

Morphological and Morphometric Changes in the Pancreas of 15-Month-Old Rats After Nicotine-Alcohol Intoxication and Correction with Turmeric

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Abstract Background: The pancreas is a highly specialized organ responsible for regulating digestive and metabolic processes. Increased exposure to nicotine and alcohol leads to significant disturbances in pancreatic morpho-functional integrity. In recent years, growing attention has been directed toward the protective effects of natural biologically active compounds such as curcumin. **Objective:** To evaluate morphological and morphometric changes in the pancreas of 15-month-old rats under nicotine-alcohol intoxication and to determine the corrective efficacy of a turmeric-based phytopreparation. **Materials and Methods:** The study was conducted on 45 outbred white rats aged 15 months, divided into three groups: control, experimental, and phytocorrection. Intoxication was induced using established experimental models, while the phytopreparation was administered intragastrically at a dose of 0.5 ml. Histological analysis was performed using hematoxylin-eosin and Van Gieson staining. Morphometric parameters of both exocrine and endocrine components were assessed. **Results:** Nicotine-alcohol intoxication caused severe pancreatic damage characterized by disorganization of acinar structures, cytoplasmic vacuolization, reduction of zymogen granules, and nuclear degeneration. Morphometric analysis revealed a decrease in acinar diameter, area, and exocrinocyte size, along with an increased nuclear-cytoplasmic ratio. More pronounced alterations were observed in the endocrine apparatus, including reductions in islet area, endocrinocyte number, and cell density. Marked stromal fibrosis developed, with increased collagen content compared to the control group. Application of phytocorrection led to partial restoration of pancreatic morphology, reduction of fibrosis, and improvement of morphometric parameters. **Conclusion:** Nicotine-alcohol intoxication induces pronounced dystrophic and fibrotic changes in both exocrine and endocrine components of the pancreas in 15-month-old rats. Administration of a turmeric-based phytopreparation reduces morphological damage and improves morphometric indices. These effects are associated with the antioxidant and anti-inflammatory properties of curcumin, supporting its potential use in the prevention and treatment of toxic pancreatic injury.

Keywords Pancreas, Intoxication, Morphology, Morphometry, Turmeric

1. Introduction

The pancreas, as a highly specialized mixed organ, plays an important role in regulating digestive processes and carbohydrate metabolism. Its parenchyma consists of acinar complexes, interlobular ducts, and hormonally active islets of Langerhans, and the micromorphological integrity of these structures ensures the functional stability of the organ [14,18].

In recent decades, due to the increasing consumption of nicotine and alcohol, inflammatory and dystrophic diseases of the pancreas have become a global medical and social problem [21]. From a morphological point of view, these changes are characterized by disorganization of acinar architecture, cytoplasmic vacuolization, reduction of zymogen granules, nuclear pyknosis, and karyorrhexis [15]. In addition, edema of the interstitial tissue, increased fibroblastic activity, and microcirculatory disturbances are observed.

Morphometric analyses demonstrate a statistically significant decrease in acinar area and volume, a relative increase in the stromal component, and a reduction in β -cell density in the endocrine apparatus [6,23]. These alterations contribute to impaired insulin secretion and the development of metabolic dysfunction.

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In recent years, therapeutic approaches based on natural biologically active compounds, particularly phytopreparations, have been considered a promising strategy for correcting toxic and inflammatory damage. Curcumin, the main polyphenolic compound in turmeric, exhibits multiple molecular mechanisms of action, including inhibition of the NF- κ B signaling pathway, suppression of cytokine expression, enhancement of antioxidant enzyme activity, and stabilization of mitochondrial homeostasis [2,17,19]. Furthermore, curcumin modulates apoptosis and promotes tissue repair by stimulating cell proliferation [12].

It should be noted that under conditions of nicotine-alcohol intoxication, especially in the context of age-related changes, the effects of curcumin-based phytopreparations on the morphological and morphometric parameters of the pancreas have not been sufficiently systematically investigated.

Aim of the study. To evaluate morphological and morphometric changes in the pancreas of 15-month-old outbred white rats under experimental nicotine-alcohol intoxication and to assess the protective role of a turmeric-based phytopreparation.

2. Materials and Methods

The study was conducted on 15-month-old outbred white rats. A total of 45 experimental animals were selected and divided into three groups: control group (n=15), experimental group exposed to nicotine-alcohol intoxication (n=15), and correction group (n=15).

The rats met representativeness criteria in terms of age, body weight, nutrition, and housing conditions. Animals in the control and experimental groups had free access to food, consisting mainly of grains and vegetables.

Nicotine intoxication was induced using the model proposed by Solomina A.S. (2011). Alcohol intoxication was modeled according to the methods of Sidorov P.I. (2002) and Knyshova L.P. (2016). The phytopreparation was administered intragastrically via a probe at a dose of 0.5 ml.

At the end of the study, animals were euthanized in the morning on an empty stomach using instant decapitation under ether anesthesia in compliance with all bioethical standards [5,8,10,11]. Tissue samples were prepared for histological analysis and stained with hematoxylin-eosin and Van Gieson stains.

3. Results

According to the study results, in the control group of rats, the exocrine pancreas was morphologically intact, with well-preserved acini, pyramidal acinar cells, and retained secretory granules. Morphometric parameters were as follows: acinus diameter $29.0 \pm 0.7 \mu\text{m}$, acinus area $860.0 \pm 30.0 \mu\text{m}^2$, epithelial height $11.6 \pm 0.4 \mu\text{m}$; exocrinocyte area

$120.0 \pm 5.0 \mu\text{m}^2$ (nucleus $18.7 \pm 0.7 \mu\text{m}^2$, cytoplasm $101.0 \pm 5.0 \mu\text{m}^2$), nuclear-cytoplasmic ratio 0.18 ± 0.01 . The number of cells per acinus was 6.7 ± 0.2 , the relative exocrine parenchyma area was $71.5 \pm 1.4\%$, and the intralobular duct diameter was $13.0 \pm 0.6 \mu\text{m}$.

In the endocrine apparatus, the islets were large and densely cellular: islet area $14.2 \pm 0.5 \times 10^3 \mu\text{m}^2$, diameter $122.0 \pm 7.0 \mu\text{m}$, number of endocrinocytes per islet 108.0 ± 4.0 , cell density $7.2 \pm 0.3 \times 10^{-3} \text{ cells}/\mu\text{m}^2$, endocrinocyte area $71.0 \pm 3.0 \mu\text{m}^2$; the relative endocrine area was $2.30 \pm 0.10\%$, with 1.65 ± 0.10 islets.

In the experimental group, intoxication induced atrophic-dystrophic changes in the exocrine part, including vacuolization of acinar cells, reduction of secretory granules, blurring of acinar borders, and dilation of ductal structures. Morphometrically, the acinus diameter decreased to $25.0 \pm 0.5 \mu\text{m}$ (-14%, $p \leq 0.05$), acinus area to $700.0 \pm 25.0 \mu\text{m}^2$ (-19%, $p \leq 0.05$), and epithelial height to $10.5 \pm 0.3 \mu\text{m}$ (-9%, $p \leq 0.05$).

Exocrinocyte area decreased to $92.0 \pm 4.0 \mu\text{m}^2$ (-23%, $p \leq 0.05$), with nucleus $15.5 \pm 0.4 \mu\text{m}^2$ and cytoplasm $76.0 \pm 4.0 \mu\text{m}^2$; the nuclear-cytoplasmic ratio increased to 0.20 ± 0.01 ($p \leq 0.05$). The number of cells per acinus decreased to 5.8 ± 0.2 ($p \leq 0.05$). The relative exocrine parenchyma area decreased to $63.0 \pm 1.3\%$, while the intralobular duct diameter increased to $20.0 \pm 0.9 \mu\text{m}$ ($p \leq 0.05$), indicating intensified chronic remodeling.

Damage to the endocrine apparatus was more pronounced: islet area decreased to $9.0 \pm 0.4 \times 10^3 \mu\text{m}^2$ (-37%, $p \leq 0.05$), diameter to $100.0 \pm 6.0 \mu\text{m}$; the number of endocrinocytes per islet decreased to 70.0 ± 3.0 (-35%, $p \leq 0.05$), and cell density to $5.6 \pm 0.2 \times 10^{-3} \text{ cells}/\mu\text{m}^2$ ($p \leq 0.05$). Endocrinocyte area decreased to $55.0 \pm 2.0 \mu\text{m}^2$ ($p \leq 0.05$), and the relative endocrine area to $1.50 \pm 0.10\%$, with 1.10 ± 0.10 islets recorded.

Thus, in 15-month-old outbred white rats under chronic intoxication, reduction of the endocrine component was more pronounced and persistent than exocrine changes.

In the control group, age-related stromal fibrosis was observed. Collagen fibers were densely arranged around vessels and ducts, as well as along interlobular septa. The collagen area fraction was $35.2 \pm 1.3\%$.

In the experimental group, fibrosis reached a maximal level. The stroma was expanded, with large collagen bundles occupying a significant portion of the parenchyma; thick fibrous capsules formed around acini, and vascular walls showed hyalinosis. The collagen area fraction increased to $58.6 \pm 2.3\%$, which was 66.5% higher than in the control group ($p \leq 0.05$).

In the phytocorrection group, a positive effect of treatment was observed. Fragmentation and more diffuse distribution of collagen fibers were noted, although the stroma remained relatively dense. The collagen area fraction decreased to $48.1 \pm 1.9\%$, which was 17.9% lower than in the intoxication group ($p \leq 0.05$).

4. Discussion

The obtained results demonstrate that nicotine–alcohol intoxication in 15-month-old outbred white rats induces profound morphological and morphometric changes in the pancreas. Signs such as disorganization of acinar structures, vacuolization, reduction of zymogen granules, and nuclear degradation confirm the activation of dystrophic and autolytic processes [6,15,20].

Morphometric findings, including a decrease in acinar diameter and area, reduction in exocrinocyte size, and an increase in the nuclear–cytoplasmic ratio, indicate disruption of cellular metabolism and a decline in secretory activity [14,9,22].

In the endocrine apparatus, a significant decrease in islet area and the number of endocrinocytes leads to β -cell reduction, thereby increasing the risk of hormonal dysfunction [23,4]. At the same time, the intensification of fibrotic processes in the stroma and the increased proportion of collagen fibers are interpreted as consequences of impaired microcirculation and chronic hypoxia [3,15]. This condition indicates activation of remodeling processes in the pancreas.

The positive changes observed in the phytocorrection group can be explained by the antioxidant and anti-inflammatory effects of curcumin contained in turmeric. It reduces the impact of free radicals, protects cell membranes, and stimulates reparative processes [2,17,19]. Partial restoration of morphometric parameters confirms the effectiveness of these mechanisms. However, the absence of complete normalization is associated with the limited regenerative capacity related to aging [1,16].

5. Conclusions

The results of the conducted experimental study scientifically demonstrated that nicotine–alcohol intoxication in 15-month-old outbred white rats has a significant negative effect on the morphological and morphometric state of the pancreas. In the exocrine part, disorganization of acinar structures, cellular dystrophy, and a reliable decrease in morphometric parameters were identified, which was noted to be associated with a reduction in secretory activity.

In the endocrine apparatus, a decrease in islet area and the number of endocrinocytes was shown to lead to β -cell reduction, which in turn may create conditions for disruption of hormonal homeostasis. At the same time, the increase in fibrotic processes in the stromal component and the rise in collagen fiber content confirmed the activation of chronic remodeling processes.

The use of a turmeric-based phytopreparation led to a partial regression of morphological changes, a reduction in the degree of fibrosis, and a relative improvement in morphometric indicators. This effect is explained by the antioxidant, anti-inflammatory, and cytoprotective properties of curcumin.

Thus, the obtained results demonstrate the effectiveness of curcumin-based phytotherapy in reducing pancreatic damage under nicotine–alcohol intoxication and substantiate its potential use in experimental and clinical studies.

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