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Herbal medicine for experimental type 2 diabetes and atherosclerosis

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Abstract

Introduction. In the present era, atherosclerosis and type 2 diabetes represent the most socially significant diseases. Furthermore, the situation is exacerbated by the prevalence of chronic stress among the Ukrainian population. Among the organs most affected by this process, the liver is of particular significance.

Aim. The objective of this study is to examine the impact of herbal preparations on the restructuring of liver tissue in the context of experimental atherosclerosis and diabetes.

Materials and methods. The study was conducted on a group of 50 male rats. The classical model of atherosclerosis proposed by Anichkov and the dexamethasone suppression model of diabetes were employed in this study. A decoction of Transcarpathia medicinal plants (prepared according to our own recipe) was used as a prophylactic agent.

Results. The experimental model of atherosclerosis and diabetes revealed the development of degenerative changes in the liver. These changes are most evident in the group that has undergone two simulated pathological processes. The prophylactic administration of traditional medicinal plants from Transcarpathia was observed to have a pronounced hepatoprotective effect.

Conclusions. The experimental induction of atherosclerosis and diabetes in animals has been observed to result in degenerative alterations to the liver parenchyma and stroma. The prophylactic administration of a decoction of medicinal plants from Transcarpathia has been demonstrated to exert a hepatoprotective effect, as evidenced by morphological studies.
Key words: atherosclerosis, type 2 diabetes, liver, herbal remedy protection.

Introduction. The prevailing political circumstances in Ukraine are exerting a deleterious impact on the health of the Ukrainian population, precipitating a marked surge in the prevalence of patients with atherosclerosis and type 2 diabetes. This phenomenon is not confined to the organs of the cardiovascular system but also affects the digestive system, particularly the liver. Domestic medical practitioners have already issued a warning that the development of acute and chronic stress in our fellow citizens represents the foundation for the proliferation and intensification of atherosclerosis and its associated manifestations [4].

Despite the fact that the famous words of N. Anichkov, "without cholesterol, there is no atherosclerosis", have been over a century old, the value of his discovery is still considered to be among the ten most important in the field of medicine by the American Academy of Sciences. The contribution of N. Anichkov to the scientific understanding of the role of cholesterol in the aetiology of atherosclerosis is considered to be on a par with R. Koch's discovery of the tuberculosis bacillus. The well-known postulate remains relevant despite the proliferation of theories regarding the origin and development of atherosclerosis. However, the data from American and European studies unequivocally confirm that cholesterol plays a pivotal role in atherogenesis. Anichkov was among the first to propose that atherogenesis has a systemic nature, a hypothesis that has since been widely accepted [8].

Recently, there has been a growing recognition of the link between atherosclerosis and type 2 diabetes. It is postulated that diabetes mellitus, a severe progressive endocrine disease, may have an etiopathogenetic relationship with atherosclerosis [10].

It is generally accepted among researchers that atherosclerosis and diabetes are symptoms of the metabolic syndrome [3]. Consequently, it may be possible to identify a common cause or relationship between the three conditions [5].

In the USA, it was estimated that high-tech methods of treating atherosclerosis did not affect total mortality, with a contribution of approximately 5% [8]. Despite the advent of novel therapeutic modalities, the management of patients with type 2 diabetes mellitus remains challenging and frequently unsatisfactory [5].

The ongoing dissemination of cardiovascular diseases in Ukraine and globally gives rise to the necessity of identifying and implementing novel approaches to their treatment and prevention [1]. It was further observed that no synthetic substances had been developed over the previous decade. The least harmful and most therapeutically effective drugs of natural origin, which are less toxic and have a milder effect, are due to the affinity of plant and animal cell metabolism. Plants, as a principal component of nutrition, are incorporated into the metabolic process and exert a beneficial influence on all organs and their functional status. They contribute to optimal bioavailability and multifaceted action due to a diverse range of biologically active compounds [7].

The primary links in the pathogenesis of atherosclerosis and type 2 diabetes are closely associated with the functional status of the gastrointestinal tract, particularly the liver. Oxidative stress, endothelial dysfunction and alterations in the lipid cytokine spectrum of the blood result in liver function disorders. The corresponding imbalance in the regulation of carbohydrate metabolism contributes to the fact that chronic hyperglycemia, which is present in type 2 diabetes, triggers a cascade of pathological reactions [3].

A substantial literature exists on the separate study of liver structure in experimental atherosclerosis and diabetes. However, these diseases were previously considered as distinct nosological entities [9].

Aim

The objective of our study was to examine the structural remodelling of the liver during the simultaneous modelling of atherosclerosis and type 2 diabetes, as well as the hepatoprotective effect of traditional medicinal plants from Transcarpathia from an evidence-based medicine perspective.

Materials and methods

The study was based on observations made on 50 white laboratory rats. The animals were distributed into five groups, with each group comprising ten individuals. Group 1 comprised intact rats, Group 2 rats that were modelled with diabetes (pre-diabetes), Group 3 rats that were modelled with experimental atherosclerosis according to Anichkov's classic method, Group 4 rats that were subjected to a simultaneous simulation of atherosclerosis and diabetes, and Group 5 rats that were administered a herbal preparation derived from traditional medicinal plants native to Transcarpathia with the objective of preventing diabetes and experimental atherosclerosis. Over the course of 30 days, rats in the third, fourth, and fifth groups were administered 0.5 g/kg of oil via intragastric injection with the aid of a probe, in conjunction with methyl-2-thiouracil, which was employed to suppress the function of the thyroid gland [2]. Over a period of 14 days, rats from the second, fourth and fifth groups were administered dexamethasone via intradermal injection in order to reproduce impaired glucose tolerance. It has been demonstrated that the reduction in glucose utilisation by adipocytes subsequent to dexamethasone injection is a consequence of its direct impact on the expression of glucose transporters GLUT 1 and GLUT 4, which results in the development of insulin resistance. The administration of dexamethasone to rats at the age of four months, at a dose of 0.125 mg/kg of body weight for 14 days, allows the reproduction of the main pathogenetic mechanisms of type 2 diabetes, namely the disruption of insulin secretion and the development of insulin resistance, which are observed in patients [6]. The fifth group of animals was administered a phytopreperation derived from traditional Transcarpathian flora, including: blueberry leaves, bean pods, flax seeds, oat straw, galega grass, dandelion root, nettle leaves, valerian root, and plantain leaves. The phytopreperation was prepared using a combination of dandelion leaves, walnut leaves, black elderberry roots and flowers, black elderberry leaves, linden flowers, St. John's wort, ergot, ergot root, and cut oat straw, in accordance with the specifications outlined by the author (2 ml in a 1:10 dilution, administered intragastrically).

The housing and manipulation of animals were conducted in accordance with the provisions set forth in the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1985) and the "General Ethical Principles of Animal Experiments," which were adopted by the First National Congress. This was also confirmed by the Bioethics Committee of the Vinnytsia National Medical University named after M.I. Pirogov (protocol No. 11 of 7 June 2012). The animals were euthanised by decapitation under light ether anaesthesia.

Results and duscussion

The massometric study demonstrated a change in the mass of the experimental animals over the course of the experiment. Consequently, over the course of the 14-day experimental period, the weight of the intact group of animals exhibited minimal variation. Concomitantly, animals with experimental diabetes exhibited a loss of approximately 20% of their initial body weight, while animals with experimental atherosclerosis demonstrated a loss of 15.2% of their weight. Animals with simultaneous modelling of both pathologies exhibited a loss of almost 16% of their body weight. In contrast, animals with experimental diabetes, atherosclerosis and after the therapeutic introduction of the herbal preparation exhibited a loss of only 5% of their initial body weight. The liver weight of animals with experimental diabetes was 13% smaller than that of the intact group, while the liver weight of animals with experimental atherosclerosis was 8% smaller. Simultaneous modelling of pathologies resulted in a 3% decrease in the organ, and prophylactic administration of the herbal preparation led to a 3% increase in the weight of the organ compared to the intact group (Table .1).

Table 1. Indicators of massomorphometric measurements of rat organs

indicator / animals	Mass primary (d)	Mass at the end of the experiment (d)	Liver (d)
1 group (n=10)	232.5±68.00	232.75±25.10	7.52±1.56
2nd group (n=10)	224.38±18.74	181.63±21.24 *	6.58±0.78 *
3 group (n=10)	230 , 6 3 ±23.16	195.5±33.25 *	6.9±1.16 *
4 group (n =10)	227.25±14.87	191.38±18.18 *	7.28±0.90 *
5 group (n =10)	213.58±12.47	201.66±21.7 *#	7.76±0.88 *#

Note: * – the difference is significant in comparison with the group of intact animals ($p \leq 0.05$), # – the difference is significant in comparison with the group of animals with experimental pathology ($p \leq 0.05$). # –

The morphological studies were conducted using common histological methods. The histological preparations were stained with hematoxylin and eosin and subsequently analysed using a system for the examination of histological sections. This system involved the display of images from a microscope on a computer monitor via a video camera and a specialised software programme.

The histological examination of the liver revealed the presence of stroma and parenchyma under light microscopy in the liver of intact rats. The stroma is constituted by a thin connective tissue capsule and layers of connective tissue with blood and lymphatic vessels and bile ducts. The parenchyma of the liver is constituted by epithelial cells, specifically hepatocytes, which are arranged in a manner that is consistent with the classic arrangement of liver lobes. The lobes of the liver in this group of rats are challenging to identify due to the lack of clear separation from one another by connective tissue layers, which is typical for this species of animals. The shape of the classic hepatic lobule is pentagonal or hexagonal with rounded corners. The portal zone, which consists of transversely cut branches of the interlobular hepatic artery, portal vein, bile duct, and lymphatic vessels, together with nerves and loose connective tissue, can be observed within this structure. It is also necessary to determine the location of these structures. The central vein of the classical liver lobe is characterised by a rounded opening and, on occasion, the presence of uniform elements of blood. From the central vein, irregularly branched rows of hepatocytes extend in a radial direction. The cytoplasm of hepatocytes is homogeneous. The nuclei of hepatocytes typically exhibit a rounded shape and contain one or two nucleoli, which can be readily discerned. The majority of hepatocytes are observed to possess a single nucleus, with binucleated cells also present in close proximity to portal tracts. In the liver plates, hepatocytes are situated in two rows, with sinusoids in the form of slit spaces situated between them. The wall of sinusoids is formed by stellate endotheliocytes and macrophages. The nuclei of endotheliocytes are characterised by a short, thin rod-like appearance, while those of macrophages exhibit a triangular, prismatic, or elongated oval shape. On occasion, fat storage cells are discovered (Fig. 1).

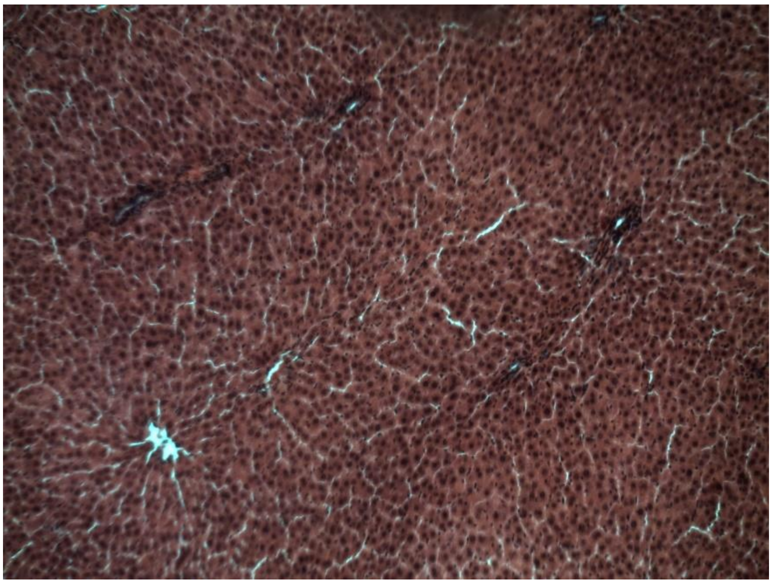

Fig. 1. Liver of an intact animal. Hematoxylin-eosin staining. Collection:10x8

Microscopic examination of liver preparations derived from rats with experimental atherosclerosis revealed that hepatocytes exhibit a pale cytoplasm with optically empty vacuoles and basophilic granules. In the livers of rats with experimental atherosclerosis, an increase in the amount of connective tissue was observed, as well as the presence of foci of haemorrhage. Additionally, lobules of the liver were distinguished by the presence of interlobular connective tissue layers, which contained macrophages, lymphocytes, cells of the fibroblastic series, and bundles of collagen fibers. A notable deviation from the standard two-layer structure of the liver plates was observed, accompanied by an expansion of the sinusoidal capillary space (Fig. 2).

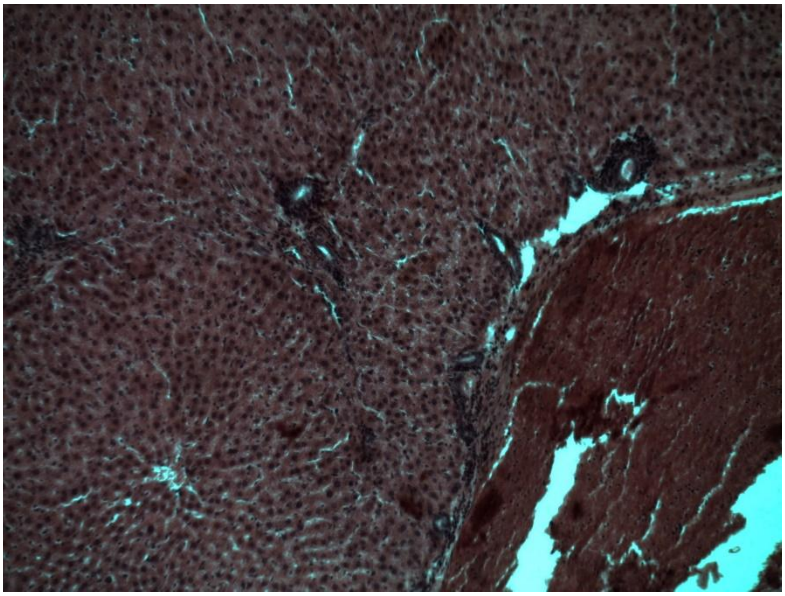

Fig. 2. Liver of an animal with experimental atherosclerosis . Hematoxylin -eosin staining. Collection: 10x8

In experimental diabetes, it was observed that the lobular structure of the liver tissue remained intact. In the centrolobular zone, there were areas where the radial arrangement of the liver beams was disrupted, and the sinusoidal capillaries exhibited marked expansion. In such areas, hepatocytes were frequently observed to be anucleated and optically vacuolated. In hepatocytes with preserved nuclei, a notable degree of swelling and hyperchromicity was observed. Some cells exhibited a markedly swollen cytoplasm, accompanied by a considerable number of optically empty vacuoles. Additionally, single foci of hepatocyte necrosis with a substantial lymphocytic infiltrate were observed in the centrolobular zone. The presence of blood clots was noted within the expanded lumina of the sinusoidal capillaries and central veins. The endotheliocytes of the sinusoidal capillaries exhibited a heterogeneous staining pattern. A significant number of macrophages were observed. Additionally, dystrophy and necrosis of hepatocytes were observed in the periportal zone. The dystrophy exhibited characteristics consistent with fatty degeneration of hepatocytes (Fig. 3)

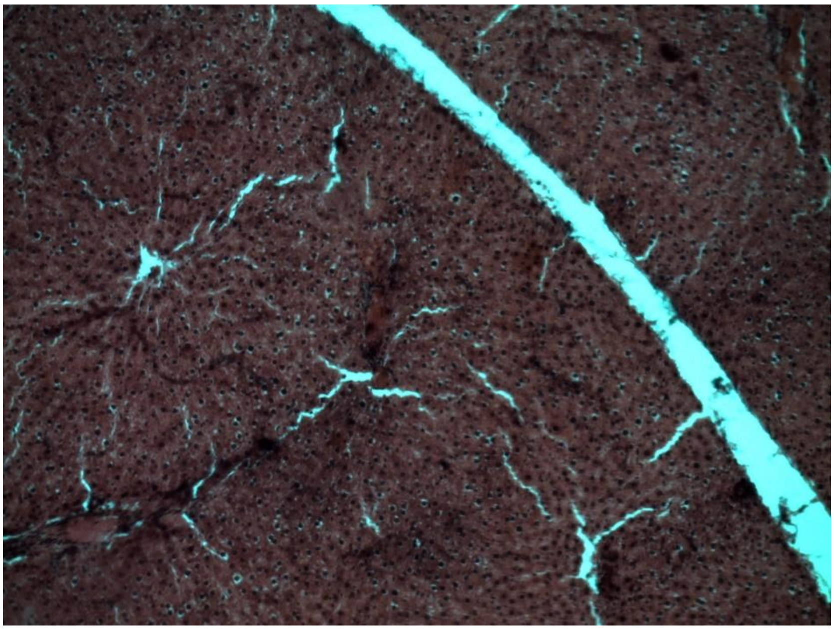

Fig. 3. Liver of an animal with experimental diabetes . Collection 10x8

The simultaneous modelling of atherosclerosis and diabetes resulted in a total loss of the lobular structure of the liver. The hepatocytes were observed to be arranged in a disorganized manner, lacking the formation of liver beams. A considerable number of anucleated cells were observed, displaying a high prevalence of optically empty vacuoles. Dystrophic and necrotic areas were observed in all zones of the classic lobules. The changes observed in the blood vessels were also more pronounced than those seen when modelling each pathology separately. Furthermore, an increase in the overall diameter of the sinusoids and central veins was observed, accompanied by a thickening of their walls and an infiltration of lymphocytes. The endothelial lining was not continuous, and the nuclei of the endotheliocytes were pyknotic when they protruded into the lumen of the sinusoidal capillaries (Fig. 4)

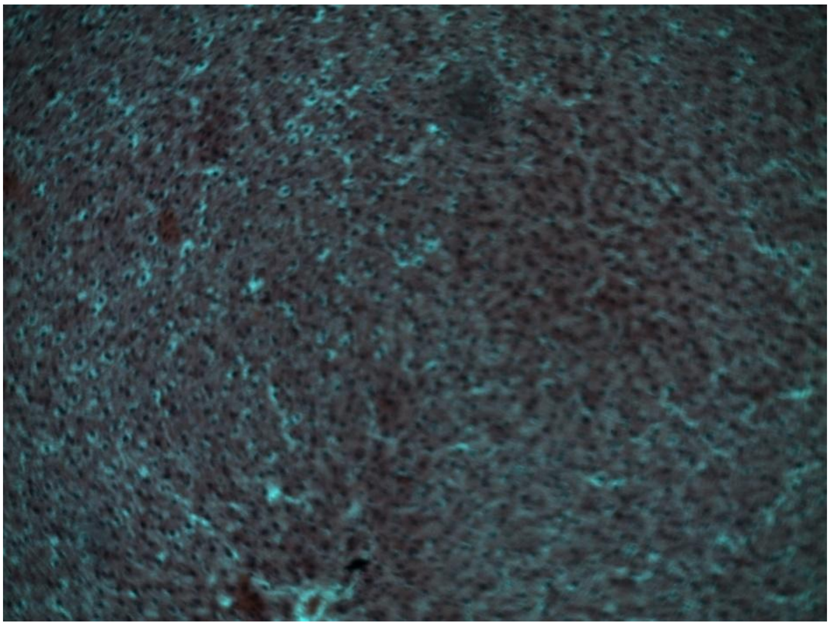

Fig. 4. Liver of an animal with simultaneous modeling of pathologies. Hematoxylin-eosin staining. Collection: 10x8

The investigation revealed the presence of dystrophic and necrotic areas in all zones of the classic lobules. Furthermore, the alterations observed in the blood vessels were more pronounced when modelling the combined pathology, as opposed to when modelling each pathology separately. The total expansion of the lumina of the sinusoids and central veins, along with their thickening and infiltration by lymphocytes, were observed. The endothelial lining was not solid, and the nuclei of the endotheliocytes were pyknotic if they protruded into the lumen of the sinusoidal capillaries.

The prophylactic administration of a decoction of traditional medicinal plants from Transcarpathia resulted in a notable reduction in the incidence of adverse changes observed in the experimental pathology. Specifically, the microscopic light-optical examination of the liver tissue of rats in the experimental group revealed slight violations of the two-layered structure of the liver beams, a slight expansion of the space of sinusoidal capillaries, and a decrease in the number of macrophages, lymphocytes, and cells of the fibroblastic series. The hepatocytes exhibited a homogeneous cytoplasm, with some displaying optically empty vacuoles (Fig. 5).

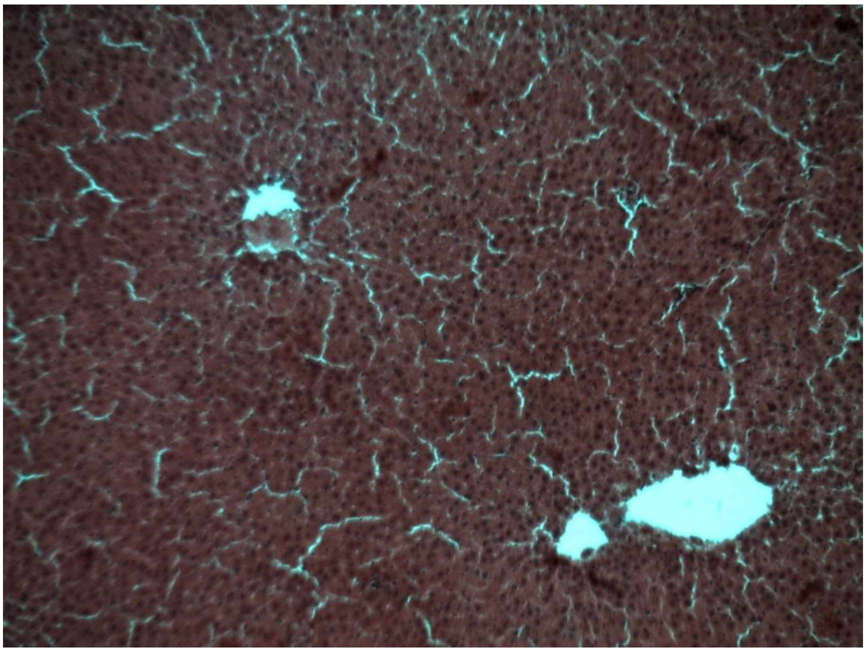

Fig. 5. Liver of an animal with therapeutic administration of a decoction of traditional medicinal plants of Transcarpathia against the background of simultaneous modeling of pathologies. Hematoxylin-eosin staining. Collection: 10x8

Conclusions .

1. In experimental models of diabetes (dexamethasone model of type 2 prediabetes) and atherosclerosis in animals, there is a reduction in body and liver weight.

2. The development of atherosclerosis and diabetes in experimental models has been observed to result in dystrophic alterations in the liver. The most significant alterations are observed when pathologies are modelled concurrently.

3. The administration of a decoction of traditional medicinal plants from Transcarpathia has been demonstrated to have hepatoprotective effects.

Prospects for further study .

Further investigation into the organoprotective effects of herbal preparations from Transcarpathia in experimental atherosclerosis and type 2 diabetes at the level of evidence-based medicine is considered a promising avenue of research.

Author's contribution

Conceptualization Żanna Białoszycka, Alina Biloshytska, methodology, Alisa Pachevska, Alina Biloshytska, software Monika Białoszycka, Alisa Pachevska, Mykyta Vasyliev, check Żanna Białoszycka, Alina Biloshytska, formal analysis Żanna Białoszycka, Alisa Pachevska, Mykyta Vasyliev, investigation Monika Białoszycka, Alina Biloshytska, resources Żanna Białoszycka, Monika Białoszycka, Mykyta Vasyliev, data curation

Monika Białoszycka, Żanna Białoszycka, Alina Biloshytska, writing-rough preparation Żanna Białoszycka, Alina Biloshytska, Mykyta Vasyliev, writing review and editing Żanna Białoszycka, Alisa Pachevska, Mykyta Vasyliev, visualization Żanna Białoszycka, Alina Biloshytska, Mykyta Vasyliev, supervision Żanna Białoszycka, Alisa Pachevska, project administration Żanna Białoszycka, Alina Biloshytska.

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Ethical approval

The minutes for this study was approved by the institutional ethics committee.

Conflict Of Interest:

The authors declare no conflict of interest.

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