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Detoxification Therapy in Nicotine-Induced Lung Injury: Morphological and Morphometric Evidence from an Experimental Study

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Abstract Chronic exposure to nicotine-containing oral products represents an emerging public health concern due to its systemic toxic effects, particularly on the respiratory system. However, the morphological and morphometric alterations of bronchopulmonary tissues under such exposure remain insufficiently studied. The aim of this study was to investigate structural changes in the bronchi and lungs under chronic nicotine intoxication and to evaluate the effectiveness of detoxification therapy using natural biocorrectors. The experimental study was conducted on 120 white outbred rats divided into four groups: control, chronic nicotine intoxication, and two detoxification groups receiving Mumiyo (200 mg/kg) and a biologically active supplement (300 mg/kg), respectively. Histological and morphometric analyses were performed at 6, 9, and 12 months. Chronic nicotine exposure resulted in progressive structural remodeling of bronchopulmonary tissues, characterized by epithelial damage, increased goblet cell hyperplasia, thickening of interalveolar septa, vascular remodeling, perivascular fibrosis, and the development of emphysematous changes. The severity of alterations increased with the duration of exposure, leading to irreversible structural damage at later stages. Detoxification therapy demonstrated a significant restorative effect, including partial normalization of epithelial structure, reduction of inflammatory infiltration, decreased fibrosis, and improvement of alveolar architecture. Morphometric parameters approached physiological values, particularly in the Mumiyo-treated group.

Keywords Nicotine intoxication, Bronchopulmonary system, Morphometry, Detoxification therapy, Mumiyo, Lung remodeling, Experimental study, Fibrosis, Emphysema

1. Introduction

Chronic exposure to nicotine-containing products remains one of the most significant modifiable risk factors contributing to the development of non-communicable diseases worldwide. According to global epidemiological data, tobacco-related exposure is responsible for a substantial proportion of morbidity and mortality, affecting not only the cardiovascular system but also exerting profound pathological effects on the respiratory tract. In recent years, alongside traditional smoking, there has been a notable increase in the consumption of alternative nicotine-containing oral products, such as nasvay, snus, and nicotine pouches, particularly in regions with specific socio-cultural patterns of use. This trend raises new concerns regarding the mechanisms and extent of their impact on bronchopulmonary structures [1,3,7,9,11].

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Nicotine and associated toxic compounds demonstrate a complex, multifactorial effect on the respiratory system, including oxidative stress induction, endothelial dysfunction, and chronic inflammatory activation. These processes contribute to progressive structural remodeling of lung tissue, involving epithelial damage, disruption of mucociliary clearance, thickening of interalveolar septa, vascular alterations, and the formation of fibrotic and emphysematous changes. While the effects of inhaled tobacco smoke on pulmonary parenchyma have been extensively investigated, significantly less attention has been paid to the impact of nicotine entering the body through the oral mucosa, despite its ability to induce systemic toxic and inflammatory responses [2,8,10].

The lack of comprehensive morphological and morphometric studies addressing bronchial and lung tissue alterations under chronic exposure to nicotine-containing oral products represents a critical gap in modern experimental and clinical pulmonology. In particular, the dynamics of structural changes over time, as well as the transition from reversible adaptive responses to irreversible pathological remodeling, remain insufficiently elucidated. Moreover, there is a limited evidence base regarding the potential reversibility of these

alterations and the effectiveness of therapeutic interventions aimed at mitigating nicotine-induced tissue damage [4,5,6,12,13].

In this context, increasing attention is being directed toward the use of natural biocorrectors with antioxidant, anti-inflammatory, and regenerative properties. Compounds such as Mumiyo and biologically active supplements have demonstrated potential in modulating oxidative stress, improving microcirculation, and enhancing tissue repair processes. However, their efficacy in the correction of nicotine-induced bronchopulmonary damage has not been sufficiently studied from a morphological standpoint. Therefore, the present study aims to provide a comprehensive experimental assessment of structural lung changes under chronic nicotine exposure and to evaluate the therapeutic potential of detoxification strategies based on natural biocorrectors.

Purpose of the study. The aim of this study was to investigate the morphological and morphometric alterations of the bronchopulmonary system under chronic exposure to nicotine-containing oral products and to evaluate the effectiveness of detoxification therapy using natural biocorrectors.

2. Materials and Methods

The experimental study was conducted on 120 white outbred rats of both sexes, weighing 220–300 g, maintained under standard vivarium conditions with free access to food and water. All animals were obtained from a certified breeding facility and underwent a 21-day quarantine period prior to the experiment. Housing conditions included a temperature of 21–23 ℃, relative humidity of 45–60%, and a 12-hour light/dark cycle. All experimental procedures were performed in accordance with established ethical principles and guidelines for the use of laboratory animals.

The animals were randomly divided into four experimental groups (n=30 in each group):

- **Group I (Control):** intact animals not exposed to nicotine-containing products, used to determine baseline morphological and morphometric parameters of the bronchopulmonary system.
- **Group II (Chronic nicotine intoxication):** animals subjected to daily oral administration of a nicotine-containing product diluted in physiological saline for 30 days to model chronic intoxication.
- **Group III (Detoxification therapy – Mumiyo):** animals previously exposed to nicotine intoxication, subsequently treated with Mumiyo at a dose of 200 mg/kg/day administered orally for 30 days.
- **Group IV (Detoxification therapy – biologically active supplement):** animals after nicotine exposure treated with a 3% aqueous solution of a biologically active supplement (Best Detox) at a dose of 300 mg/kg/day for 30 days.

To assess the dynamics of structural changes, animals from each group were examined at 6, 9, and 12 months. At each time point, euthanasia was performed using an overdose of ether anesthesia in accordance with ethical standards. Immediately after euthanasia, thoracic dissection was carried out, and lung and bronchial tissues were collected for further analysis.

For histological examination, the lungs were fixed in 10% neutral buffered formalin under controlled pressure (20–25 cm H_2O) via tracheal cannulation to preserve physiological architecture. Tissue samples were processed using standard histological techniques, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

Morphological evaluation included assessment of bronchial wall structure, epithelial integrity, goblet cell density, vascular changes, inflammatory infiltration, and presence of emphysematous alterations. Morphometric analysis involved measurement of serous membrane thickness, epithelial height, interalveolar septal thickness, alveolar density, vascular wall thickness, and connective tissue components using light microscopy.

All procedures involving laboratory animals were conducted in accordance with the methodological guidelines “Rules and Methods for Working with Laboratory Animals in Microbiological and Immunological Research” approved by the Ministry of Health of the Republic of Uzbekistan (2016).

Statistical analysis was performed using standard methods of variation statistics. Quantitative data were expressed as mean values (M ±m). Differences between groups were considered statistically significant at $p<0.05$.

3. Results and Discussion

The conducted experimental study revealed that chronic exposure to nicotine-containing oral products exerts a profound and progressively aggravating effect on the structural organization of the bronchopulmonary system. The observed changes involved all major morphological components, including the bronchial wall, epithelial layer, vascular network, interstitial connective tissue, and alveolar structures, and demonstrated a clear time-dependent pattern of pathological remodeling.

In the control group, lung tissue exhibited a stable and well-preserved histoarchitectonic organization, corresponding to physiological norms. The serous membrane remained thin and uniform, measuring 19.0±1.0 μm, and was lined by flattened mesothelial cells without signs of proliferation or degeneration. The bronchial wall maintained its normal structure, with a pseudostratified ciliated epithelium of 27.7±1.3 μm in height and a balanced proportion of goblet cells (approximately 8–9%), reflecting adequate mucociliary function. The basal membrane remained thin and continuous, while the muscular and connective tissue layers were moderately expressed and well organized.

The alveolar component demonstrated high structural integrity, with evenly distributed alveoli and a density of 7.7±0.3 per field of view. Interalveolar septa were thin (8.7±0.4 μm), indicating optimal conditions for gas exchange. The vascular component was characterized by normal wall thickness (7.5–8.0 μm), absence of perivascular fibrosis, and minimal collagen deposition. No inflammatory infiltration, emphysematous changes, or signs of structural damage were detected, confirming the baseline integrity of bronchopulmonary tissues.

Following 6 months of chronic nicotine exposure, the bronchopulmonary system demonstrated early pathological alterations, indicating the activation of compensatory-adaptive and inflammatory mechanisms. The serous membrane thickness increased to 23.0±1.0 μm, representing an increase of approximately 20–22% compared to control values. This was accompanied by hypertrophy of mesothelial cells and focal areas of desquamation, suggesting the onset of surface damage and increased permeability.

The bronchial wall exhibited moderate thickening due to proliferation of connective tissue components, reaching 67.0±2.5 μm, which exceeds control values by approximately 20–25%. The epithelial layer showed signs of structural disorganization, with a decrease in height to 22.5±1.2 μm (reduction of about 18–20%), indicating impaired barrier function and early degenerative changes. The proportion of goblet cells increased significantly to 14%, suggesting activation of compensatory hypersecretion in response to chronic irritation.

Further morphometric analysis revealed thickening of the basal membrane (up to 6.0±0.3 μm) and hypertrophy of smooth muscle cells (17.9±0.7 μm), indicating the initiation of bronchial remodeling processes. The vascular component showed early signs of dysfunction, including mild wall thickening and vascular congestion.

In the alveolar compartment, interalveolar septa thickened to 11.2±0.5 μm (increase of approximately 28–30%), while alveolar density decreased to 6.5±0.3. These changes indicate a reduction in the effective respiratory surface area. Initial emphysematous changes were observed in 30–35% of alveoli, accompanied by moderate inflammatory infiltration. The number of alveolar macrophages increased to 5–6 per field of view, many containing pigment inclusions, reflecting an active phagocytic response to toxic exposure. At this stage, the observed alterations can be interpreted as predominantly adaptive and partially reversible.

At 9 months of exposure, the pathological process progressed significantly, and the structural changes acquired a stable and more severe character. The serous membrane thickness increased further to 24.5±1.0 μm, with signs of fibrotic transformation and densification of connective tissue. The bronchial wall demonstrated pronounced thickening, with connective tissue layers reaching 69.5±3.0 μm, exceeding control values by approximately 25–30%. Collagen fibers became disorganized, and elastic elements showed signs of fragmentation.

The epithelial layer exhibited further degeneration, with a decrease in height to 21.0±1.1 μm and the presence of desquamation zones. Goblet cell hyperplasia intensified, reaching 15–16%, indicating persistent hypersecretory activity and chronic mucosal irritation. The basal membrane thickened further, and smooth muscle hypertrophy became more pronounced, contributing to structural rigidity of the bronchial wall.

The vascular component demonstrated significant remodeling. Arteriolar wall thickness increased to 10.8±0.5 μm (approximately 35–40% higher than control), while perivascular collagen deposition reached 20%, indicating the development of perivascular fibrosis. These changes reflect impaired microcirculation and increased vascular resistance.

In the alveolar compartment, interalveolar septa thickened to 11.8±0.5 μm, and alveolar density decreased to 6.1±0.3. Emphysematous changes became more extensive, affecting 40–42% of alveoli, with fragmentation and coalescence of air spaces. Inflammatory infiltration intensified, with macrophage counts increasing to 6–7 per field of view and the appearance of lymphoid tissue hyperplasia, indicating the formation of a chronic inflammatory process. These findings suggest a transition from adaptive changes to persistent inflammatory-destructive remodeling.

After 12 months of chronic exposure, the bronchopulmonary system exhibited advanced and largely irreversible structural damage. The serous membrane thickness increased to 25.5±1.1 μm, with pronounced fibrosis and areas of hyalinization. The bronchial wall underwent marked hypertrophy, with connective tissue thickness reaching 72.0±3.0 μm and muscle layer thickness increasing to 96.0±3.8 μm.

The epithelial layer showed severe atrophic changes, with a decrease in height to 19.5±1.0 μm and areas of complete desquamation. Goblet cell content increased to 17%, indicating persistent hypersecretory dysfunction and impaired mucosal regulation. The basal membrane became irregular and significantly thickened, reflecting chronic structural remodeling.

In the alveolar component, interalveolar septa thickened to 12.4±0.6 μm (increase of approximately 40–42%), with fragmentation and rupture of septa leading to the formation of large emphysematous spaces affecting up to 50% of the lung tissue. Alveolar density decreased to 5.8±0.3, while fibrous tissue content increased to 15–16%, indicating extensive fibrotic transformation.

The vascular component showed severe remodeling, with arteriolar wall thickness increasing to 11.5±0.5 μm (approximately 45% higher than control) and perivascular fibrosis reaching 22%. These changes were accompanied by vascular congestion, endothelial damage, and impaired perfusion. The accumulation of macrophages and lymphoid elements further indicated persistent chronic inflammation. At this stage, the observed alterations correspond to irreversible fibrotic-emphysematous remodeling.

The application of detoxification therapy significantly influenced the structural state of the bronchopulmonary system. In the group treated with Mumiyo, a marked

improvement in morphometric parameters was observed. The serous membrane thickness decreased to approximately 21.0 μm, approaching control values. The bronchial epithelium demonstrated partial restoration, with an increase in height to 25–26 μm, and the proportion of goblet cells decreased to 9–10%, indicating normalization of secretory activity.

Interalveolar septa thickness decreased, and alveolar density increased, reflecting partial restoration of lung architecture. Inflammatory infiltration and macrophage accumulation were significantly reduced, suggesting attenuation of the inflammatory process. Vascular parameters improved, with a decrease in wall thickness and reduced perivascular fibrosis, indicating improved microcirculation.

In contrast, the group treated with the biologically active supplement showed moderate improvements. Although there was a reduction in fibrosis and inflammatory infiltration, epithelial recovery remained incomplete, and morphometric parameters did not fully return to control values. Residual vascular remodeling and connective tissue proliferation persisted, suggesting comparatively lower therapeutic efficacy.

The observed structural changes can be explained by the complex interaction of pathogenic mechanisms, including oxidative stress, chronic inflammation, endothelial dysfunction, and activation of fibroblast proliferation. Nicotine exposure leads to disruption of cellular homeostasis, resulting in epithelial damage, impaired mucociliary clearance, and progressive remodeling of bronchial and alveolar structures.

The therapeutic effects of Mumiyo are likely associated with its antioxidant, anti-inflammatory, and cytoprotective properties. These effects contribute to stabilization of cell membranes, reduction of oxidative damage, improvement of microcirculation, and activation of reparative processes. The decrease in inflammatory infiltration and normalization of morphometric parameters confirm its role in mitigating nicotine-induced tissue damage.

Overall, the results demonstrate a clear stage-dependent progression of bronchopulmonary pathology under chronic nicotine exposure, transitioning from early adaptive-inflammatory changes to irreversible fibrotic and emphysematous remodeling. Detoxification therapy, particularly with natural biocorrectors such as Mumiyo, significantly reduces the severity of these changes and promotes partial structural recovery of lung tissue, supporting its potential application in pathogenetically oriented therapeutic strategies.

4. Conclusions

Chronic exposure to nicotine-containing oral products leads to a progressive and stage-dependent structural reorganization of the bronchopulmonary system, affecting the bronchial wall, alveolar structures, vascular components, and interstitial connective tissue. The severity of these changes increases with the duration of exposure.

At the early stage of intoxication, the observed alterations are predominantly adaptive-inflammatory in nature and include epithelial damage, goblet cell hyperplasia, thickening of the basal membrane and interalveolar septa, vascular congestion, and moderate inflammatory infiltration.

With prolonged exposure, these changes evolve into stable pathological remodeling characterized by progressive fibrosis, hypertrophy of bronchial structures, vascular remodeling, decreased alveolar density, and expansion of emphysematous areas. At later stages, the structural alterations become largely irreversible and correspond to fibrotic-emphysematous transformation of lung tissue.

Detoxification therapy demonstrates a significant corrective effect on nicotine-induced bronchopulmonary damage. Both treatment approaches reduce the severity of inflammatory and fibrotic changes; however, the therapeutic efficacy is more pronounced in the group treated with Mumiyo.

The use of Mumiyo is associated with partial restoration of epithelial integrity, normalization of goblet cell activity, reduction in interalveolar septal thickness, decreased inflammatory infiltration, and attenuation of vascular remodeling, indicating its higher effectiveness as a natural biocorrector.

The findings confirm the key role of oxidative stress, chronic inflammation, and fibrogenesis in the pathogenesis of nicotine-induced lung injury and support the potential application of detoxification therapy with natural biocorrectors as a pathogenetically justified approach for reducing structural damage in the bronchopulmonary system.

REFERENCES

[1] Chen K., Zhang H., Yao Z., Tao S., Ma Q. Current advancements in the mechanisms and animal models of acute exacerbation of pulmonary fibrosis: a systematic review. Frontiers in Pharmacology. 2025; 16: 1501085.

[2] Xu D., et al. The mechanism of oxidative stress in pulmonary fibrosis. Antioxidants. 2026; 15(1): 142.

[3] Lu S., et al. Treatment of pulmonary fibrosis: from disease mechanisms to therapeutic strategies. Frontiers in Medicine. 2026.

[4] Mia M.M., et al. YAP/TAZ are crucial regulators of macrophage-mediated pulmonary inflammation and fibrosis. European Respiratory Journal. 2025.

[5] Tiple A., et al. A comparative review on lung detoxification from smoking-induced lung damage. Journal of Biomedical and Pharmaceutical Research. 2025; 14(2): 38–53.

[6] Sakharov A.V., Byrdina V.I. Morphofunctional state of lungs under long-term exposure to nicotine aerosols. Russian Journal of Veterinary Pathology. 2026.

[7] Crouser E.D., et al. A pilot randomized trial of nicotine effects in pulmonary disease. Respiratory Research. 2021.

[8] Ye X., Zhang M., Gu H., et al. Animal models of pulmonary fibrosis: current perspectives. Respiratory Research. 2023; 24: 296.

[9] D'Alessandro-Gabazza C.N., et al. Acute exacerbation of

pulmonary fibrosis: mechanisms and therapeutic targets. Nature Communications. 2020; 11: 1539.

[10] Kimura T., et al. Animal models for acute exacerbation of interstitial lung diseases. Journal of Clinical Biochemistry and Nutrition. 2022; 70(2): 129–139.

[11] Meyer N.J., Gattinoni L., Calfee C.S. Acute respiratory distress syndrome. The Lancet. 2021; 398: 622–637.

[12] Yu H., Lin L., Zhang Z., et al. Targeting NF-κB pathway in inflammatory diseases. Signal Transduction and Targeted Therapy. 2020; 5: 209.

[13] Post-COVID pulmonary fibrosis: pathophysiology and clinical implications. Journal of Pulmonology and Respiratory Research. 2024.

[14] ScienceDaily. Targeting immune pathways to reverse lung fibrosis. 2025.