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MORPHOLOGICAL CHANGES IN THE LIVER IN EXPERIMENTAL DIABETES

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Introduction

Diabetes is one of the intensively developing diseases, and chronic hyperglycemia causes protein glycosylation, glucose autoxidation, and a sharp increase in the active forms of oxygen. Chronic hyperglycemia causes high oxidative stress. As a result, the amount of free radicals increases. This causes damage to the heart, kidney, blood vessels and nervous system of vital organs [15].

In the liver, expansion of the central vein of the sinusoids, damage to the cells of the wall of the central veins is observed. Apoptosis of liver cells occurs [1,2,3].

Hepatocyte nuclear chromatin condensation, endoplasmic reticulum damage, and loss occur [4,5]

A sharp decrease in mitochondria is observed. As a result, the process of energy production is disturbed and ATF deficiency begins. It has been proven in experimental experiments that this situation also occurs in kidney cells [14]

In the case of chronic hyperglycemia, the content of Ca^{+2} ions in mitochondria increases, which directly affects cell function. Increased liver resistance to glucose leads to the breakdown of mitochondria[6,7,8].

Diabetes is accompanied by an increase in lipids in the blood and accumulation in the liver [9,10,11]

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Chinese scientists have identified epigallocatechin gallate in green tea and proved that this substance reduces blood glucose levels in diabetes and prevents a number of other pathological conditions. It has been proven that it reduces the amount of glycosylated proteins in diabetes and improves the morphology of the pancreas [12].

Arab scientists treated the changes that occur in the liver in diabetes with the help of an extract prepared from pomegranate peel[13].

In a healthy body, the amount of leptin and adiponectin depends on the body mass. If the synthesis of these substances from adipocytes decreases, insulin resistance in tissues increases.

Diabetic rats were treated with Shifo biologically active additive(BAA) for 15 days, and mainly dystrophic and slow-growing changes were detected in the histioarchitectonics of the liver.

The purpose of the study:

To identify morphological changes in the liver in diabetes and to correct them.

Research Material

Metformin drug (Russian pharmaceutical company "Biosintez, PAO") was used to restore morphological changes in the liver in experimental diabetes, and **"Shifo** " and "As-GAM" BAAs (prepared in the laboratory of the Bioorganic Institute) were used for comparison.

Research design. In the study , 120 white adult rats weighing 180-220 g were used in the laboratory of the Institute of Bioorganics, fed on a standard diet . All animal studies were conducted in accordance with WHO recommendations regarding the use of experimental animals and precautions. The experiments were carried out on healthy, male white laboratory rats with

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a body weight of 180 ± 20 g, which were quarantined for 10-14 days. The animals are the following five: Group I – negative control (healthy); Group II alloxan +metformin pharmacopoeia drug; Group III (alloxan + healing BAA); IV group (alloxan +As-GAM BAA); Group V - positive control (alloxan + dis. water); consists of the included groups of animals. The diabetes model was induced by a single intraperitoneal injection of alloxan at a dose of 130 mg/kg body weight. Animals were fasted for 24 hour to induce diabetes. During the experiment, the amount of glucose in the blood of the animals was measured. Diabetic animals were selected for the experiment and infusions of the researched drugs Shifo BAA - 100 mg/kg, As-GAM BAA - 100 mg/kg and the comparative drug metformin at a dose of 50 mg/kg were administered for treatment for 21 days. Shifo and As-GAM biologically active food additives were measured in doses of 100 mg/kg and injected into the stomach of rats using a special probe after boiling for 5 minutes and cooling at room temperature. The rats of the positive control group were given an equal volume of distilled water for 14 days.

Research methods

On the 15th day of the study, rats in all groups were decapitated and livers were removed from the rats. Morphological examinations were carried out at the Republic Pathological Anatomy Center. Liver cut during slaughtering of animals was kept in a neutral solution of 10% phosphate buffered formalin for 48 hours and washed in running water for 2-4 hours. Slices are dehydrated in 70, 80, 90, 96, 96, 100% alcohol and chloroform and embedded in a mixture of paraffin and wax. Hematoxylin-eosin staining of sections cut with a sled microtome from deparaffinized sections was performed.

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Results and Discussion

Group 1 (healthy group). The wall of the sinusoids is covered with flat rows of endotheliocytes, between the hepatocytes and the endothelium, the perisinusoidal space, the space of Disse, is located. Special macrophages along the sinusoids Kupffer cells are found in the sinusoidal spaces, in front of the wall, sometimes in the spaces of Disse (Fig. 1). Most of the hepatocytes have 1 and 2 nuclei, and the cytoplasm has a homogeneous pink eosinophilic appearance. Medial and centrolobular hepatocytes are roughly the same size, and most are radial and arranged in pairs. The average size of hepatocytes is 30-50 μm, and it decreases closer to the center.

Group 2. Group treated with metformin. The following changes were found in the liver tissue of metmorphine-corrected rats with alloxan-induced diabetes under experimental conditions. Liver capsule is uneven in thickness, signs of fullness in its veins were found. The lumps have the same appearance, and a loosely formed fibrotic tissue was detected in its perimeter. Sinusoids were sharply enlarged and the perisnusoidal spaces were also enlarged in various ways. The most expanded branches of the sinusoidal spaces correspond to the medial and centrolobular branches of the lobes and are considered as signs of intoxication in these metabolic syndromes. Foci of necrosis appeared, and the cytoplasm of hepatocytes around them was stained with oxyphil, the vacuole underwent dystrophic changes. Due to fatty dystrophy, centrolobular hepatocytes were shown to be hydropic dystrophy. (See Figure 2).

Sparse fibrous tissue is developing around the triads, focal infiltration of lymphocytes and histiocytes at a size of 200x in the interval is characterized by the replacement appearance of the reparative regeneration process, i.e., the

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appearance of fibrosis of the liver, formed in the periportal areas. Liver tissue in the samples showed progressive liver fibrosis consisting of sparse fibrous structures around the lobes. The width of the sinusoids was mainly determined around the central vein (see Figure 3).

Group 3. (Shifo BAA). Morphological changes in the liver tissue after administration of "Shifo" BAA - 100 mg/kg drug for 15 days to experimental alloxan diabetic rats were studied. According to the obtained results, the following were determined: no drastic changes were detected in the liver slices, mainly in the perilobular branches of the slices, dystrophically changed hepatocytes with medium and small drops of fat were detected. Fatty dystrophic changed hepatocytes increased in size and sinusoids in these branches were found to be narrowed. 2 nucleoli were detected in the nuclei of most hepatocytes . (See Figures 4-5).

For the most part, no signs of dampness were detected in bile capillaries. No signs of cholestasis were detected in the collecting ducts. At the same time, signs of intrahepatic cholestasis were not detected in all areas of the slices. Morphological signs of this type are considered a positive effect of "Shifo" BAA. The fact that the sinusoidal spaces in the slices are of the same width, the radial structure of the hepatocytes in the slices is of the same size compared to those in the other groups, and the number of 2-nuclear hepatocytes has increased, means that the reparation process is moving in a positive direction.

Group 4. AS-GAM biologically active. As-GAM is biologically active in experimental alloxan diabetic rats Morphological changes in liver tissue after treatment for 15 days were studied. According to the obtained results, the following were determined. Liver capsule was of normal thickness, moderate

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signs of fullness were found in its vessels. The central vein of the lobes is almost the same width. Sinusoids have the same width (Fig. 6). Focal proliferation and foci of basement membrane-like fibrous structures were formed in the endothelium of the sinusoidal wall, these changes were evaluated as the effect of alloxan diabetes on the liver. (See Figure 7). According to Rappaport, Kupffer cells were mainly located along the wall of the 2nd area of sinusoids, hepatocytes subjected to necrobiosis and migrated to various toxic metabolites. Around necrotic hepatocytes, 1-3 lymphocytes were detected at 200x field of view.

Sinusoids in this area are expanded and tissue components of destruction were detected around them. Reparative regeneration processes in hepatocytes were determined in the 2nd area according to Rappaport, and mitotic foci were visible. In place of necrotic hepatocytes, hepatocytes with light-stained cytoplasm with small nuclei appeared, and homogeneous fluid traces were detected in the surrounding area. This showed that the alteration process developed in hepatocytes and non-infectious injuries developed. It is the changes that have occurred against the background of alloxan diabetes, and the detection of hepatocytes with pale cytoplasm is considered to be one of the signs of forced detoxification in hepatocytes of area 2 according to Rappaport under the influence of As-GAM BAA substance.

Group 5. Alloxan diabetes and water-corrected group. Liver capsule is of normal thickness, average fullness of capsule vessels and poorly formed interstitial swellings were revealed. The histioarchitectonics of the liver is devoid of sharp changes, most of the changes in the hepatocytes are dystrophic, necrobiotic and developing liver fibrosis . Along the sinusoids, under the endothelial cells, sparsely located parallel foci of fibrous structures

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are identified, and these changes are considered to be the foci of fibrosis developing as a complication of diabetes. It is the development of foci of perihepatocellular fibrosis along the sinusoids, which is a reversible process, and reticulin fibers are counted. Foci of perihepatocellular fibrosis were also detected in the troectorial image with clear contours in the form of weakly formed sparse fibers at the border of the medial and perilobular hepatocytes of the lobes (see Fig. 8). Signs of cholestasis in the form of foci were detected in bile capillaries. Increased eosinophilic inclusions in the cytoplasm of hepatocytes in the centrolobular areas of the lobes and frequent detection of hyaline droplet dystrophy mean that the 1st and 2nd active areas according to Rappaport have not fully performed their function. (See Figure 8).

The portal vein is unevenly full, most of the hepatocytes have compression atrophic changes at 40x and 100x magnification, the size is different, the histioarchitectonics of the particles are slightly elongated along the perimeter of the trachea. (See Figure 9).

In the perilobular branches, hepatocytes have medium-drop fatty dystrophic changes, fibrosis and sclerotic changes formed at the site of necrobiosis and necrotic hepatocytes, the presence of perihepatocellular fibrosis foci (see Fig. 8), infiltration of lymphocytes and histiocytes around the triad, interstitial edema, the formation of sparse fibrous structures and procollagen fibers the activation of proliferation of fibroblasts, which provides synthesis, is considered as a complication of diabetes, and the effect of Alloxan substance on liver tissue .

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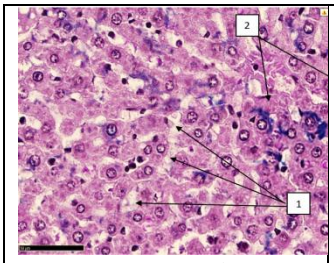
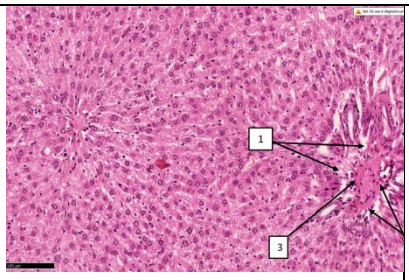


Figure 1. Control group. Hepatocytes look the same. Sinusoids are of the same width (1), the cytoplasm of medial and centrolobular hepatocytes has the same eosinophilic inclusions. Paint G.E. The size is 40x10.



Picture 2. Group 3. Sample-7. Metmorphine-corrected group. Fibrous tissue developing around the portal tract (1), weakly formed lymphocytic infiltration foci (2), and hyaline fibrinoid foci on the wall of the hepatic artery were detected (3). Paint G.E. The size is 20x10.

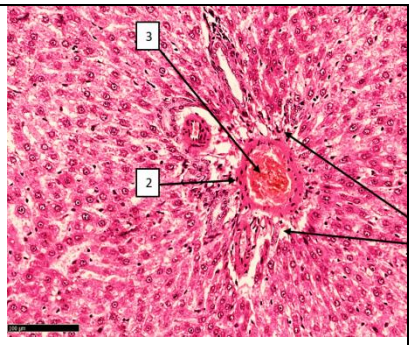


Figure 3. Group 3. Sample-10. Metmorphine-corrected group. Fibrous tissue developing around the portal tract (1), weakly formed lymphocytic infiltration foci in the interval (2), the hepatic artery appears full and the vessel wall is thickened (3). Paint G.E. The size is 20x10.

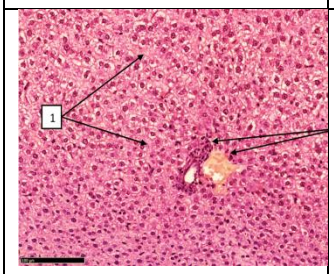


Figure 4. A group of rats accepted by "Shifo" BAA. Sample-3. No changes were detected in the histioarchitectonics of the liver. Hepatocytes with small fatty dystrophic changes and mildly hyaline droplet dystrophy were found mainly in perilobular branches (1), low-level venous filling in the perilobular vein, poorly formed landscape of lymphocytic and histiocytic infiltration around the bile duct (2). Paint G.E. Size 4x10.

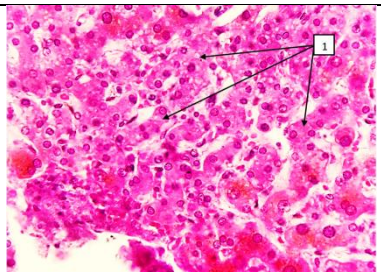


Figure 5. A group of rats accepted by "Shifo" BAA. Sample-5. No changes were detected in the histioarchitectonics of the liver. Hepatocytes with small fatty dystrophic changes and mild hyaline droplet dystrophy were found mainly in perilobular branches (1). Paint G.E. Size 4x10.

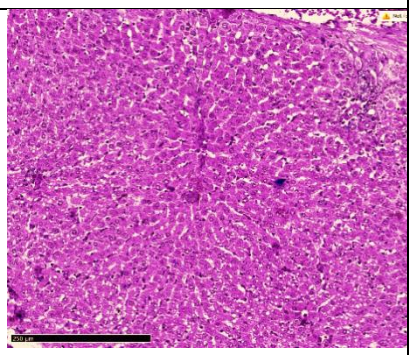


Figure 6. Group 4. As-GAM-corrected group. The histioarchitectonics of the liver tissue has not changed. The lobes are preserved in shape, the sinusoidal spaces are expanded. The central veins are of the same width. Paint G.E. Size 4x10.

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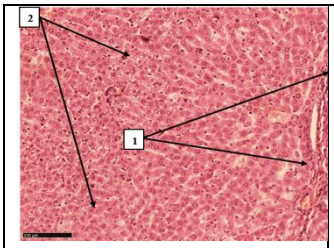

Figure 7. Group 4. Sample-35. As-GAM BAA-corrected group. Around the portal tract, weakly formed lymphocytic infiltration foci were detected in the space of sparse fibrous connective tissue (1), no signs of cholestasis were detected in the bile capillaries. Sinusoids are of different widths, and hydropic and medium droplet-like dystrophied hepatocytes are found in the focus (2). Paint G.E. The size is 20x10.

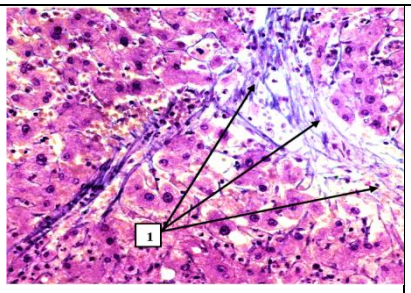

Figure 8. Group 5. Alloxan + water group of rats that received liver tissue. In the histioarchitectonics of the liver, foci of developing fibrosis were detected in the perilobular area (1), sparse fibrous fibrous tissue and foci of lymphohistiocytic infiltration were detected around the perimeter of the perilobular vein, Dye G.E. Size 4x10.

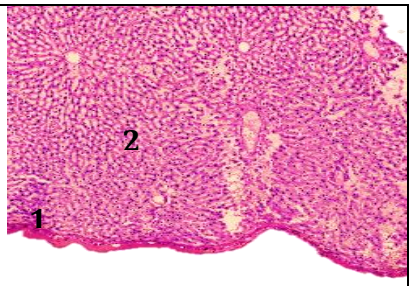

Figure 9. Group 5. Alloxan + water group of rats that received liver tissue. liver capsule unevenly thickened (1). Foci of bridge-like necrosis were found in the liver lobes (2), sinusoids were sharply expanded, and a cavity and a center of hemorrhage were formed in the space. Paint G.E. Size 4x10.

Discussions

Diabetes mellitus is a disease with complex clinical symptoms, which primarily damages the liver [17;18;19]. One of the main symptoms is hyperglycemia, which damages many organs, including the histological structure of hepatocytes [20; 21; 22]. The liver is an organ involved in the detoxification of toxic products in the body. During diabetes there is an increase in active forms of oxygen in cells and hyperglycemia [16]. This leads to a violation of the metabolism of liver cells as well as all cells. Brazilian scientists studied healthy rats that did not suffer from diabetes and found that the general structure of the liver was preserved. Anomalous distribution of fibroblasts was not observed[23]. Fat vacuoles, enlarged sinusoids, liver fibrosis, and steatohepatitis were found in diabetic rats [26; 27]. The structures of hepatocyte mitochondria, granular endoplasmic reticulum and nuclei were found to be changed [23; 24; 25].

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In our experimental experiment, the effect of 2 different BAAs prepared from local plants and metformin imported from abroad on liver morphology was studied.

Foci of necrobiosis and necrosis were detected under the influence of metformin drug. In place of necrotic hepatocytes, empty cystic enlarged foci appeared, and traces of homogeneous serous fluid were detected in the surrounding area. This shows that the alteration process has developed in hepatocytes and injuries without an infectious factor have occurred, and these are the changes that occurred against the background of alloxan diabetes, and it has been shown that under the influence of Metmorphin, the process of neoglycogenesis in hepatocytes has slowed down. Liver fibrosis developed around the liver lobes. The width of the sinusoids is determined mainly around the central vein. The drug metformin reduces blood glucose levels, but it has a low positive result due to side effects on the liver.

In rats treated with BAA, there was no damping-off in the bile ducts. The uniform width of the sinusoidal spaces of the liver lobes, the uniform radial structure of hepatocytes, and the increased number of 2-nuclear hepatocytes indicate an increased reparation process. At 40x and 100x magnification, the cytoarchitectonics of most hepatocytes are the same, and the histioarchitectonics of the slices are typical, indicating the recovery of the morphofunctional areas of the liver in alloxan diabetes mellitus.

The hepatoprotective factor of As-GAM, albeit small, is explained by the detection of mitotic foci in hepatocytes with light cytoplasm, instead of hepatocytes subjected to destruction and necrobiosis. no signs of cholestasis are detected in bile capillaries. Weakly formed interstitial swellings around bile vessels are detected, and these are considered residual morphological signs of cholestasis formed on the background of alloxan diabetes mellitus.

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In rats of the untreated group, the development of perihepatocellular fibrosis leads to the development of the basement membrane between the hepatocytes and sinusoids, and the sharp obstruction of the morphofunctional surfaces of the liver. It ends with alloxan diabetes leading to development of cirrhosis of the liver over a certain period of time (on average 60-80 days). Lymphocytic and macrophage infiltration foci develop around damaged hepatocytes. In some areas of the interlobular areas of the liver, there are also foci of necrosis and bleeding into their cavities.

Summary

In an experimental model of diabetes, Shifo and As-GAM BAAs were observed to effectively lower blood glucose levels and improve liver and pancreas morphology. Hepatoprotective property of Shifo BAA was determined. No cases of necrosis or fibrosis were observed in rats given this BAA. It was found that the regeneration process in hepatocytes increased. No fibrosis was observed in rats given As-GAM BAA. A partial restoration of regeneration was found.

No liver regeneration was observed in rats of the group treated with metformin. Glycogen production was inhibited and necrotic, dystrophic changes developed.

Conflict of interest

The authors declare no conflict of interest in publishing this article.

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References:

1.Aboonabi A, Rahmat A, Othman F. Effect of pomegranate on histopathology of liver and kidney on generated oxidative stress diabetic induced rats. J Cytol Histol. 2015; 6(1).

2.Al-Attar AM, Alsalmi FA. Influence of olive leaves extract on hepatorenal injury in streptozotocin diabetic rats. Saudi J Biol Sci. 2019; 26(7): 1865–1874, doi: 10.1016/j. sjbs.2017.02.005, indexed in Pubmed: 31762669

3. Rodríguez V, Plavnik L, Tolosa de Talamoni N. Naringin attenuates liver damage in streptozotocin-indu1,2,3ced diabetic rats. Biomed Pharmacother. 2018; 105: 95–102, doi: 10.1016/j. biopha.2018.05.120, indexed in Pubmed: 29852394.

4. Alshathly MR. Efficacy of ginger (zingiber officinale) in ameliorating streptozotocin-induced diabetic liver injury in rats: histological and biochemical studies. J Microsc Ultrastruct. 2019; 7(2): 91–101, doi: 10.4103/JMAU. JMAU_16_19, indexed in Pubmed: 31293891.

5. Farid O, Zeggwagh NA, Ouadi FEl, et al. aqueous extract exhibits antidiabetic and hepatoprotective effects in streptozotocin-induced diabetic rats. Endocr Metab Immune Disord Drug Targets. 2019; 19(3): 292–301, doi: 10.217 4/1871530318666181005102247, indexed in Pubmed: 30289084.

6.Chang JYA, Yu F, Shi L, et al. Melatonin affects mitochondrial fission/fusion dynamics in the diabetic retina. J Diabetes Res. 2019; 2019: 8463125, doi: 10.1155/2019/8463125, indexed in Pubmed: 31098384

7.Arruda AP, Hotamisligil GS. Calcium homeostasis and organelle function in the pathogenesis of obesity and diabetes. Cell Metab. 2015; 22(3): 381–397, doi: 10.1016/j. cmet.2015.06.010, indexed in Pubmed: 26190652.

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Eureka Journal of Physical and Chemical Research (EJPCR)
ISSN 2760-490X (Online) Volume 01, Issue 02, December 2025

https://eurekaoa.com/index.php/1

8. Rogers RS, Wheatley JL, Archer AE, et al. Heat shock protein 72 regulates mitochondrial integrity and function in the prevention of hepatic insulin resistance. FASEB J. 2016; 30(suppl 1): 1015–1011
9.Seng YH, Chang CW, Chiang W, et al. Adlay bran oil suppresses hepatic gluconeogenesis and attenuates hyperlipidemia in type 2 diabetes rats. J Med Food. 2019; 22(1): 22–28, doi: 10.1089/jmf.2018.4237, indexed in Pubmed: 30673500
10. Bae JS, Lee JY, Lee DH, et al. Quantitative evaluation of hepatic steatosis using normalized local variance in a rat model: comparison with histopathology as the reference standard. Korean J Radiol. 2019; 20(9): 1399–1407, doi: 10.3348/kjr.2019.0068, indexed in Pubmed: 31464118
11. Lisha V, John P, Sujith S, et al. Effect of Averrhoa bilimbi fruit powder on Histopathology and the functional Indices of the Liver and Kidney of Rats fed with high fat diet. Pharma Innov J. 2019; 8(1): 48–51.
12.Zhongtao Feng, Xiumei Hou, Chuanan Zhu, Jiabin Zhu, Chunxiao Jiang. Epigallocatechin gallate ameliorates morphological changes of pancreatic islets in diabetic mice and downregulates blood sugar level by inhibiting the accumulation of AGE-RAGE. RESEARCH ARTICLE J Cell Biochem. 2019;120:8510–8520.. DOI: 10.1002/jcb.28139
13. K.A.J. Faddladdeen. Ameliorating effect of pomegranate peel extract supplement against type 1 diabetes-induced hepatic changes in the rat: biochemical, morphological and ultrastructural microscopic studies. journals.viamedica.pl . Folia Morphol., 2021, Vol. 80, No. 1,pp. 149–157 DOI: 10.5603/FM.a2020.0034
14. Yildiz BO, Haznedaroglu IC. Rethinking leptin and insulin action: therapeutic opportunities for diabetes. Int J Biochem Cell Biol 2006;38:820–30.

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Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online) Volume 01, Issue 02, December 2025

https://eurekaoa.com/index.php/1

15. Soon YY, Tan BK. Evaluation of the hypoglycemic and anti-oxidant activities of Morinda officinalis in streptozotocin-induced diabetic rats. Singapore Med J 2002;43:077–85.
16. Ferrell JM, Chiang JYL. Circadian rhythms in liver metabolism and disease. Acta Pharm Sin B. 2015; 5(2): 113–122.
17.Duru OK, Middleton T, Tewari MK, et al. The landscape of diabetic kidney disease in the united states. Curr Diab Rep. 2018; 18(3): 14.CrossRefPubMed
18. George B, Cebioglu M, Yeghiazaryan K. Inadequate diabetic care: global figures cry for preventive measures and personalized treatment. EPMA J. 2010; 1(1): 13–18.CrossRefPubMed
19. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2018; 14(2): 88–98.CrossRefPubMed
20. Smith BW, Adams LA. Nonalcoholic fatty liver disease and diabetes mellitus: pathogenesis and treatment. Nat Rev Endocrinol. 2011; 7(8): 456–465.CrossRefPubMed
21.Targher G, Lonardo A, Byrne CD. Nonalcoholic fatty liver disease and chronic vascular complications of diabetes mellitus. Nat Rev Endocrinol. 2018; 14(2): 99–114.CrossRefPubMed
22.Ahmadieh H, Azar ST. Liver disease and diabetes: association, pathophysiology, and management. Diabetes Res Clin Pract. 2014; 104(1): 53–62.CrossRefPubMed
23. Amanda Natália Lucchesi, Lucas Langoni Cassettari, César Tadeu Spadella. Alloxan-Induced Diabetes Causes Morphological and Ultrastructural Changes in Rat Liver that Resemble the Natural History of

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ISSN 2760-490X (Online) Volume 01, Issue 02, December 2025

https://eurekaoa.com/index.php/1

Chronic Fatty Liver Disease in Humans. J Diabetes Res. 2015; 2015: 494578. doi: 10.1155/2015/494578

24. Sarin S.K., Choudhury A. Acute-on-chronic liver failure: Terminology, mechanisms and management. Nat. Rev. Gastroenterol. Hepatol. 2016;13:131–149. doi: 10.1038/nrgastro.2015.219. [PubMed] [CrossRef] [Google Scholar]

25. Adams L.A., Angulo P. Recent concepts in non-alcoholic fatty liver disease. Diabet. Med. 2005;22:1129–1133. doi: 10.1111/j.1464-5491.2005.01748.x. [PubMed] [CrossRef] [Google Scholar]

26. Mohamed J., Nafizah A.N., Zariyantey A.H., Budin S. Mechanisms of diabetes-induced liver damage: The role of oxidative stress and inflammation. Sultan Qaboos Univ. Med. J. 2016;16:e132. doi: 10.18295/squmj.2016.16.02.002. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

27. Skat-Rørdam J., Højland Ipsen D., Lykkesfeldt J., Tveden-Nyborg P. A role of peroxisome proliferator-activated receptor γ in non-alcoholic fatty liver disease. Basic Clin. Pharmacol. 2019;124:528–537. doi: 10.1111/bcpt.13190. [PMC free article] [PubMed] [CrossRef] [Google Scholar].