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MORPHOMETRIC CHANGES IN THE LIVER UNDER THE INFLUENCE OF "SHIFO" AND "AS-GAM" FOOD SUPPLEMENTS

Ibragim R. Askarov
Andijan State University Professor of the Department of Chemistry, Doctor of Chemistry, Honored Inventor of Uzbekistan, Chairman of the TABOBAT Academy of Uzbekistan
https://orcid.org/0000-0003-1625-0330

Guyoxon A. Mominova
Andijan State Medical Institute Associate Professor, DSc
https://orcid.org/0000-0003-3531-7772
E-mail:guyoxonmuminova@gmail.com

Feruzaxon L. Sayidjanova
Andijan State Medical Institute Assistant Professor, Department of Pathological Anatomy and Forensic Medicine
https://orcid.org/0009-0003-8464-0047

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Annotation
This article presents the results of morphometric determination of the effect of herbal food additives "Shifo" and "As-GAM" on liver morphology in the alloxan diabetes model and comparison with the synthetic drug Metformin

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INTRODUCTION. In recent years, the practice of preparing food supplements from natural plants and using them as substitutes for chemical drugs has been widely observed all over the world. This ensures a reduction in toxic effects on the body.

Many plant-based dietary supplements are used to control diabetes. In order to reduce the toxic effects, we also used the plant-based dietary supplements "Shifo" and "As-GAM" to correct diabetes.

LITERATURE ANALYSIS AND METHODS. Diabetes mellitus is a complex, multisystem disease that primarily affects the vital organ liver. Hyperglycemia observed in diabetes mellitus damages many organs, including the histological structure of hepatocytes [1]. According to the literature, in diabetes mellitus, enlargement of the central vein of the sinusoids in the liver, damage to the cells of the central vein wall, and apoptosis of hepatocytes are detected [2]. Condensation of the chromatin of the hepatocyte nucleus, damage and loss of the endoplasmic reticulum occur, and mitochondria are sharply reduced [3]. This is due to the fact that in chronic hyperglycemia, the amount of Ca^{+2} ions in mitochondria increases, and increased hepatic resistance to glucose leads to mitochondrial fragmentation [4]. The appearance of fatty vacuoles, sinusoid enlargement, liver fibrosis, and steatohepatitis were detected in hepatocytes of diabetic rats [5]. Changes in mitochondria, rough endoplasmic reticulum, and nuclear structures were also noted in hepatocytes [6]. The data presented here support our findings.

The literature provides information on the hepatoprotective properties of the plant extracts we are investigating. Studies have shown that treatment with oat extract reduced serum liver enzymes, and the oat extract-treated group did not show any alcohol-induced liver damage. It also significantly prevented the development of pathological changes (macrovesicular and microvesicular) in liver cells of alcoholic liver degeneration, and also ensured the integrity of liver cells [7].

Another plant, wild rose extract, has been shown in studies to reduce hepatic steatosis and restore gut microbiota and metabolite parameters [8].

The antioxidant phenolic compounds in hawthorn prevent liver cell necrosis in diabetes [9; 10].

The hepatoprotective and antioxidant effects of ethanolic extract of yarrow were demonstrated by histopathological and biochemical studies in a rat liver injury model [11].

Coriander seed extract has been shown to increase the levels of enzymes such as SOD, catalase, and GP in the liver and to promote the regeneration of liver cells in liver necrosis. It has also been shown to reduce the levels of NF-κB, TNF-α, and caspase 3 and necrosis in liver injury [8].

We corrected an experimental diabetes model using the food supplements "As-GAM" and "Shifo" prepared on the basis of these plants. We evaluated the morphological studies based on morphological criteria.

Research methods. The research team fixed 1.5x1.5 cm sections of liver tissue taken from autopsy in a 10% phosphate-buffered formalin solution for at least 48 hours.

10% phosphate buffered formalin solution for fixing tissue and organ sections.

1. Formalin (40% formaldehyde) - 100 ml
2. Sodium monophosphate, monohydrite - 4 g
3. Sodium biphosphate, anhydrous - 6.5 g
4. The volume of the solution should be brought to 1 liter with distilled water.

Method for dehydrating tissue sections for paraffin embedding.

1. Formalin buffer solution 24 hours
2. Wash in running water for 2-3 hours
3. Ethanol 70 1 hour
4. Ethanol 80 2 hours
5. Ethanol 90 1 hour
6. 3 96-liter alcohol bottles for 30 minutes each
7. Leave Ethanol 100 overnight
8. Absolute ethanol-xylene (1:1) 20 minutes
9. 3 xylene 37° C for 20 minutes
10. Xylene-paraffin (1:1) 56°C 25 minutes
11. Paraffin 1 56° 1 hour
12. Paraffin 2 56° 1 hour
13. The pieces were prepared by pouring them into paraffin.

In the first stage of morphological research, tissue samples are fixed in 10% neutral formalin solution for 72 hours. Then, the materials are passed through alcohol in increasing order (70, 80, 90, 100%) for dehydration and finally through chloroform and xylene for degreasing. The obtained paraffin blocks were cut into 4-5 μm thick sections on microtome, mounted on glass slides, stained with hematoxylin-eosin and placed under coverslips. The stained histological preparations were examined using a ZEISS (Primo Star, 64 MP camera, 40, 100, 400 magnification, made in Germany) light microscope and micrographs were taken.

RESULTS AND DISCUSSION.

Table 1.

Evaluation of morphological changes in the liver of research rats based on the criteria of RGKnoudell et.al. (1996)

	AD	metformin	Shifo	As-Gam
The degree of dystrophic changes in hepatocytes	3	3	2	2
The degree of development of necrosis in the liver parenchyma	2	2	0	2
The degree of development of lymphoid infiltration is less than 1/3 of the portal tracts.	3	3	1	1
The degree of development of sclerosis - the expansion of the portal tracts due to fibrosis	3	2	1	1
The rate of hepatocyte regeneration	2	2	4	2
Total	13	12	8	8

As can be seen from the data presented in the table, the used OTCs were found to be effective in diabetes mellitus, and were more effective than metformin in terms of eliminating dystrophic changes, necrosis, infiltration, sclerosis, and regeneration properties. "Shifo" OTC was more effective than As-GAM OTC in eliminating necrosis and showing higher hepatocyte regeneration indicators (Table 2).

Table 2

Criteria for assessing the degree of fibrosis in the morphological changes in the liver of research rats

	AD		metformin		Shifo		As-GAM	
Developed morphological units	METAVIR	Ishak	METAVIR	Ishak	METAVIR	Ishak	METAVIR	Ishak
No fibrosis	F3	3	F2	2	F0	0	F2	2
Portal fibrosis of multiple portal tracts	F3	3	F2	2	F1	1	F1	1
Portal fibrosis of multiple portal tracts	F2	2	F2	2	F0	0	F1	1
Multiple bridging fibrous barriers	F2	2	F1	1	F1	1	F0	0
Multiple bridging fibrous barriers	F1	1	F1	1	F0	0	F0	0
Incomplete cirrhosis	F0	0	F0	0	F0	0	F0	0
Full-blown cirrhosis	F0	0	F0	0	F0	0	F0	0
Total score for accumulated morphological units	2.2	2.2	1.6	1.6	1	1	1.3	1.3

OTCs reduced the degree of fibrosis and morphological changes in the liver of study rats and were found to be more effective than metformin.

Thus, the data obtained on the above morphological changes in the modeled diabetes group were analyzed, and the following changes were determined in the effect of Alloxan on the liver tissue

of the untreated group of diabetics, which were induced experimentally under experimental conditions. In the processes of liver fibrosis formed against the background of diabetes, accompanied by dystrophic, necrobiotic and sclerotic changes in hepatocytes, the direct effect of Alloxan on the liver stimulated the occurrence of the reparative regeneration process in the form of substitution, and instead of the dystrophic and necrobiotic changes that developed in hepatocytes, sclerotic changes were formed and continued with the formation of foci of lymphohistiocytic infiltration around the triads. In the untreated group of alloxan-induced diabetes, the changes in liver tissue were assessed according to the above criteria within 15 days, and the effect was negative, and if the process continues for longer than 60-80 days without treatment, the likelihood of developing liver cirrhosis was increased.

In the group treated with metformin, the above morphological changes were observed, and the use of metformin for the correction of alloxan-induced diabetes mellitus in experimental conditions was considered to be a direct effect of metformin on the liver, inhibiting the process of neoglycogenesis and stimulating the process of reparative regeneration in the form of substitution, which was accompanied by dystrophic and necrobiotic changes in hepatocytes, mainly in the liver tissue, which was formed against the background of diabetes mellitus. When evaluated according to the above criteria, it is estimated that the use of metformin in the treatment of diabetes mellitus had a positive effect on the liver, with side effects on the liver, compared to groups with therapeutic doses, with side effects, compared to other groups.

Therefore, based on the data obtained on the above morphological changes, the use of the drug "Shifo" OOQ-100 mg/kg for the correction of experimentally induced allopurinol diabetes mellitus did not lead to drastic changes in the liver tissue, but only continued in the form of the development of dystrophic changes. When evaluated according to the above criteria, it is estimated that the drug "Shifo" OOQ-100 mg/kg gave a positive result compared to other groups in terms of high therapeutic efficacy and the absence of side effects on the liver tissue.

Based on the data obtained on the above morphological changes in the group treated with “As-GAM ” , the following morphological aspects of the side effects that occurred in the liver tissue as a result of the use of the “As-GAM” OQ preparation for the correction of alloxan-induced diabetes mellitus under experimental conditions were determined. In the liver tissue, in the processes accompanied by liver fibrosis, fatty and protein dystrophic and necrobiotic changes in hepatocytes, the direct effect of "As-GAM" OQ on the liver did not lead to negative consequences, but rather to some extent suppressed foci of perihepatocellular fibrosis, sharp changes in areas 1 and 2, which are responsible for metabolism according to Rappaport, also had positive changes compared to the group in which "As-GAM" OQ was used, reparative regeneration in hepatocytes was manifested in the form of restitution, and the preservation of hepatocytes with fatty dystrophic changes in the form of small droplets indicated a positive change in the process. When evaluated according to the above criteria for determining liver damage and fibrosis, the drug "As-GAM" was used in the treatment of diabetes mellitus and showed that the side effects on the liver were more than in the 2 groups at therapeutic doses, and the side effects were lower than in the other groups, which was confirmed by the positive results on the above-mentioned morphological changes.

CONCLUSION. In the alloxan diabetes model, “Shifo” and “As-GAM” dietary supplements improved liver morphology. In rats given “Shifo” dietary supplements, necrosis and fibrosis were not observed, and the regeneration process in hepatocytes was enhanced. In rats given “As-GAM” dietary supplements, fibrosis was not observed, and partial restoration of regeneration was observed. In the group of rats treated with metformin, liver regeneration was not observed, and necrotic and dystrophic changes developed.

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