



**URGANCH DAVLAT TIBBIYOT INSTITUTI
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**IMMUNOHISTOCHEMICAL EXAMINATION OF GASTRIC TISSUE IN LIVER INJURY
UNDER EXPERIMENTAL CONDITIONS**



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Annotation. The expression of the Ki-67 proliferation marker is an important criterion for assessing the proliferative activity of gastric mucosa cells. During the study, the level of immunohistochemical expression of the Ki-67 marker in the gastric tissues of 3 and 6-month-old white crossbred rats with liver injury in the control group and experimental conditions was studied. In the gastric mucosa of 3–6-month-old white crossbred rats in the control group, it was observed that Ki-67 positive cells were mainly located in the proliferative zones of the glands, especially in the neck. The expression of the marker at a physiological level indicated that the natural renewal processes of gastric epithelial cells were preserved. The presence of the Ki-67 index at a normal level indicates that the balance between cell proliferation and apoptotic processes is maintained. It was found that the expression of the Ki-67 marker in the stomach of rats 3 months after experimentally induced liver injury significantly increased compared to the control group. This phenomenon was assessed as a compensatory-regenerative response to the dystrophic and inflammatory changes that developed in the gastric mucosa.

Keywords: liver injury, stomach, immunohistochemical examination, rats.



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Annotatsiya. Ki-67 proliferatsion marker ekspressiyasi oshqozon shilliq qavati hujayralarining proliferativ faolligini baholashda muhim mezon hisoblanadi. Tadqiqot davomida nazorat guruhi hamda tajriba sharoitida jigar shikastlanishi chaqirilgan 3 va 6 oylik oq zotsiz kalamushlar oshqozon to'qimalarida Ki-67 markerining immunogistokimyoviy ifodalanish darajasi o'rganildi. Nazorat guruhidagi 3–6 oylik oq zotsiz kalamushlar oshqozonining shilliq qavatida Ki-67 pozitiv hujayralar asosan bezlarning proliferativ zonalarida, ayniqsa bo'yin (neck) qismida joylashgani kuzatildi. Markerning fiziologik darajadagi ekspressiyasi oshqozon epiteliy hujayralarining tabiiy yangilanish jarayonlari saqlanib qolganligini ko'rsatdi. Ki-67 indeksining me'yoriy darajada bo'lishi hujayralar proliferatsiyasi va apoptotik jarayonlar o'rtasidagi muvozanat saqlanganidan dalolat beradi. Tajriba sharoitida chaqirilgan jigar shikastlanishidan keyingi 3 oylik kalamushlar oshqozonida Ki-67 markerining ekspressiyasi nazorat guruhiga nisbatan sezilarli oshgani aniqlandi. Bu holat oshqozon shilliq qavatida rivojlangan distrofik va yallig'lanish o'zgarishlariga kompensator-regenerativ javob sifatida baholandi.

Kalit so'zlar: jigar shikastlanishi, oshqozon, immunogistokimyoviy tekshiruv, kalamushlar.

ИММУНОГИСТОХИМИЧЕСКОЕ ИССЛЕДОВАНИЕ ЖЕЛУДОЧНОЙ ТКАНИ ПРИ ПОВРЕЖДЕНИИ ПЕЧЕНИ В ЭКСПЕРИМЕНТАЛЬНЫХ УСЛОВИЯХ

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Аннотация. Экспрессия маркера пролиферации Ki-67 является важным критерием оценки пролиферативной активности клеток слизистой оболочки желудка. В ходе исследования изучался уровень иммуногистохимической экспрессии маркера Ki-67 в желудочной ткани 3- и 6-месячных белых крыс с повреждением печени в контрольной группе и экспериментальных условиях. В слизистой оболочке желудка 3–6-месячных белых крыс контрольной группы было обнаружено, что Ki-67-положительные клетки располагались



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преимущественно в пролиферативных зонах желез, особенно в области шейки. Экспрессия маркера на физиологическом уровне указывала на сохранение естественных процессов обновления эпителиальных клеток желудка. Наличие индекса Ki-67 на нормальном уровне свидетельствует о поддержании баланса между процессами пролиферации и апоптоза клеток. Было установлено, что экспрессия маркера Ki-67 в желудке крыс через 3 месяца после экспериментально вызванного повреждения печени значительно увеличилась по сравнению с контрольной группой. Это явление было оценено как компенсаторно-регенеративный ответ на дистрофические и воспалительные изменения, развившиеся в слизистой оболочке желудка.

Ключевые слова: повреждение печени, желудок, иммуногистохимическое исследование, крысы.

Relevance of the Study. Almost half of the world's population suffers from diseases of the gastrointestinal tract. Statistics show that the prevalence of gastritis among gastrointestinal diseases is more than 80%. Today, this serious disease is often observed not only in adults, but also in school-age children and students. The most common cause of gastritis is malnutrition: hasty and fragmentary eating, unchewed or dry food; too hot or too cold food; eating spicy foods (mainly spicy and very salty foods). Most often, diseases develop in people who are in a state of neuro-psychic stress, neglect healthy eating, abuse alcohol and smoke [1].

Functional dyspepsia (FD) is the most common nosology in the group of functional diseases of the gastrointestinal tract. According to population studies, from 10 to 30% of the general population report dyspeptic complaints [2], but only a quarter of them consult a doctor. Thus, among all cases of visits to general practitioners, the share of patients with dyspeptic syndrome is 2-5% of patients [3]. Dyspeptic symptoms account for 20-40% of complaints of a gastroenterological nature, according to the literature, organic causes are identified in 40% of patients, and in the rest, dyspepsia is functional. Approximately 50% of patients with FD show a decrease in working capacity and daily household activities [4]. Consequently, FD significantly affects the physical, social, emotional and psychological functioning of the patient, which leads to a decrease in the quality of life [5].

Numerous fundamental studies devoted to the problem of the complex effect of exogenous and endogenous influences on the human body have proven their depressive effect on the regulatory systems of the body. At the same time, it remains relevant for researchers to study the morphometric and immunohistochemical parameters of experimental intestinal scarring processes after hormonal therapy of gastric tissue, which is sensitive to disruption of homeostasis.

Aim of the Study To investigate the morphological characteristics of the stomach under conditions of experimental liver injury.

Materials and Methods. A total of 120 outbred white rats aged 3 and 6 months were used in the experimental study. All laboratory animals were maintained under standard vivarium conditions and kept under identical environmental parameters. The study was conducted in accordance with the "Rules for Conducting Research Using Experimental Animals" approved by the Ethics Committee of the Bukhara State Medical Institute (Protocol No. 18, January 16, 2018).

Prior to the experiment, all animals underwent a quarantine period for the identification of existing diseases, assessment of physical condition and age, and prevention of infectious diseases entering the vivarium. Experimental procedures were initiated only after exclusion of pathological conditions.

During the initial stage of the experiment, animals were randomly assigned to either the experimental or control groups. Feeding trials and preparatory procedures were subsequently performed. At the second stage, liver injury was induced in the experimental group of outbred white rats. Comprehensive investigations, including morphological and immunohistochemical analyses, were conducted to evaluate changes in the stomach.

At the final stage, the collected morphological data were analyzed and systematized, followed by statistical processing. Particular attention was paid to the adequacy and reliability of the results



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and to the formulation of valid conclusions and recommendations. White rats weighing 120–130 g and maintained under standard vivarium conditions were used. The animals were divided into two groups:

Group I – Control group (standard diet);

Group II – Experimental group with induced liver injury;

Group III – laboratory animals treated with cinnamon for liver damage in experimental conditions.

At the end of the experiment, the animals were euthanized by decapitation, and histological examinations were performed. The obtained data were recorded, statistically processed, and presented in the form of a research report.

For immunohistochemical staining, tissue samples were sectioned at a thickness of 4–6 μm using a microtome, mounted on glass slides, and covered with poly-L-lysine-coated coverslips. Immunohistochemical staining was performed using the avidin–biotin immunoperoxidase technique following deparaffinization and rehydration of tissue sections. Antigen retrieval was carried out under pressure using 0.01 M citrate buffer (pH 6.0). Endogenous peroxidase activity was blocked by incubating the sections in 3% hydrogen peroxide solution for 10 minutes. The sections were washed with Tris-NaCl buffer (pH 7.6), followed by incubation with specific antibodies for marker expression detection and visualization using the DAB+ chromogen system.

The stained sections were examined microscopically. Immunohistochemical results were evaluated using QuPath 4.4.0 software. Morphometric analysis was performed in five microscopic fields at magnifications of $\times 200$ –400. The percentage of positively stained cells was calculated relative to the total number of cells in the selected area. Expression levels were classified as follows:

Low expression: $<20\%$

Moderate expression: 20–60%

High expression: $>60\%$

Results. Comparative evaluation of immunohistochemical expression of Ki-67 marker in the gastric tissue of 3- and 6-month-old white outbred rats in the control, experimental and biocorrection groups showed that this marker is an important indicator in determining the proliferative activity, regenerative potential of epithelial cells and compensatory-restorative processes after liver damage. In the control group, Ki-67 expression reflected the physiological renewal processes of the gastric mucosa, while in the experimental group, this proliferative activity significantly decreased against the background of liver damage. In the biocorrection group, the re-increase in Ki-67 expression indicated the activation of regeneration and reparative processes in gastric epithelial cells under the influence of sambucus nigra. The file shows the percentage of positive expression of Ki-67 marker in the control, experimental and biocorrection groups with sambucus nigra using the QuPath-0.5.1 program.

In 3-month-old rats, the positive expression of Ki-67 in the control group was 25.20%. After liver injury under experimental conditions, this indicator decreased to 13.28%. Thus, in the 3-month-old experimental group, the expression of Ki-67 decreased by 11.92% compared to the control group, which is approximately a 47.3% decrease. This indicates that liver injury suppresses the proliferative activity in the gastric mucosa, limiting the physiological renewal and regenerative capabilities of epithelial cells. Morphologically, this process was explained by dystrophic changes in the epithelial cells of the mucosa, signs of local inflammation, and disruption of tissue homeostasis.

In the 3-month-old biocorrection group, the positive expression of Ki-67 was 19.35%. This indicator increased by 6.07% or approximately 45.7% compared to 13.28% in the experimental group. Thus, biocorrection with yarrow significantly restored the proliferative activity that had decreased as a result of liver injury in 3-month-old rats. However, the indicator in the biocorrection group did not fully reach the 25.20% in the control group, remaining 5.85% or 23.2% lower than the control. This

indicates that the recovery process has begun, but the proliferative potential of the gastric epithelial layer has not yet fully returned to the physiological level (Figure 1).

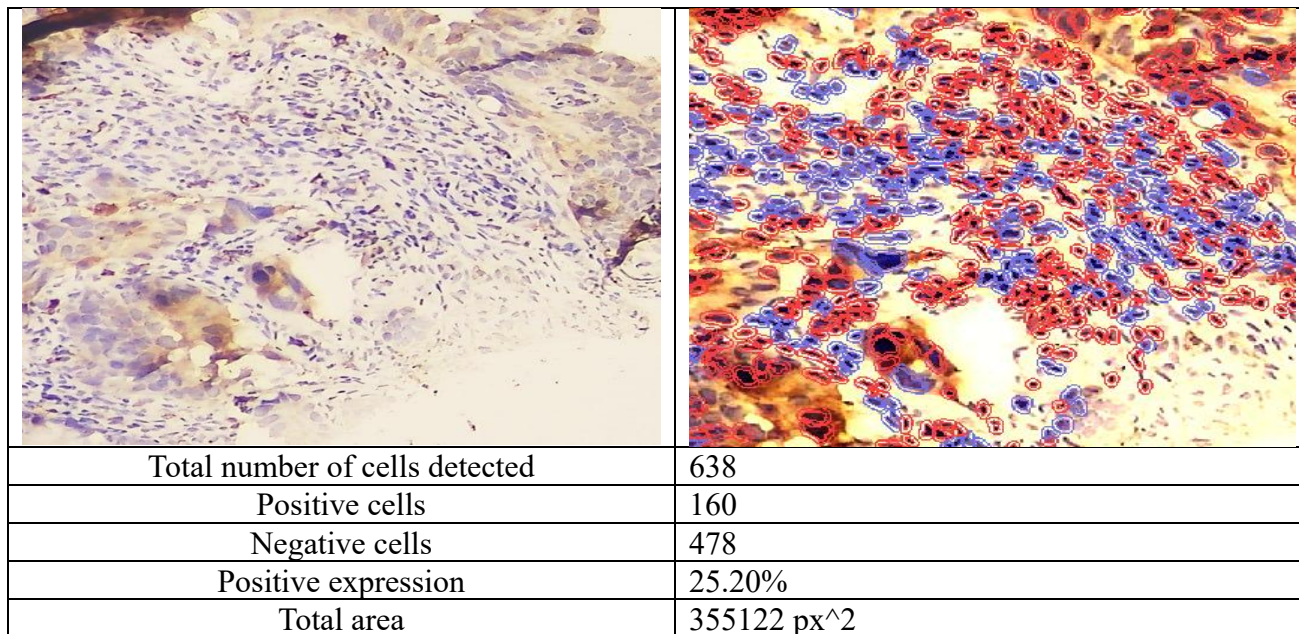
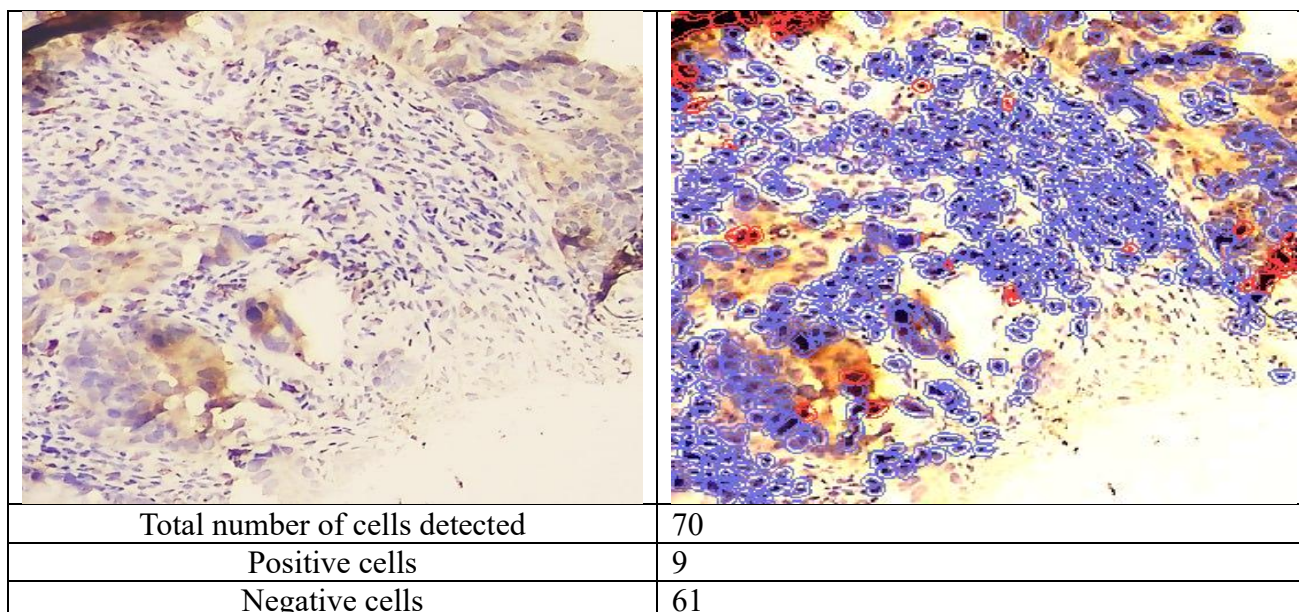


Figure 1. Immunohistochemical study of the expression of Ki-67 marker in the stomach of 3-month-old white outbred rats in the control group. Stained by the Dab chromogenic method. Image magnified 200 times. Scanned and the level of expression was determined using the QuPath-0.5.1. program. Expressed cells are in red.

In 6-month-old rats, the positive expression of Ki-67 in the control group was 26.28%. In the experimental group, this figure decreased to 17.85%. Thus, in the 6-month-old experimental group, the expression of Ki-67 decreased by 8.43% or approximately 32.1% compared to the control group. This result indicates that liver injury also reduced the proliferative activity of gastric epithelial cells in 6-month-old rats. At the same time, the relatively higher preservation of Ki-67 expression in the 6-month-old experimental group compared to the 3-month-old experimental group indicated that compensatory-regenerative mechanisms may be more stable in a more mature organism (Figure 2).



Positive expression	13.28%
Total area	528105 px ²

Figure 2. Immunohistochemical study of Ki-67 marker expression in the stomach of 3-month-old white outbred rats after experimental liver injury. Stained by the Dab chromogenic method. Image magnified 200 times. Scanned and expression levels were determined using QuPath-0.5.1. Expressed cells are in red.

In the 6-month biocorrection group, Ki-67 positive expression was 21.83%. This is an increase of 3.98% or approximately 22.3% compared to 17.85% in the experimental group. Thus, biocorrection with cinnamon increased the proliferative activity of epithelial cells in 6-month-old rats, enhancing reparative and adaptive processes in the gastric mucosa. However, this indicator was 4.45% or 16.9% lower than the 26.28% in the control group. This indicated that although biocorrection had a positive effect, immunohistochemical changes after liver injury were not completely normalized.

When comparing the 3- and 6-month groups, the Ki-67 expression in the control group was 25.20% at 3 months and 26.28% at 6 months, increasing by 1.08% or 4.3% over the 6-month period. This indicates that the physiological proliferation and renewal processes in gastric epithelial cells are somewhat more stable over the 6-month period. In the experimental group, the expression was 13.28% at 3 months and 17.85% at 6 months, and the 6-month group showed a higher result of 4.57% or 34.4%. This indicates that the compensatory proliferative response in 6-month-old rats after liver injury was more active than in 3-month-old rats. In the biocorrection group, the increase was 19.35% at 3 months and 21.83% at 6 months, and in the 6-month group, an increase of 2.48% or 12.8% was observed. This confirms that under the influence of cinnamon, regenerative processes were activated in both age groups, but this effect was relatively more stable in 6-month-old rats (Figure 3).

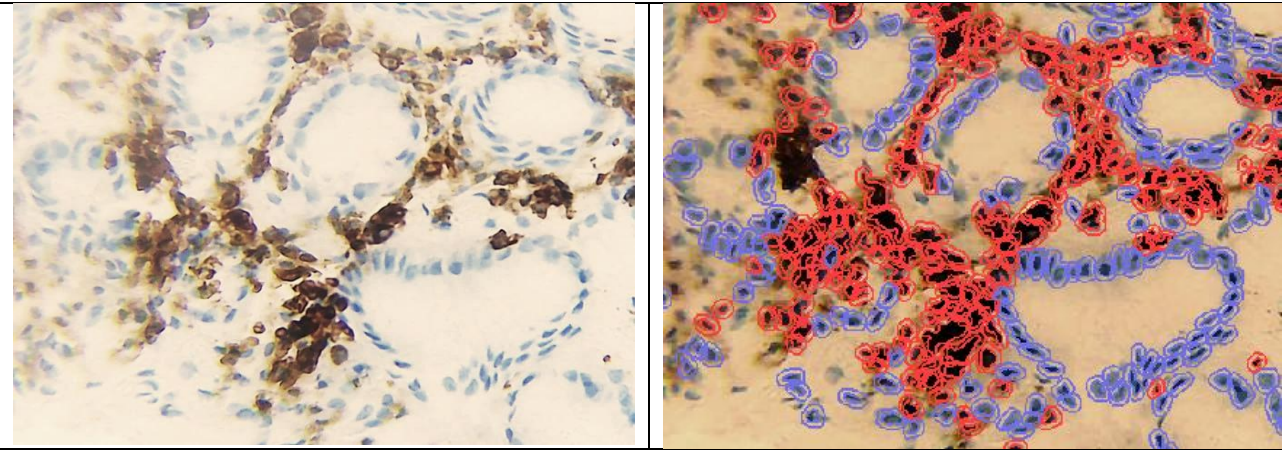
	
Total number of cells detected	327
Positive cells	63
Negative cells	264
Positive expression	19.35%
Total area	205056 px ²

Figure 3. Biocorrection of gastric tissues of 3-month-old white outbred rats after experimental liver injury with stellate starch and study of the expression of the immunohistochemical marker Ki-67. Stained by the Dab chromogenic method. Image magnified 200 times. Scanned and the level of expression was determined using the QuPath-0.5.1. program. Expressed cells are in red.

In general, the results obtained on the immunohistochemical expression of the Ki-67 marker showed that liver injury disrupts proliferative-regenerative processes in the gastric mucosa. The



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decrease in Ki-67 expression in the experimental group compared to the control group confirms the weakening of the regenerative ability of epithelial cells, the reduced regenerative potential of the mucosa, and the occurrence of morphofunctional instability in the gastric tissue. In the group biocorrected with Zarchoba, the re-increase in Ki-67 expression indicated the activation of regeneration processes in gastric epithelial cells, the enhancement of tissue repair mechanisms, and the partial reduction of the negative effect of liver injury on the gastric tissue.

Conclusion. The expression of the Ki-67 proliferation marker is an important criterion for assessing the proliferative activity of gastric mucosa cells. During the study, the level of immunohistochemical expression of the Ki-67 marker in the gastric tissues of the control group and 3- and 6-month-old white crossbred rats with liver injury induced under experimental conditions was studied. In the gastric mucosa of 3–6-month-old white outbred rats in the control group, Ki-67 positive cells were observed to be located mainly in the proliferative zones of the glands, especially in the neck. The expression of the marker at a physiological level indicated that the natural renewal processes of gastric epithelial cells were preserved. The presence of the Ki-67 index at a normal level indicates that the balance between cell proliferation and apoptotic processes was maintained. It was found that the expression of the Ki-67 marker in the stomach of 3-month-old rats after experimentally induced liver injury significantly increased compared to the control group. This was assessed as a compensatory-regenerative response to the dystrophic and inflammatory changes that developed in the gastric mucosa. The increased proliferative activity, especially in glandular epithelium and superficial epithelial cells, indicated the activation of reparative regeneration processes of the mucosa. At the same time, the uneven distribution of Ki-67 positive cells in some areas indicates an imbalance of proliferative processes. In animals of the 6-month experimental group, Ki-67 expression was detected at a higher level, which indicated the continuation of chronic trophic disorders and compensatory proliferation in the gastric mucosa against the background of prolonged liver failure. In some preparations, an increase in the number of Ki-67 positive cells was observed, along with a violation of the architectonics of the glands, thickening of the epithelium and expansion of the proliferative zone. This indicates that the cell cycle is activated under the influence of a chronic pathological process and that reparative mechanisms are under tension. In the groups where biocorrection was used, the expression of the Ki-67 marker showed a tendency to decrease compared to the experimental group. The approach of the marker to the normative indicators indicates the physiological trace of regenerative processes in the gastric mucosa and the reduction of inflammatory-dystrophic changes. The regulation of proliferative activity as a result of biocorrection is explained by the partial restoration of the structure of the glandular epithelium, improvement of microcirculation and stabilization of trophic processes.

List of used literature

1. Улугбекова Г. Ж., Парпиева С. Б. Исследования слизистой оболочки желудка // Экономика и социум. – 2022. – №. 7 (98). – С. 383-386.
2. Hassani M. Liver structure, function and its interrelationships with other organs: a review // International Journal Dental and Medical Sciences Research. – 2022. – Т. 4. – №. 1. – С. 88-92.
3. Nie S., Yuan Y. The role of gastric mucosal immunity in gastric diseases // Journal of Immunology Research. – 2020. – Т. 2. – С. 1-8.
4. Rahmani S. et al. Treatment of non-alcoholic fatty liver disease with curcumin: A randomized placebo-controlled trial // Phytotherapy Research. – 2016. – Т. 30. – №. 9. – С. 1540-1548.
5. Yang J. et al. Clinical characteristics of drug-induced liver injury and primary biliary cirrhosis // World Journal of Gastroenterology. – 2016. – Т. 22. – №. 33. – С. 7579.