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CHANGES IN LIVER MORPHOLOGY IN THE PRESENCE OF HERBAL PREPARATIONS IN ITS ACUTE TOXIC LESION

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ABSTRACT
The results of studying the influence of various hepatoprotective phytopreparations on the morphology of the liver in its acute toxic lesion are presented. It was revealed that of all the studied hepatoprotective drugs, geranyl, catacin and carsil give a relatively good effect in the correction of toxic hepatitis. The action of geraniol is associated with increased protein synthesis, increased immunoregulatory function of the liver and proliferation of bile ducts. It was established that pharmacotherapy of acute toxic hepatitis with catacin and carsil leads to the restoration of damaged liver parenchyma. During pharmacotherapy of acute toxic liver damage with cavergal, small foci of necrosis and hemorrhage were preserved in the liver tissue together with the restoration of the affected parenchymal foci, were revealed the diffusely distributed foci of inflammatory lymphoproliferative infiltration.
KEY WORDS: *hepatoprotector, geranyl, catacin, karsil, Kupffer cells.*

Currently, herbal remedies are widely used to treat toxic liver lesions. Widely used are drugs such as Karsil, Essential, Silibor, Silymarin, Phosphogliv and others that have a versatile effect[5, 8, 10, 12]. The elaboration and study of the mechanism of their hepatoprotective action will not only expand the arsenal of effective domestic hepatoprotectors, but also introduce them into clinical practice. In recent years, staff of the Institute of Chemical Engineering of the Academy of Sciences of the Republic of Uzbekistan have created drugs based on bioflavonoids and proanthacyanidins [9]. Preliminary studies have shown their anti-hypoxic and hepatoprotective properties [7]. However, morphological studies can be evidence of their hepatoprotective effect. All of the above was the subject of an upcoming study.

The aim of the study: morphologically evaluate the effectiveness of various hepatoprotectors synthesized in ICP in acute toxic liver lesion.

MATERIALS AND RESEARCH METHODS

In the experiment, 160 white nondescript male rats weighing 180-220 were used. The model of acute toxic lesion (ATG) was reproduced by a single injection of heliotrin at a dose of 200 mg / kg of animal body weight in 75 rats, 8 rats made up the intact group. Mortality on days 1-3 was 10.7% (8 rats). On the 3rd day of the introduction of the toxicant, the surviving 67 animals were divided

into 5 groups: 1) ATG + physiological saline at a dose of 5 ml / kg body weight (control) (15 rats); 2) ATG + karsil (comparison group) (13 rats); 3) OTG + catacin (13 rats); 4) ATG + geranyl (13 rats); 5) ATG + cover (13 rats). The drugs were administered intragastrically at 100 mg / kg for 12 days daily. After the final administration of the preparations, the animals were killed, the liver pieces were fixed in a 10% solution of neutral formalin. The histological sections obtained on this microtome were stained with hematoxylineosin and examined under a Lake microscope under the lenses: 10, 20, 40.

RESULTS AND ITS DISCUSSION

When toxic hepatitis is reproduced with the introduction of heliotrin in the liver, the development of massive centrallobular necrosis and hemorrhage is observed, which in places penetrate into the blood vessels and into the area of the periportal parenchyma of the liver with the formation of bridging necrosis (Fig. 1).

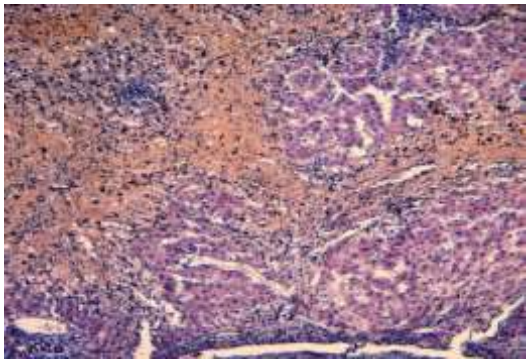

Fig 1. Toxic hepatitis. Penetration of foci of necrosis and hemorrhage in the periportal zone with the formation of bridge necrosis. Coloring: GE. Uv:approx.10. vol.10.

In the surviving periportal liver tissue, an expansion of sinusoids, Disse spaces, foci of inflammatory lymphohistiocytic infiltration around necrosis and vessels of the portal tracts is revealed.

Pharmacotherapy of acute heliotrin liver damage with catacin leads to a decrease in necrotic phenomena. The trabecular arrangement of hepatocytes persists, but due to the expansion of sinusoids, the liver cells are somewhat compressed and elongated. In the cytoplasm of hepatocytes, eosinophilic protein content is detected. The nucleus of hepatocytes in a state of moderate hypertrophy and hyperchromasia in the form of an increase in chromatin concentration and hypertrophy of the nucleoli (Fig. 2).

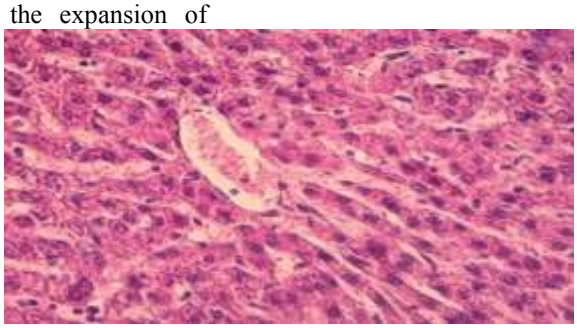

Figure 2. Catacin. Plethora of veins, hyaline droplet degeneration of hepatocytes, hyperchromasia of nuclei. Coloring: G.E. Uv: approx. 10, vol. 40.

During pharmacotherapy with geranyl in the liver tissue, proliferative activity of stromal tissue structures and an increase in the area of both the cytoplasm and the nuclear structures of hepatocytes were noted. Pathomorphological changes from the stroma manifested themselves in the form of an increase in the proliferative activity of Kupffer cells in the form of hypertrophy and hyperchromasia of nuclei. In some of them, signs of the appearance of phagocytized particles appeared. Also, single lymphoid cells appeared in the space of the disse. On the part of the liver parenchyma, the preservation of the beam and lobular structure of hepatocytes was noted. Hepatic cells are expanded in volume due to increased protein synthesis in the form of hyaline droplet cytoplasmic dystrophy and carbohydrate vacuolar dystrophy of nuclei karyoplasm (Fig. 3).

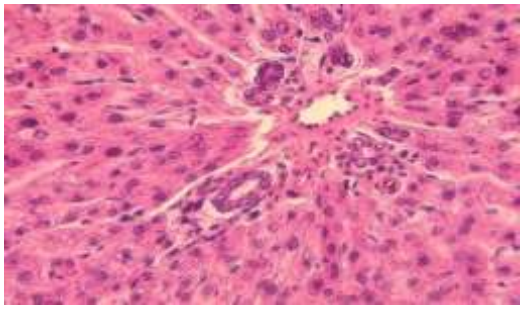

Fig 3. Geranyl. Proliferation of the bile ducts, thickening of the artery wall due to sclerosis and inflammatory infiltration. Coloring: G.E. Uv: approx. 10, vol. 40.

In this series, proliferation of the bile ducts in the form of neoplasms of the small ducts due to proliferation and accumulation of cholangiocellular epithelium, which are located along the periphery of the portal tracts, is observed in the liver tissue from the portal tracts, some penetrate the hepatic parenchyma. In the center of the portal tracts there is an artery, the wall of which is thickened due to sclerosis and the appearance of inflammatory lymphohistiocytic infiltration in the circle. In this zone, hepatocytes retain the beam structure, in the cytoplasm of which protein hyaline droplet degeneration is determined.

Thus, under the influence of geronyl in the liver tissue, parenchyma is restored, protein synthesis of hepatocytes in the form of hyaline droplet dystrophy is enhanced, stabilization of stromal tissue structures in the form of Kupffer cell hypertrophy, preservation of small lymphoid infiltration along the portal tracts are also noted, and bile secretion is also increased proliferation of bile ducts.

When correcting acute toxic liver damage with a cavergal in the liver tissue, both parenchyma and stroma are restored, but with the preservation of small foci of necrosis and hemorrhage in the centrallobular sections of the lobules and the appearance of a focus of inflammatory lymphoproliferative infiltration around the preserved microcenters of necrosis and hemorrhage. Moreover, the presence of small foci of necrosis and hemorrhage was noted in the central parts of the liver lobes, around which the presence of inflammatory infiltration from lymphohistiocytic cells was determined (Fig. 4).

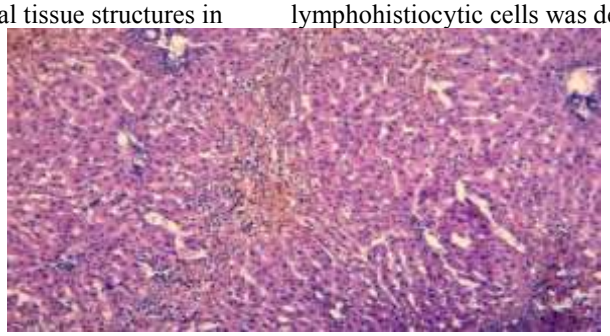

Fig 4. Kavergal. Preservation of foci of necrosis and hemorrhage in the center of the lobules of the liver, the appearance of inflammatory infiltration. Coloring: G.E. Uv: approx. 10, vol. 10.

The expansion of sinusoids and the space of disse was revealed. The preserved foci of necrosis and hemorrhage in the central part of the lobules are also clearly visible and are represented by the decay of cellular elements, hematogenous pigments and the appearance of hypertrophic macrophages and active lymphoid cells. Hepatocytes are expanded in volume, swollen due to protein hyaline droplet degeneration with preservation of the beam structure.

Thus, during pharmacotherapy of acute toxic liver damage with a cavergal in the liver tissue, along with the restoration of the affected foci of the parenchyma, small foci of necrosis and hemorrhage remained, diffusely distributed foci of inflammatory lymphoproliferative infiltration were detected.

Pharmacotherapy of acute toxic liver damage with carlsil was characterized by the restoration of damage to the liver parenchyma and immunoregulation of the stroma-parenchymal message in the form of lymphohistiocytic infiltration along the portal tracts. From the side of the liver parenchyma, the development of hyaline droplet and small-droplet vacuole protein dystrophy was noted, indicating an increase in synthetic processes from the side of hepatocytes. At the same time, the area of the portal tracts was expanded due to pronounced lymphohistiocytic infiltration, expansion and vacuolization of the periportal zone and thickening of the vessel wall (fig. 5).

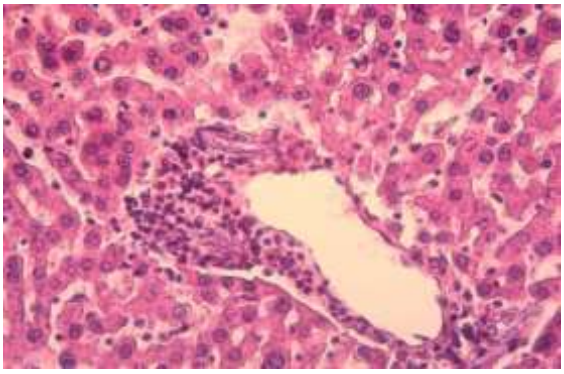

Figure 5. Carsil. Periportal lymphohistiocytic infiltration, expansion of sinusoids, protein dystrophy of hepatocytes. Coloring: G.E. Uv: approx. 10, vol. 40.

In the liver parenchyma, there is the presence of diffuse lymphoid in-filtration between the liver beams and along the sinusoids, which is also a sign of strengthening the protective and immune function of the organ. In the liver parenchyma, there is a pronounced expansion of sinusoids and dissolution space with the presence of lymphoid cells in their lumen and moderate hypertrophy of Kupffer cells.

Thus, with the introduction of carcil, the processes of repairing damage to the liver parenchyma and immunoregulation of the stroma-parenchymal relationship in the form of lymphohistiocytic infiltration along the portal tracts are activated.

The data obtained show that the cause of hepatic insufficiency in many pathological conditions is a decrease in oxygen supply, activation of the immune-mediated and mitochondrial apoptosis pathways, fibroblast growth factors, causing irreversible fibrosis processes leading to chronicity of the pathological process [17, 18, 19]. Damage and destruction of hepatocytes is the starting point in the activation of other cell populations [14, 19].

Improving the functioning of the enzyme systems of the organ by hepatoprotectors, in our opinion, is due to the chemical structure of these compounds [4, 11, 16, 20]. The mechanism of the protective action of flavonoids is associated with an increase in the activity of antioxidant enzymes and restoration of hepatocyte cell membranes [5, 8]. Most flavonoids have an anti-inflammatory effect, inhibiting the enzymes responsible for the synthesis of cytokines, prostaglandins, thromboxanes and leukotrienes [2]. The metabolic effect of this group of hepatoprotectors is associated with the stimulation of protein biosynthesis and the acceleration of regeneration of damaged hepatocytes, due to the specific stimulation of RNA polymerase 1, activation of transcription and translation [2, 4]. Apparently, the positive changes that we identified in the structure of hepatocytes are associated with the activation of synthetic processes. In the studies of Abdullaev G.R. (2016) in rats with emotional pain stress, a decrease in lipid peroxidation processes using catacin was found, the drug increased the energy potential of cells [1, 3]. This drug has an antihypoxic effect in various forms of hypoxia and is superior in activity to known antihypoxants [15]. A study of the chronic toxicity of catacin showed a lack of cumulative properties [6]. Proanthocyanidin geranyl exhibited antihypoxic properties in a carotid artery occlusion model [7]. Apparently, the pronounced hepatoprotective properties of catacin and geranyl are associated with their antihypoxic and antioxidant effects. Kavergal has a pronounced antihypoxic and antioxidant activity and membrane-protective action, increases the body's resistance to adverse environmental factors.

CONCLUSIONS

1. Of all the hepatoprotective drugs, geranyl, catacin and karsil gave a relatively good effect in the correction of toxic hepatitis.

2. Pharmacotherapy of acute toxic hepatitacatacin and karsil leads to the restoration of damaged liver parenchyma and immunoregulation of the stroma-parenchymal ratio, the development of hyaline droplet and small droplet vacuole protein dystrophy.

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