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# MORPHOMETRIC CHARACTERISTICS OF THE RAT SMALL BRONCHI IN CONSUMPTION OF THE COMPLEX OF FOOD ADDITIVES

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The paper presents the data of the morphometric study of the small bronchi of the lungs of rats under the complex effect of food additives. It has been established that consumption of the complex of food additives leads to a change in the morphometric parameters of the structural components of the small bronchi of the rat lungs, which at the early stages is manifested by a significant decrease in the morphometric parameters of the outer diameter and lumen with a significant increase in the height of the epitheliocytes in the small bronchi of all orders due to the primary endogenous impact of the components of the food additive complex, which is associated with spasm of the exchange blood vessels and the progressive phenomena of hypoxia. Subsequently, the impact of the alterative factor, which prevails over the protective mechanisms of the body, is manifested by the development of bronchospasm in the small bronchi of the 3rd order, the appearance of inflammatory infiltration in the bronchial walls and the formation of bronchial hyperreactivity, which is characteristic of the development of diseases of the respiratory system, including asthma.

**Keywords:** rats, lungs, small bronchus, monosodium glutamate, sodium nitrite, Ponceau-4R, morphometric study.

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# МОРФОМЕТРИЧНА ХАРАКТЕРИСТИКА МАЛИХ БРОНХІВ ЛЕГЕНЬ ЩУРІВ ПРИ ВЖИВАННІ КОМПЛЕКСУ ХАРЧОВИХ ДОБАВОК

У роботі представлені дані морфометричного дослідження малих бронхів легень щурів при комплексній дії харчових добавок. Встановлено, що вживання комплексу харчових добавок призводить до зміни морфометричних показників структурних компонентів малих бронхів легень щурів, що на ранніх стадіях виражається достовірним зменшенням морфометричних парметрів діаметру зовнішнього та просвіту з достовірним збільшенням висоти епітеліоцитів в малих бронхах усіх порядків внаслідок первинної ендогенної дії складових комплексу харчових добавок, що пов'язане зі спазмом судин обмінної ланки та наростаючими явищами гіпоксії. В подальшому, дія альтеративного фактору, яка переважає над захисними механізмами організму, виражається посиленням розвитку бронхоспазму у малих бронхах 3-го порядку, появою запальної інфільтрації в стінках бронхів та формуванні бронхіальної гіперреактивності, характерної для розвитку захворювань органів дихання, в тому числі і астми.

**Ключові слова:** щури, легені, малий бронх, глутамат натрію, нітрит натрію, Понсо-4R, морфометричне дослідження.

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It has been reported that experimental simulation of various diseases in animals is one of the key methods of studying the patterns of the development of various pathological processes; therefore, an objective comparative assessment of experimental data and their subsequent extrapolation to humans is impossible without knowledge of the basic morphometric parameters of the organs and tissues in the normal condition [1]. Consequently, the use of the morphometric method makes it possible to objectively assess changes in the structural elements of organs and tissues, affected by the various endogenous and exogenous factors [11, 14].

Currently, a comprehensive experimental morphofunctional study of lung structures of rats at the organ, tissue and cellular levels in dynamics [8] is of great interest. The up-to-date concept of the development of diseases of the respiratory system, including bronchial asthma, is based on the idea of the key role of persistent inflammation in the bronchial wall in response to the impact of various factors that lead to hyperreactivity of the bronchi and bronchial obstruction [2].

The lack of thorough research on the impact of food additives on the body, and especially under its combined effect, causes considerable controversy in the scientific community, since the available data do not give a final answer regarding the varying degrees of human susceptibility to the impacts of food additives, and no data on their combined effect have been found to date [6].

The use of the complex of monosodium glutamate, sodium nitrite and Ponceau 4R is based on our analysis of the content of food additives of domestic and foreign origin, since manufacturers most often use a complex of food additives to disguise the low-quality and low-grade production [14].

A review of the potential health hazards of monosodium glutamate was made by the international group of scientists, who linked the consumption of monosodium glutamate to cardiotoxicity, hepatotoxicity, neurotoxicity, low-grade inflammation, metabolic disorder, pretumor changes and behavioral changes. A critical analysis of the existing publications shows that many of the negative health reports on the effect of monosodium glutamate are uninformative because they are based on excessive dosage that does not correspond to the normal rates, commonly consumed in food products [15].

In Ukraine, E-250 food additive (sodium nitrite) is widely used as a color retainer and preservative in the production of various types of meat products [3]. It has been established that the most pronounced changes in the activity of inflammatory processes were noted within 72 hours after sodium nitrite entered into the body of sexually immature rats poisoned by tobacco smoke. Disruption of energy supply system occurs simultaneously with the development of inflammatory processes, which is manifested by inhibition of the activity of mitochondrial enzymes in the liver and lungs of rats of all age groups after intoxication. Notably, succinate dehydrogenase and cytochrome oxidase activities, which are most pronounced in sexually immature rats, are inhibited [5].

In the food industry, food colorants (E100-E182) are widely used, which make it possible to give products the intended color or shade. Colorants, entering the body as haptens, binding to proteins such as serum albumin and others, become full-fledged antigens to which antibodies are synthesized. Permissible sanitary and hygienic standards are usually exceeded, which increases their allergenicity [7].

Thus, the detailed analysis of all available scientific sources in the leading databases worldwide allows us to state that investigations of the impact of complex of food additives on the organs of the respiratory system are quite limited and requires further thorough study.

**The purpose** of the paper was to establish the dynamics of changes in the metric parameters of the small bronchi of the 1st, 2nd and 3rd orders of the rat lungs in normal conditions and under the combined effect of the food additives, namely, monosodium glutamate, sodium nitrite and Ponceau-4R.

**Material and methods.** 84 mature outbred male rats were involved into the study. The rats of control group (n=10) consumed drinking water and were administered with saline orally. The rats of the experimental group, with access to water *ad libitum*, were administered with 0,6 mg/kg sodium nitrite, 20 mg / kg monosodium glutamate and 5 mg / kg Ponceau 4R in 0.5 ml of distilled water once daily per os. The doses of food additives were twice lower the allowable normal rate in food products. The "open field" test was used to evaluate the rats' adaptive behavior [13]. The animals were sacrificed within 1, 4, 8, 12 and 16 weeks under thiopentone anesthesia overdose. After animals' euthanasia, the fragments of the lungs were fixed in 2.5 % glutaraldehyde solution and 10 % formalin solution. Subsequently, the pieces of the lungs were embedded into epon-812 and paraffin, using the conventional technique [10]. Sections of 5-10 μm thick were obtained using the ARM 3600 microtome. Semi-thin sections were obtained using the UMTP-7 ultramicrotome. After staining with hematoxylin and eosin, as well as methylene blue, the sections were placed in polystyrene and studied under the light microscope. The digital microscope, equipped with the Levenhuk D740T digital microphoto attachment, and adapted software have been used for microphotography and morphometric study. Statistical processing of morphometric data was performed using the *Excel* program [4]. The housing of the animals and experimental part of the study has been carried out in compliance with the "General ethical principles used for animal experiments", adopted at the First National Congress on Bioethics and requirements of the international principles of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" [9].

**Results of the study and their discussion.** The findings of the morphometric study of the small bronchi of the 1st order of the lungs of the control rats have established that the mean values of the outer diameter and lumen diameter were 237.68±9.19 and 163.30±9.73 μm, respectively, and the height of the epitheliocytes was 23.05± 2.26 μm (Table 1).

Within one week after consumption of the complex of food additives the mean values of the outer diameter of the first-order small bronchi significantly decreased by 9.26 %, accounting for 215.66±8.34 μm; the values of the lumen diameter were also by 38.87 % significantly lower compared to control values and accounted for 99.82±3.34 μm ($p<0.05$). The height of the epitheliocytes significantly increased by 70.15 %, accounting for 39.22±3.31 μm ($p<0.05$) compared to control group.

On week 4 of the experiment, consumption of the complex of monosodium glutamate, sodium nitrite and Ponceau 4R led to a significant increase in the outer diameter of small bronchi of the 1st order by 52.73 % (329.37±10.64 μm) compared to the previous period of the experiment, that also was by 38.58 % significantly greater compared to the values of the control group ($p<0.05$). The lumen diameter increased significantly by 152.81 % compared to the values of the week 1 of the experiment, and by 54.53 % compared to the values of the control group, accounting for 252.35±12.72 μm ($p<0.05$). The mean

values of the height of epitheliocytes were 18.44±1.18 μm, which was by 52.98 % significantly lower compared to the values of the week 1 of the experiment, and by 20.00 % significantly lower than the values in the control group of animals (p<0.05).

Table 1

**Morphometric parameters of the first-order small bronchi of the rat lungs**

| Parameters | Small bronchi of the 1st order | | |
|---|---|---|---|
| | Outer diameter | Lumen diameter | Height of the epitheliocytes |
| Control | 237.68±9.19 | 163.30±9.73 | 23.05±2.26 |
| Week 1 | 215.66±8.34 * | 99.82±3.34 * | 39.22±3.31 * |
| Week 4 | 329.37±10.64 *.** | 252.35±12.72 *.** | 18.44±1.18 *.** |
| Week 8 | 213.32±9.85 *.** | 102.89±10.48 *.** | 22.98±2.30 ** |
| Week 12 | 268.32±8.43 *.** | 131.79±10.52 *.** | 25.08±2.24 |
| Week 16 | 248.67±9.17 ** | 189.21±11.70 *.** | 29.97±2.29 *.** |

Note * - P<0.05 compared to the control group; ** - P<0.05 compared to the previous time period of the observation.

On week 8 of consumption of the complex of pollutants, the mean values of the outer diameter of the small bronchi of the 1st order were by 35.23 % significantly lower compared to the previous time period of the experiment, accounting for 213.32±9.85 μm, and were by 10.25 % significantly lower compared to the values of the control group (p<0.05). The lumen diameter responded with significant decrease in the mean values of the morphometric parameters by 59.23 % compared to the values of week 4 of the experiment, accounting for 102.89±10.48 μm, that was by 36.99 % significantly lower compared to the values in the control group (p<0.05). The mean values of the height of the epitheliocytes were by 24.62 % significantly greater compared to the values of the previous time period of the experiment, accounting for 22.98±2.30 μm, that was by 0.30 % insignificantly lower compared to the control values (34.44 %) (p<0.05).

On week 12 of the consumption of the complex of food additives, the mean values of the outer diameter of the small bronchi of the 1st order accounted for 268.32±8.43 μm, that was by 25,78 % significantly greater compared to the values of week 8 of the experiment and by 12.89 % significantly greater compared to the values in the control group of animals (p<0.05). The lumen diameter was by 28.09 % significantly greater compared to the previous values and accounted for 131.79±10.52 μm, that was by 19.30 % significantly lower compared to the values in the control group (p<0.05). The height of the epitheliocytes insignificantly increased by 9.14 %, accounting for 25.08±2.24 μm, that also was by 8.81 % insignificantly greater compared to the values in the control group of animals (p<0.05).

On week 16 of the experiment, the values of the outer diameter of the small bronchi of the 1st order accounted for 248.67±9.17 μm, that was by 7.32 % significantly lower compared to the values of the previous time period of the experiment and by 4.62 % insignificantly greater compared to the control values (p<0.05). The lumen diameter was by 43.57 % greater compared to the values of week 12, accounting for 189.21±11.70 μm, that was also by 15.87 % significantly greater compared to the values in the control group (p<0.05). By the end of the experiment, the mean values of the height of the epitheliocytes of the small bronchi of the 1st order were by 19.50 % significantly greater compared to the values of the previous time period of the observation that was also by 30.02 % significantly greater compared to the control values, accounting for 29.97±2.29 (p<0.05).

The findings of the morphometric study of the small bronchi of the 2nd order of the lungs of the control rats have shown that the outer diameter and lumen diameter were 208,64±8,97 μm and 126,62±10,87 μm, respectively, and the mean values of the height of the epitheliocytes was 18,11±1,09 μm (Table 2).

On week 1 of the consumption of the complex of food additives insignificant constriction of the outer diameter by 0.64 % (207.31±9.42 μm; (p<0.05)) was established. The parameters of the outer diameter were by 18.46 % (103.24±9.50 μm (p<0.05)) significantly lower compared to the control group. The height of the epitheliocytes of the second-order small bronchi was 36.87±2.41 μm, that was by 103.59 % significantly greater compared to the values in the control group (p<0.05).

On week 4 of the experiment the outer diameter was 222.30±12.37 μm, that was by 7.23 % insignificantly greater compared to the values on week 1, as well as by 6.55 % (p<0.05) insignificantly greater compared to the control group of animals. The mean values of the lumen diameter were by 31.98 %

significantly greater compared to the values of the previous time period of the experiment, accounting for 136.26±12.04 μm, and was by 7.61 % insignificantly greater compared to the control values (p<0.05). The values of the height of the epitheliocytes of the second-order small bronchi was by 49.72 %, significantly lower compared to the previous time period of the experiment and were by 2.37 % insignificantly greater compared to the values in the control group of rats, accounting for 18.54±1.25 μm (p<0.05).

Table 2

**Morphometric parameters of the second-order small bronchi of the rat lungs**

| Parameters | Small bronchi of the 2nd order | | |
|---|---|---|---|
| | Outer diameter | Lumen diameter | Height of the epitheliocytes |
| Control | 208.64±8.97 | 126.62±10.87 | 18,11±1,09 |
| Week 1 | 207.31±9.42 | 103.24±9.50 * | 36,87±2,41 * |
| Week 4 | 222.30±12.37 | 136.26±12.04 ** | 18,54±1,25 ** |
| Week 8 | 193.97±11.60 ** | 90.76±9.44 *.** | 15.52±1.14 *.** |
| Week 12 | 216.19±9.75 ** | 72.31±8.54 *.** | 18.93±1.07 ** |
| Week 16 | 157.73±11.94 *.** | 45.16±2.46 *.** | 20.59±1.17 * |

Note * - P<0.05 compared to the control group; ** - P<0.05 compared to the previous time period of the observation.

On week 8 of the consumption of the complex of food additives, the mean values of the outer diameter were by 12.74 % (193.97±11.60 μm) significantly lower that was by 7.03 % insignificantly lower compared to the values of the control group (p<0.05). The lumen diameter of the second-order small bronchi was by 33,39 % and 28,32 % significantly lower compared to the values of the previous time period of the experiment and values of the control group, respectively, where its mean values were 90.76±9.44 μm (p<0.05). The height of the epitheliocytes was by 16.29 % (15.52 μm) significantly lower compared to the values on week 4 and by 14.30 % (p<0.05) compared to the values in the control group.

On week 12, consumption of the complex of food additives, involving monosodium glutamate, sodium nitrite and Ponceau 4R, led to significant increase in the mean values of the outer diameter of the second-order small bronchi of the rat lungs by 11.46 %, compared to the previous time period of the study and accounted for 216.19±9.75 μm; however, the values were by 3.62 % (p<0.05) insignificantly greater compared to the values of the control group. The mean values of the lumen diameter were by 20.33 % (72,31±8,54 μm) significantly lower compared to the values on week 8 and was also by 42.89 % (p<0.05) significantly lower compared to the mean values in the control group. The height of the epitheliocytes was by 21.97 % significantly greater compared to the previous time period of the study that was by 4.53 % insignificantly greater compared to the values in the control group with the mean value of 18.93±1.07 μm (p<0,05).

On week 16 of the experiment the mean values of the outer diameter accounted for 157.73±11.94 μm, that was by 27.04 % significantly lower compared to the findings of the previous time period of the experiment and also was by 24.40 % significantly lower compared to control values (p<0.05). The lumen diameter significantly constricted by 37,55 % (45.16±2.46 μm), that was by 64.33 % significantly lower compared to the values of the control group (p<0.05). The mean values of the height of the epitheliocytes of the second-order small bronchi were by 8.77 % insignificantly greater compared to week 12 of the experiment that was by 13.69 % significantly greater compared to the control group of rats and on week 16 accounted for 20.59±1.17 μm (p<0,05).

The findings of the morphometric study of the small bronchi of the 3rd order of the lungs of the control group have shown that the mean value of the outer diameter and lumen diameter were 169.80±11.30 μm and 96.23±9.50 μm, respectively, and the height of the epitheliocytes was 14,83±1,16 μm (Table 3).

On week 1 of the experiment the outer diameter was by 22,26 % significantly lower compared the control group and accounted for 132.00±9.59 (p<0.05). Significant constriction of the lumen diameter by 26.16 % to 71.06±7.37 μm (p<0.05) was also noted. The height of the epitheliocytes of the third-order small bronchi accounted for 27.35±2.26 μm, that was by 84.42 % significantly greater compared to the values on the control group (p< 0.05).

On week 4 of the study, the constriction of the outer diameter to 114.29±10.61 μm was established, that was by 13.42 % lower compared to the previous time period of the experiment and by 32.69 % significantly lower compared to the values in control group (p<0.05). The lumen diameter was by 57.30 % significantly lower compared to the findings on week 1 of the experiment and accounted for 30.34±2.43 μm, that was also by 68.47 % significantly lower compared to the values in the control group of animals

(p<0.05). The mean values of the height of the epitheliocytes accounted for 16.27±1.28 μm, that was by 40.51 % significantly lower compared to the values of the previous time period of the experiment as well as by 9.71 % insignificantly greater compared to the control values (p<0.05).

Table 3

**Morphometric parameters of the third-order small bronchi of the rat lungs**

| Parameters | Small bronchi of the 3rd order | | |
|---|---|---|---|
| | Outer diameter | Lumen diameter | Height of the epitheliocytes |
| Control | 169.80±11.30 | 96.23±9.50 | 14.83±1.16 |
| Week 1 | 132.00±9.59<br>* | 71.06±7.37<br>* | 27.35±2.26<br>* |
| Week 4 | 114.29±10.61<br>*,** | 30.34±2.43<br>*,** | 16.27±1.28<br>** |
| Week 8 | 109.06±10.36<br>* | 59.09±5.71<br>*,** | 12.02±1.11<br>*,** |
| Week 12 | 140.94±9.19<br>*,** | 42.20±2.61<br>*,** | 14.54±1.30<br>** |
| Week 16 | 109.36±10.22<br>*,** | 33.03±6.15<br>*,** | 15.51±1.16 |

Note * - P<0.05 compared to the control group; ** - P<0.05 compared to the previous time period of the observation.

On week 8 of the combined effect of monosodium glutamate, sodium nitrite and Ponceau 4R, the mean values of the outer diameter of the third-order small bronchi of rat lungs accounted for 109.06±10.36 μm, that was insignificantly similar to the values of the previous time period of the study and was by 35.77 % (p<0.05) significantly lower compared to the values in the control group. The lumen diameter was by 94,76 % significantly greater compared to the findings of week 4 and accounted for 59.09±5.71 μm, though was by 38.60 % significantly lower compared to its value in the control group (p<0.05). The height of the epitheliocytes was by 26.12 % significantly lower compared to the findings of the previous time period of the experiment and accounted for 12.02±1,11 μm and was by 18.95 % insignificantly lower compared to the values in the control group (p< 0.05).

On week 12 of the pollutants' impact on the third-order small bronchi of the rat lungs, the mean values of the outer diameter accounted for 140.94±9.19 μm, that was by 29.23 % significantly greater compared to the value on week 8 and by 17.00 % significantly lower compared to the value in the control group of rats (p<0.05). The height of the epitheliocytes accounted for 14.54±1.30 μm, that was by 20.97 % significantly greater compared to the value of the previous time period of the study and by 1.96 % insignificantly lower compared to the findings in the control group of animals (p <0.05).

At the end of the experiment of consumption of the complex of food additives the mean values of the outer diameter of the third-order small bronchi accounted for 109.36±10.22 μm, that was by 22.41 % and 35.39 % significantly lower compared to the values on week 12 and the values in the control group of animals, respectively (p<0.05). The lumen diameter was by 21.73 % and 65.68 % significantly lower compared to the values of the previous time period of the experiment and the values in the control group of rats, respectively, and on week 16 its values accounted for 33.03±6.15 μm (p<0.05). The height of the epitheliocytes was by 6.67 % insignificantly greater compared to the values in the previous time period of the study that was also by 4.59 % insignificantly greater compared to the values in the control group of animals and accounted for 15.51±1.16 μm (p<0.05).

Thus, consumption of the complex of food additives leads to changes in the morphometric parameters of the small bronchi of the rat lungs, that, at the early stages, is manifested by a significant constriction of the outer and lumen diameters of the small bronchi of all orders (Fig. 1a and Fig. 1b).

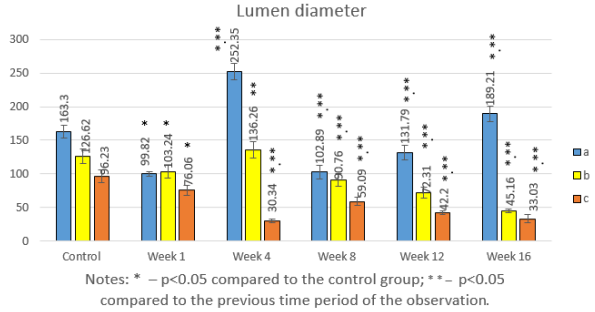



Fig. 1a. The dynamics of changes in the morphometric parameters of the outer diameter of the small bronchi of the rat lungs throughout the experiment: a – small bronchi of the 1st order, b – small bronchi of the 2nd order, c – small bronchi of the 3rd order.

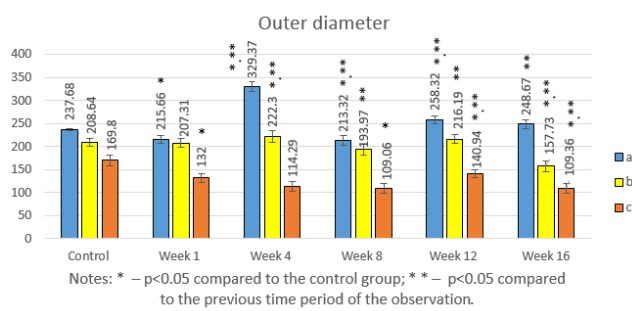



Fig. 1b. The dynamics of changes in the morphometric parameters of the lumen diameter of the small bronchi of the rat lungs throughout the experiment: a – small bronchi of the 1st order, b – small bronchi of the 2nd order, c – small bronchi of the 3rd order.

The above changes, at the initial stages, are caused, first of all, by the primary endogenous effect of the components of the complex of food additives, which was manifested by the constriction of the outer and lumen diameters of the small bronchi, associated with spasm of the exchange vessels, and the response of the loose fibrous connective tissue, with the progressive phenomena of hypoxia, which is part of the tunica adventitia, tunica submucosa and layers of the endomysium between the bundles of smooth muscle tissue of the muscular layer. These changes are confirmed by earlier studies on the effect of the complex of food additives on the state of the microcirculation [14] and are identified with the primary effect on the organs and tissues of other etiological factors [10, 11]. Following the experiment, the outer diameter of the small bronchi of the 1st and 2nd orders enlarges, indicating the development of nonspecific inflammation and swelling of the tunica adventitia in response to the development of hypoxia with the activation of mast cells (Fig. 2a and Fig. 2b) and the presence of leukocyte infiltration; the enlargement of the lumen diameter is apparently explained by the impact of sodium nitrite, as one of the components of the complex of food additives, on the smooth muscles of the muscular layer [12].

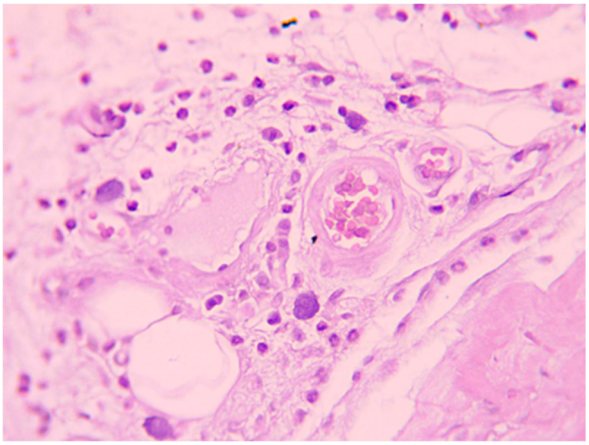


Fig. 2a. Mast cell activation on week 1 of consumption of the complex of food additives. H&E stain. Oc. lens: 10×magnification; ob. lens: 40× magnification.

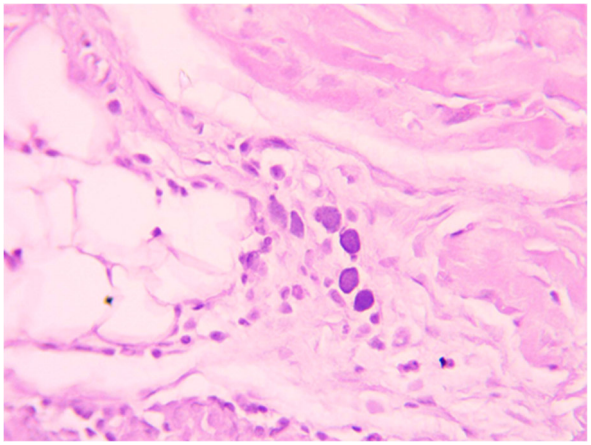


Fig. 2b. Origination of the mast cell chain and perivascular edema on week 4 of consumption of the complex of food additives. H&E stain. Oc. lens: 10×magnification; ob. lens: 40× magnification.

The small bronchi of the 3rd order responded with a significant constriction of both the outer and lumen diameters (Fig. 1a and Fig. 1b), which is connected, first of all, with the presence of a very thin tunica adventitia and tunica submucosa, as a result of which the impact of the alterative factor prevails over the body's protective mechanisms, which is manifested by progressive development of bronchospasm. At the end of the experiment, the compensatory and restorative reactions did not lead to a complete recovery of the morphometric parameters of the small bronchi, which was manifested by a significant constriction of the lumen diameter of the small bronchi of the 2nd and 3rd orders and responded by the compensatory dilatation of the small bronchi of the 1st order, which was manifested by the significant enlargement of the lumen diameter by 15.57 % compared to the parameters of the control group ($p<0.05$). The endogenous effect of the complex of monosodium glutamate, sodium nitrite and Ponceau-4R with subsequent leukocyte infiltration and the development of nonspecific inflammation led to changes in the morphometric parameters of the height of the epitheliocytes of the small bronchi of the rat lungs. The above phenomenon, at the early stages, was manifested by the significant increase in small bronchi of all orders, which is associated with goblet-cell hyperplasia (Fig. 3), which is apparently associated with the release of tumor necrosis factor from bronchiole mast cell granules, which induces the process of production of mucous secretion through cholinergic receptors on the membranes of goblet cells [2].

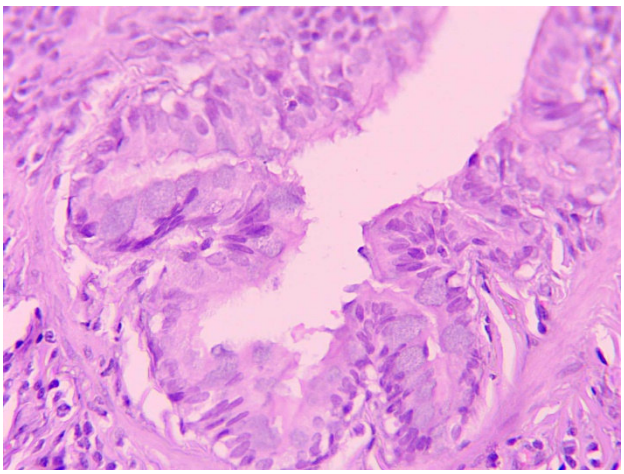
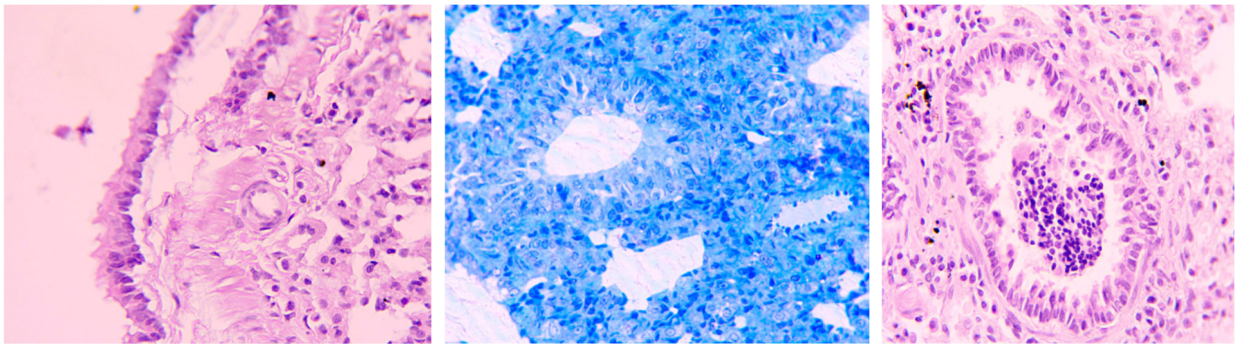


Fig. 3. The phenomena of goblet cell hyperplasia in the epithelial lining of the small bronchi of the rat lungs on week 1 of consumption of the complex of food additives. H&E stain. Oc. lens: 10×magnification; ob. lens: 40× magnification.

Subsequently, consumption of the complex of food additives led to an increase in the number of leukocytes in the mucous membrane due to the tension and strengthening of the local protective barrier,

namely eosinophils (Figs. 4a, 4b and 4c), the activity of which is associated with the production of both growth factors and the cytotoxic effect of the main protein on the ciliated epithelium, which is accompanied by increased desquamation of epitheliocytes [2] and is confirmed by a decrease in the mean values of the height of the cells in the middle terms of the experiment.



a b c

Fig. 4. Leukocyte infiltration of the mucous membrane of the small bronchi of the rat lungs on week 12-16 of the experiment: a – accumulation of eosinophils in the tunica submucosa; b – migration of eosinophils through the epithelium; c – leukocytes in the lumen of small bronchi. H&E stain (a, c) and methylene blue (b). Oc. lens: 10×magnification; ob. lens: 40× magnification.

Notably, bronchial cells potentiate the development of the inflammatory reaction by producing E selectin, which activates the adhesion and degranulation of eosinophils, which, due to their combined action, significantly contributes to the formation of bronchial hyperreactivity, characteristic of the asthma development [2]. At the end of the experiment, an increase in the mean values of the height of epitheliocytes is associated with an increase in the number of tall interstitial cells in the single-layer pseudostratified ciliated epithelium of small bronchi due to a compensatory-restorative reaction and an increase in the regenerative process, in response to the impact of the alterative factor; however, only in small bronchi of the 3rd order the height of epitheliocytes did not significantly differ from the control values, and in the small bronchi of the 1st and 2nd orders no complete recovery occurred.

## Conclusion

Consumption of the complex of food additives leads to a change in the morphometric parameters of the structural components of the small bronchi of the rat lungs, which at the early stages is manifested by a significant decrease in the morphometric parameters of the outer and lumen diameters with a significant increase in the height of the epitheliocytes in the small bronchi of all orders due to the primary endogenous impact of the components of the food additive complex, which is associated with spasm of the exchange blood vessels and the progressive phenomena of hypoxia. Subsequently, the impact of the alterative factor, which prevails over the protective mechanisms of the body, is manifested by the development of bronchospasm in the small bronchi of the 3rd order, the appearance of inflammatory infiltration in the bronchial walls and the formation of bronchial hyperreactivity, which is characteristic of the development of diseases of the respiratory system, including asthma.

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## FEATURES OF LIPOPEROXIDATION AND MORPHOLOGICAL CHANGES OF THE LUNGS IN EXPERIMENTAL DIABETES MELLITUS

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In recent decades, diabetes has become one of the most significant medical and social problems. The prevalence and incidence of diabetes have increased dramatically in the last few years. The experiments were performed on white male rats with streptozotocin-induced diabetes. Biochemical analysis has shown that in the conditions of experimental diabetes there is an intensification of lipid peroxidation processes throughout the study period, as evidenced by a significant increase in the content of active products of thiobarbituric acid ($p<0.001$). The probable increase in the level of secondary products of lipid peroxidation leads to a violation of the ultrastructural organization of the components of the respiratory part of the lungs, as indicated by the results of our electron microscopic study. We found that the most expressed changes of dystrophic-destructive nature are observed in the hemocapillaries of the alveolar wall. Red blood cells sludges, adhesion, and aggregation of white blood cells and platelets are observed in the lumen of microvessels that promote the capillary-trophic insufficiency.

**Key words:** streptozotocin-induced diabetes, lipid peroxidation, respiratory part of the lungs.

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## ОСОБЛИВОСТІ ЛІПОПЕРОКСИДАЦІЇ ТА МОРФОЛОГІЧНІ ЗМІНИ ЛЕГЕНЬ ПРИ ЕКСПЕРИМЕНТАЛЬНОМУ ЦУКРОВОМУ ДІАБЕТІ

За останні десятиліття цукровий діабет став однією з найактуальніших як медичних так і соціальних проблем. Поширеність та захворюваність цукровим діабетом різко зросла протягом останніх років. Експерименти проводено на білих щурах-самцях з стрептозотоцин-індукованим діабетом. Біохімічні дослідження сироватки крові показали, що в умовах змодельованого цукрового діабету спостерігається інтенсифікація процесів перекисного окиснення ліпідів протягом всього періоду дослідження про що свідчить достовірне збільшення вмісту активних продуктів тіобарбітурової кислоти ($p<0.001$). Вірогідне підвищення рівня вторинних продуктів перекисного окиснення ліпідів призводить до порушення ультраструктурної організації компонентів респіраторного відділу легень на що вказують результати проведеного нами електронномікроскопіного дослідження. Встановлено, що найбільш виражені зміни дистрофічно-деструктивного характеру спостерігаються в гемокапілярах альвеолярної стінки. У просвіті мікросудин відмічаються еритроцитарні сладжі, адгезія та агрегація лейкоцитів і тромбоцитів, що сприяє розвитку капіляротрофічної недостатності.

**Ключові слова:** стрептозотоцин-індукований діабет, перекисне окиснення ліпідів, респіраторний відділ легень.

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In recent decades, diabetes mellitus (DM) has become one of the most significant medical and social problems [7, 9, 12]. Despite the use of modern treatment strategies, the prevalence and incidence of DM have risen sharply in recent years, indicating a global epidemic. Scientists predict that in the 21st century diabetes will be a disease that reduces life on a global scale [6, 11]. According to the World Health Organization and the International Diabetes Federation (IDF), the number of people with DM worldwide will