THE EFFECT OF CHITOSAN DERIVATIVES ON THE LIVER STRUCTURE OF RATS WITH ACUTE HEPATITIS

Galieva Z. I
Tashkent Medical Academy

Abstract: *In 30 rats with acute toxic liver damage caused by the administration of CCl4 in olive oil over a span of four days, at a dosage of 2.5 milligrams per kilogram of body weight, biochemical indicators of liver damage were studied. To reproduce acute toxic liver damage, 30 rats were administered CCI4 4 times at a dose of 2.5 ml/kg body weight subcutaneously for 4 days. No mortality was observed. Pharmacotherapy of acute toxic liver damage was carried out 24 hours after the final administration of the toxicant. The animals were separated into the following groups: control group (10 rats) with ATH + placebo (H2O); comparison group (10 rats) with ATH + comparison drug Carsil at a dose of 100 mg/kg; main group (10 rats) with ATH + LMWC at a dose of 25 mg/kg. The drugs were administered as a suspension intragastrically through a special tube for 12 days. In the control group, the development of syndromes of cytolysis, cholestasis, mesenchymal inflammation, and hepatic cell failure, a decrease in catalase activity, and an elevation in the content of MDA, FASL, and NF-kB was established, which coincided with the morphological signs of hepatocyte destruction. Low-molecular chitosan obtained from Bombyx mori pupae to a certain extent restored the histiostructure of the liver of rats with ATH, reduced the processes of lipid peroxidation and apoptosis, cytolysis, cholestasis and hepatocellular failure. In terms of hepatoprotective action, it was not inferior to the classical hepatoprotector Carsil.*

Keywords: *liver, carbon tetrachloride, low molecular weight chitosan, carsil.*

INTRODUCTION

Chitosan is a biocompatible and biodegradable polymer that is completely safe and non-toxic. It is a cationic aminopolysaccharide of natural origin, a copolymer of glucosamine and N-acetylglucosamine, obtained by partial deacetylation of chitin. Chitosan can be categorized based on molecular weight: high molecular weight (HMW) chitosan ranges from 190 to 375 kDa with a degree of deacetylation greater than 75%, while low molecular weight (LMW) chitosan ranges from 20 to 190 kDa with a degree of deacetylation less than 75% [1]. Higher molecular weight chitosan exhibits increased activity, but low and medium molecular weight chitosan have superior antimicrobial properties [2]. However, their hepatoprotective properties have not yet been studied.

Objective To investigate the effect of low molecular weight chitosan derived from Bombyx mori silkworm pupae on liver structure using an acute tetrachloromethane hepatitis model.

Materials and Methods The experimental studies were conducted in accordance with the requirements of the Helsinki Declaration on the Humane Treatment of Animals (Strasbourg, 1985). Experiments were conducted on 26 sexually mature male rats with an initial weight of 160-180 g, kept on a standard diet in the laboratory of pharmacology and toxicology at the TMA biomedical technology center. To induce acute toxic liver injury (ATI), rats were administered CCl_4 subcutaneously at a dose of 2.5 ml/kg body weight for 4 days, with no observed lethality. Pharmacotherapy with OTG was performed 24 hours after the final administration of the toxicant. The animals were divided into 3 groups of 6 rats each: control group received 0.5 ml of H_2O, comparison group received carsil at a dose of 100 mg/kg, and the main group received NMX at a dose of 25 mg/kg intragastrically for 12 days. After 24 hours from the last drug administration, the animals were decapitated under light ether anesthesia, and their livers were removed. For histological studies, liver pieces were fixed in a mixture of 10% formalin, ethyl alcohol, and acetic acid, and then embedded in paraffin. Sections of 4-5 μm thickness were stained with hematoxylin and eosin. The preparations were visualized using Polyvar and Leica DMRE microscopes with a digital video surveillance system and the Videotest-4 image analysis program.

Results The studies indicated that in the control group, the morphological picture was characterized by diffuse periportal mesenchymal-cellular infiltration, lysis, and fatty transformation of hepatocytes with displacement of nuclei.

Several lobes of the liver exhibited dust-like fatty degeneration of hepatocytes under low magnification. The liver lobules showed slit-like narrowing of blood vessels, fine-drop fatty degeneration of hepatocytes, and a dilated central vein, with the beam structure of hepatocytes preserved.

The periportal tracts had a cellular reaction and single fatty inclusions.

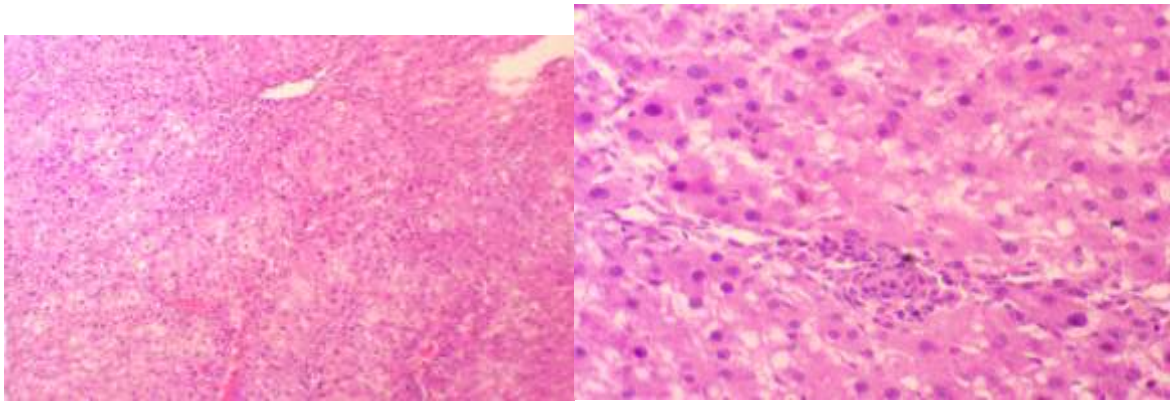

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Fig. 1. Liver of a rat with ATG. Under low magnification of the objective lens, liver lobules with slit-like narrowing of the vascular lumen, fine-drop fatty degeneration of hepatocytes are seen (a). Magnification 10.0. Hematoxylin and eosin staining. Under high

magnification of the objective lens, periportal cellular infiltration, lysis, and fatty transformation in hepatocytes are noted (Figure 1b). Magnification 40.0. Hematoxylin and eosin staining.

Under high magnification of the objective lens, periportal cellular infiltration, lysis of individual hepatocytes, and fatty transformation in hepatocytes are observed (Figure 1b). In rats with acute tetrachloromethane hepatitis (ATH), a decrease in the recovery reaction and an increase in signs of proliferation of immature connective tissue with an abundance of cellular structures were noted. These results indicate the adequacy of the chosen acute ATH model.

During experimental pharmacotherapy with the hepatoprotector Carsil at a dose of 100 mg/kg for 12 days, signs of venous hyperemia, sharp expansion of the central vein lumen, and vascular congestion were observed. Sinusoidal spaces and Kupffer cells were also identified. Hepatocytes exhibited a beam structure, and in the middle sections of the lobule, single hepatocytes with dust-like fatty degeneration of a focal nature were noted (Figure 2a).

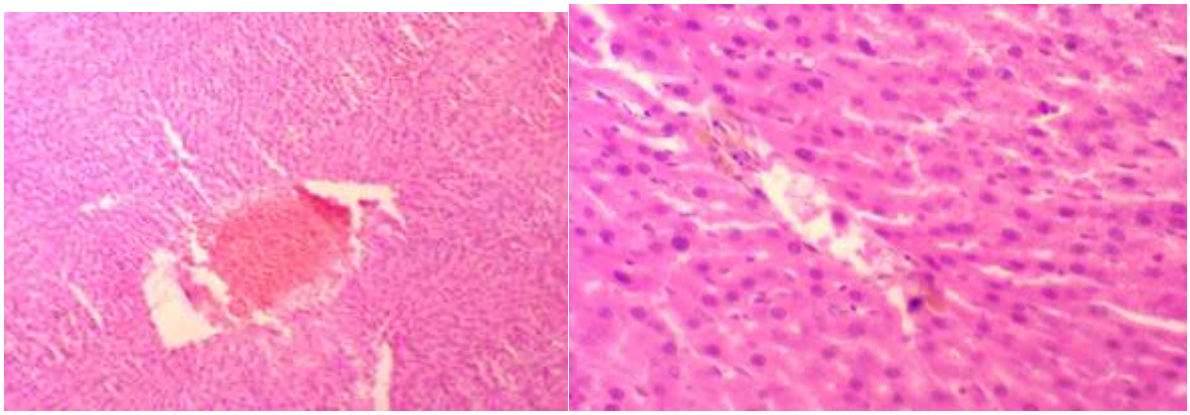

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Figure 2. Liver of a rat with ATG treated with Carsil. The central vein is sharply dilated and full-blooded, and in the middle sections of the lobule, there are single hepatocytes with dust-like fatty degeneration of a focal nature (a). Magnification 4.0 (a). The beam structure of the liver is preserved, nuclei in the hepatocytes are visible, and in the lobule, the lumen of the central vein is dilated and contains erythrocytes (b). Magnification 40.0. Hematoxylin and eosin staining.

In some areas, the beam structure of hepatocytes had a parallel orientation. Under high magnification of the objective lens, single mononuclear cells were observed in the Disse space. Hepatocytes are round-polygonal in shape, with pink-reddish cytoplasm and hyperchromically stained nuclei (Figure 2b).

In animals with ATG that underwent pharmacotherapy with NMH, focal accumulation of histiogenic cells around the vessels and fatty inclusions in hepatocytes

were detected under high magnification of the objective lens (Figure 3a). Signs of a mesenchymal-cellular reaction were noted along the periportal tracts, with an accumulation of lymphocytes and histiocytes in the Disse space, slit-like lumens of the vessels, and dystrophic changes in hepatocytes, including Councilman bodies, but the beam structure was preserved (Figure 3b).

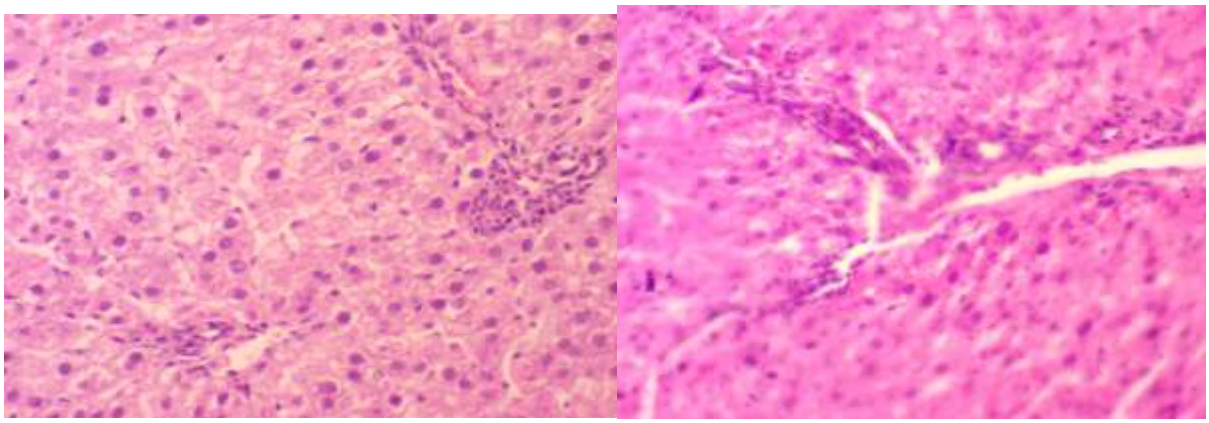

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Figure 3. Liver of a rat with ATG treated with NMX. Focal accumulation of histiogenic cells around the vessels and fatty inclusions in hepatocytes (a). Hematoxylin and eosin staining. Magnification: 40.0. Mesenchymal-cellular reaction along the periportal tracts, slit-like vessels, and preserved hepatocytes (b). Hematoxylin and eosin staining. Magnification: 40.0.

Based on the results obtained, the following conclusions can be made:

1.Low-molecular chitosan derived from Bombyx mori pupae partially restores the histological structures of the liver in rats with ATG and, in terms of morphological features, is not inferior to the classical hepatoprotector Rukarsil.

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