidi) hamda antioksidant himoya tizimiga (superoksiddismutaza, katalaza fermentlari) ta’siri o‘rganildi. Natijalar shuni ko‘rsatdiki, benzketozon qon zardobida yara patogenezida hal qiluvchi rol o‘ynaydigan lipidlarning peroksidli ochilishi mahsulotlarining yuqori darajasini pasaytiradi. Bundan tashqari, ushbu preparat antioksidant fermentlarning pasaygan faolligini oshiradi va me’da yara nuqsonlarining reparativ regeneratsiyasini tezlashtiradi.

**Kalit so‘zlar:** Benzketozon, me’da yarasi, peroksidli ochilish, diyen konyugatlari, katalaza.

**Introduction.** Gastropathies involve various pathological processes leading to gastric mucosal damage. One such key mechanism is lipid peroxidation (LPO) [1,9].

The overproduction of reactive oxygen species (ROS) stimulates free-radical LPO, which is accompanied by the destruction of cell membranes and damage to macromolecules, including proteins, lipids, and DNA. This results in the disintegration of intracellular and outer membranes, ultimately leading to cell death. Polyunsaturated fatty acids are the most frequent targets of ROS; their primary oxidation products are diene conjugates, secondary products include ketodienes and conjugated trienes, intermediate products are represented by malondialdehyde (MDA), and the final products are Schiff bases [2,3,4,5,7.8,11].

**Aim of the study.** The study aimed to evaluate the effects of benzketozone, methyluracil, and glycyram on LPO parameters (diene conjugates, malondialdehyde) and antioxidant defense systems (superoxide dismutase and catalase enzymes) in rats with immobilization stress-induced gastric ulcers.

**Materials and Methods.** In the first series of experiments, gastric ulcers were induced in rats using the immobilization stress model. To evaluate the prophylactic effects, the test compounds were administered orally 48 hours, 24 hours, and 30 minutes prior to immobilization. Rats in the comparison group received starch mucilage. Following immobilization, the rats were decapitated, and their stomachs were excised for examination. Primary focus was placed on assessing destructive damage to the gastric mucosa: the number of animals with ulcers was recorded, the severity and area of ulcerative lesions were measured, and the Pauls index was calculated.

In the blood serum of the rats, conjugated dienes (CD), malondialdehyde (MDA), total protein content, superoxide dismutase (SOD), and catalase (CAT) enzyme activities were measured using established methods. Total lipids were determined using the "Lachema" biotest (Czech Republic). As in the previous series, all study drugs were administered orally 48 hours, 24 hours, and 30 minutes before immobilization [4, 6,10].

**Results and Discussion.** The results indicated that immobilization stress led to a 1.6-fold increase in serum CD levels in the ulcer-induced experimental group compared to the control group. Although CD levels remained slightly elevated under the influence of the studied drugs compared to the controls, they showed a statistically significant decrease relative to the untreated experimental group.

Specifically, under the effect of methyluracil, CD levels were 26% higher than in the control group but 23% lower than in the experimental group. Glycyram exhibited a more pronounced effect, normalizing serum CD levels relative to the control group and reducing them by 38% compared to the experimental group.

Administration of benzketozone at a dose of 25 mg/kg resulted in serum CD levels that were 34% higher than the control values but 18% lower than the experimental group. At a dose of 50 mg/kg, this parameter was 23% higher than the control and 25% lower than the experimental group. The most potent effect on CD levels was observed at a benzketozone dose of 75 mg/kg; in this case, the values were nearly identical to the control group and were 38% lower than those of the experimental group.

Serum MDA levels. MDA is one of the key markers for determining the intensity of lipid peroxidation (LPO). Immobilization stress resulted in a sharp increase in serum MDA levels in the experimental ulcer group, reaching a 3.7-fold increase (369%) compared to the control group.
The administration of the studied agents led to a less pronounced increase in this parameter, bringing it closer to the control values. Specifically, in rats treated with methyluracil, serum MDA levels were 2.7 times (265%) higher than in the control group, yet 28% lower than in the untreated experimental group. Glycyram demonstrated a significantly more potent effect on this LPO product; under its influence, serum MDA levels were 24% higher than in the control group and 66% lower than in the experimental group.

When benzketozone was administered at doses of 25 and 50 mg/kg, MDA levels remained 2.6 (262%) and 1.7 (172%) times higher than the control values, respectively, representing a decrease of 29% and 53% compared to the experimental group. The most significant effect of benzketozone

on MDA levels was observed at a dose of 75 mg/kg. In this group, serum MDA levels nearly returned to baseline, exceeding the control values by only 10%, while showing a 70% reduction compared to the experimental group.

SOD and Catalase Enzyme Activity. The activity of antioxidant defense enzymes in the blood serum of the experimental group animals significantly decreased. Specifically, both SOD and catalase activities were 2.2 times lower than those in the control group.

The administration of the studied drugs led to an increase in enzyme activity compared to the untreated experimental group. Methyluracil increased SOD functional activity 3.0-fold relative to the experimental group and restored it to a level 1.4 times that of the control group values. Similarly, catalase activity under methyluracil treatment increased 3.0-fold compared to the experimental group and reached 1.4 times the control level.

Under the influence of glycyram, SOD activity was 3.5 times higher than in the experimental group, showing a 1.6-fold recovery relative to the control. Catalase activity increased 3.1-fold compared to the experimental group and 1.5-fold relative to the control group.

Benzketozone, administered at doses of 25, 50, and 75 mg/kg, increased SOD activity 2.7, 3.1, and 3.6 times, respectively, compared to the experimental group (corresponding to 1.2, 1.4, and 1.7 times the control levels). Catalase activity also showed a dose-dependent increase of 2.7, 3.0, and 3.3 times compared to the experimental group, which was 1.3, 1.4, and 1.5 times higher than the control values, respectively.

**Conclusions**

1. In rats with immobilization stress-induced gastric ulcers, lipid peroxidation (LPO) processes in the blood serum- which play a critical role in the pathogenesis of the disease- are accompanied by a significant decline in the antioxidant defense system. The administration of benzketozone in these cases markedly attenuated the observed disturbances. According to these parameters, benzketozone demonstrated superior efficacy compared to methyluracil and was found to be virtually equivalent to glycyram.

2. Benzketozone effectively reduces the elevated levels of LPO products in the blood serum that are crucial to ulcer pathogenesis, enhances the diminished activity of antioxidant defense enzymes, and accelerates the reparative regeneration of gastric ulcers.

3. The anti-ulcer mechanism of benzketozone and its ability to accelerate healing are characterized by the strengthening of local protective factors in the gastric mucosa, the suppression of LPO

processes, and the stimulation of antioxidant and reparative regeneration without affecting the stomach's secretory activity.

**References**

1. Arkhipova A.A., Anishchenko V.V. Characteristics of gastric ulcers complicated by bleeding. Acta Biomedica Scientifica. 2020;5(1):42-46. (In Russ.) DOI: 10.29413/ABS.2020-5.1.5

2. Bogomolova S.S., Nil E.A., Akhomgotova D.A., Babakhanova A.A., Tyultyaeva L.A. Gastric and duodenal ulcers in geriatrics: endoscopic features. Russian Journal of Geriatric Medicine. 2025;(5):423-425. (In Russ.) DOI: 10.37586/2686-8636-3-2025-423-425

3. Gadzhiev D.N., Sushkov S.V., Allakhverdiev V.A., Klimova E.M., Gadzhiev N.D. Immune disorders in acute ulcerative gastroduodenal bleeding. Pirogov Russian Journal of Surgery. 2015;(6):32-34. (In Russ.) DOI: 10.17116/hirurgia2015632-34

4. Gadzhiev N.D., Allakhverdiev V.A. Features of disorders in the cytokine system and lipid peroxidation in acute gastroduodenal ulcer bleeding. Kazan Medical Journal. – 2017. – Vol. 98. – No. 5. – Pp. 686-691. DOI: https://doi.org/10.17750/KMJ2017-686

5. Ivashkin V.T., Baranskaya E.K., Shifrin O.S., Yurieva E.Yu. The role of antacids in modern therapy of peptic ulcer disease. RMJ (Russian Medical Journal). – 2002. – Vol. 4. – No. 2. – Pp. 106-118. https://www.rmj.ru/articles/bolezni_organov_pishchevareniya

6. Khamraev A.A. Inhibitory effect of conventional therapy on certain mechanisms of gastric protective barrier synthesis. Infection, Immunity and Pharmacology. – 2005. – No. 2. – Pp. 87-89.

7. Morozov V.P., Perelygin V.G., Sovrensky V.M. Lipid peroxidation in blood and tissues in patients with peptic ulcer disease. Klinicheskaya Meditsina. 1998;(2):75-77. (In Russ.) Available from: https://arar.sci.am/Content/91015/file

8. Perekhodov S.N., Milyukov V.E., Bartosh N.O., Krasnoperova M.S. Modern assessment of epidemiology and complications of gastric and duodenal ulcers. RUDN Journal of Medicine. 2024;28(2):230-245. (In Russ.) DOI: 10.22363/2313-0245-2024-28-2-230-245

9. Ragimova Sh.I. Modern diagnostic methods and the antioxidant effect of glutathione in gastroduodenal bleeding in patients with high surgical and anesthetic risk. Bulletin of Surgery in Kazakhstan. – 2021. – No. 1. – Pp. 24-30.

10. Sidorenko N.D. Lipid peroxidation and antioxidant defense in chronic gastroduodenitis in children (literature review). International Journal of Applied and Fundamental Research. 2015;(2-1):59-61. (In Russ.) Available from: https://applied-research.ru/ru/article/view?id=6376

11. Smirnova O.V., Sinyakov A.A., Titova N.M. State of lipid peroxidation and antioxidant defense in chronic gastritis associated with Helicobacter pylori infection in middle-aged men. Russian Journal of Infection and Immunity. 2020;10(4):741-746. (In Russ.) DOI: 10.15789/2220-7619-TSO-1234