WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979, Volume 7, Issue 1, January- 2026

# MORPHOLOGICAL PECULIARITIES OF THE RETINA IN TOXIC HEPATITIS

Rasulov X. A.
Department of Anatomy, Histology, and Pathological Anatomy
Professor, DSc Tashkent State Medical University

Gulnoza. O. Khidirova
Associate Professor, PhD,

Abbos. B. Burkhonov
khidirovagulnoza1980@gmail.com
orcid.org/0000-0001-7245-2493

**ABSTRACT**

Toxic hepatitis is accompanied not only by liver damage but also by systemic disorders, including alterations in the visual system. In recent years, special attention has been paid to the morphological changes in the retina, as it is a highly sensitive structure reflecting the general condition of the organism. In toxic liver injury, degenerative processes, photoreceptor dystrophy, disturbances of the retinal pigment epithelium, microcirculatory disorders, and enhanced apoptosis of nerve cells are observed. Histological and histochemical studies reveal imbalances in protein, lipid, and carbohydrate metabolism, leading to structural and functional insufficiency of the retina.

**Materials and Methods** The study was conducted on 30 white rats of both sexes (180–220 g), maintained under standard vivarium conditions. All procedures complied with the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986) and were approved by the local bioethics committee. Animals were divided into three groups: control (n = 10), toxic hepatitis (n = 10), and toxic hepatitis + hepatoprotector (silymarin, 100 mg/kg/day orally for 21 days, n = 10).

**Results** All animals in the control group maintained normal activity, body weight, and intact ocular morphology. In the toxic hepatitis group, animals demonstrated lethargy, reduced food intake, and signs of hepatotoxicity. In control animals, the retina displayed well-preserved laminar organization with clear boundaries of all layers, normal vascular architecture, and absence of glial proliferation. Morphological changes at this level—such as dystrophy, degeneration, cellular structural disorganization, apoptosis, and vascular damage—may precede or

accompany impaired visual function. Studying such alterations helps to elucidate how toxic hepatitis affects not only the liver but also target organs such as the eyes.
**Conclusion** The present experimental study demonstrated that toxic hepatitis leads to pronounced morphological and histochemical alterations in the retina. These changes included disruption of retinal layer integrity, degeneration of photoreceptor and ganglion cells, disturbances of the microvascular network, and activation of glial elements. The identified alterations reflect microcirculatory disturbances, metabolic disorders, and hypoxic processes, indicating a close relationship between toxic liver injury and pathology of the visual analyzer.

**Keywords:** toxic hepatitis, retina, morphological changes, photoreceptor dystrophy, pigment epithelium, microcirculation, endogenous intoxication, histochemistry, apoptosis, hepatoprotective therapy.

## Introduction

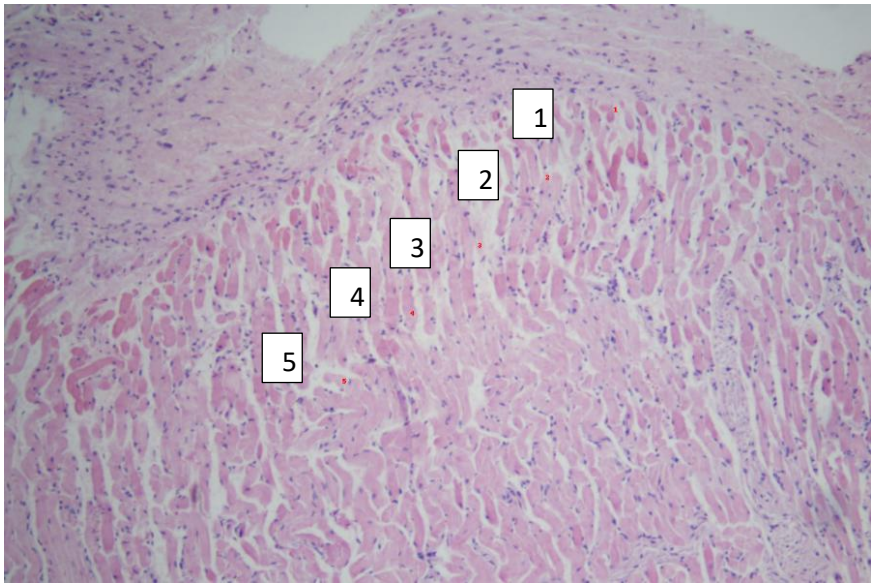
Toxic hepatitis represents an important medical problem caused by liver injury under the influence of poisons, medications, chemical agents, alcohol, industrial toxins, and endogenous intoxication. The liver, being critically involved in detoxification, metabolism, and synthetic functions, when impaired, disrupts systemic homeostasis, which may lead to a wide range of systemic consequences. One of the organs highly sensitive to metabolic disturbances, hypoxia, and toxic exposure is the eye, particularly the retina. The retina is a complex neuro-sensory structure composed of multiple layers, including photoreceptors, pigment epithelium, vascular networks, and neural elements. These changes correlate with the severity of hepatocyte injury and the degree of endogenous intoxication. Thus, the study of morphological changes in the retina in toxic hepatitis has not only fundamental but also practical significance: it allows the retina to be considered as a marker of systemic disorders and provides a basis for evaluating the effectiveness of therapy, including hepatoprotective agents. Although official statistical data on toxic (non-viral) hepatitis in Uzbekistan remain incomplete, the literature indicates that infectious-allergic and toxic hepatitis, along with cirrhosis, represent a significant proportion of liver pathologies in Central Asia, including Uzbekistan. Research in Uzbekistan has addressed toxic hepatitis, including studies on the effectiveness of hepatoprotective therapy in 120 patients with toxic hepatitis. Moreover, experimental studies have been conducted on the effects of maternal chronic toxic hepatitis on the development of offspring organs. The frequency and geographical distribution of liver injuries caused by chemical substances remain insufficiently

studied both globally and in Uzbekistan. Most national statistics and prevention programs in Uzbekistan focus primarily on viral hepatitis types A, B, and C. For instance, there has been an observed increase in hepatitis A cases among children, along with intensified measures for vaccination and screening against viral hepatitis B and C. At the same time, data on toxic hepatitis—especially those associated with chemical and industrial pollutants or drug-induced liver injury—and its effects on other organs (including the visual system) are lacking or fragmentary. In this context, the need for an in-depth study of retinal morphological changes in patients with toxic hepatitis becomes evident, particularly: determining the nature and extent of histological changes; identifying correlations between the severity of hepatic damage and the degree of ophthalmic morphological alterations; assessing the potential of retinal changes as markers of systemic intoxication; and evaluating possibilities for vision monitoring and prevention of ocular complications in patients with toxic hepatitis. Such research is of great interest to hepatologists, ophthalmologists, and pathologists, and may have direct clinical implications. Timely identification of retinal morphological changes can aid in therapeutic adjustments, including the use of hepatoprotectors, detoxification measures, and interventions aimed at protecting visual function.

## Materials and Methods

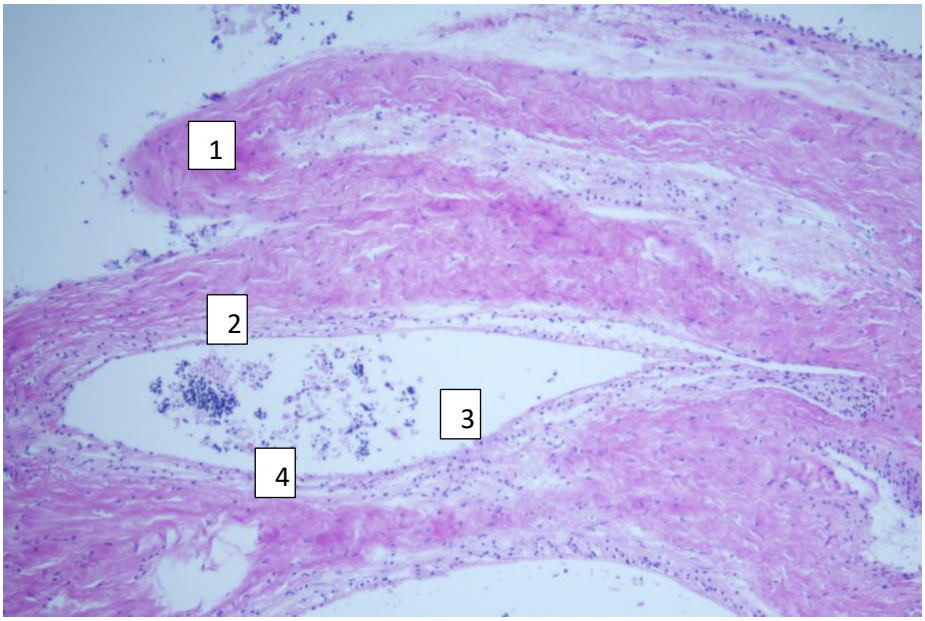
In the toxic hepatitis group, marked structural changes were observed by day 7, which intensified by days 14 and 21. Toxic hepatitis was induced by intraperitoneal injection of carbon tetrachloride (0.5 ml/100 g body weight, dissolved in sunflower oil 1:1) every other day for 7 days. Model validation was based on serum ALT, AST, and bilirubin levels, as well as liver histopathology. On day 30, animals were euthanized under ketamine–xylazine anesthesia. Liver and eye samples were fixed in 10% neutral formalin, dehydrated, and embedded in paraffin. Sections (4–5 μm) were stained with hematoxylin–eosin (H&E) for general morphology, PAS reaction for carbohydrates, Nissl staining for neuronal integrity, and Bielschowsky–Gross silver impregnation for reticular fibers. Retinal assessment included measurement of layer thickness, ganglion cell density, outer-to-inner nuclear layer ratio, and vascularization index. Histological analysis revealed stratified retinal architecture with metabolic disturbances, focal disorganization, vascular wall thickening, and mild degenerative changes, without massive necrosis.

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979, Volume 7, Issue 1, January- 2026




**Retina, H&E staining ×400.**

**1** – Ganglion cell layer **2** – Inner nuclear layer **3** – Outer nuclear layer (photoreceptors) **4** – Nerve fiber layer **5** – Retinal pigment epithelium and choroid Ganglion cell layer – a single row of large basophilic nuclei. Inner nuclear layer – a denser row of small dark-violet nuclei. Outer nuclear layer – basophilic nuclei of photoreceptors, compactly arranged. Nerve fiber layer – a light zone between the cellular layers. Pigment epithelium and choroid – located in the lower part of the specimen, adjacent to the vascular coat. Hematoxylin and eosin (H&E): general retinal morphology. Reticulin silver impregnation evaluation of reticulin fibers, capillaries, and glial elements. Succinic dehydrogenase (SDH) activity assessment of mitochondrial metabolic activity. Acid phosphatase (ACP) activity evaluation of lysosomal function and inflammatory response. Microscopy and Morphometric Analysis slides were examined under a Leica DM500 light microscope with ×10, ×40, and ×100 oil immersion objectives. Digital images were captured and analyzed using ImageJ software for morphometric evaluation of retinal layers, vascular density, and glial cell proliferation.




**Retina, PAS reaction, ×400**

**1** – thickened vascular wall (violet-pink, brightly stained area) **2** – vascular lumen (light area inside) **3** – perivascular tissue (loose zone surrounding the vessel) **4** – retinal pigment epithelium and choroid (lower layer with PAS-positive inclusions).

Vascular structures with thickened walls are visible, showing an intense PAS-positive reaction (pink-violet staining). This indicates the accumulation of glycoproteins and hyaline-like masses within the vascular wall. The inner surface of the vessels is uneven in places, with evidence of endothelial disorganization. In the vascular lumens, clumps of cellular elements and possible fragments of destroyed erythrocytes are observed. Perivascularly, edema and loosening of connective tissue, along with single-cell infiltration, are noted. PAS-positive inclusions are most pronounced in the intima and media of the vessels, which is characteristic of wall damage under toxic influence (e.g., toxic hepatitis or systemic metabolic disorders). Schiff staining revealed pathological thickening and homogenization of vascular walls, accumulation of glycoproteins and carbohydrate-containing structures, reflecting dystrophic and sclerotic changes associated with toxic injury.

## Results

In the toxic hepatitis group, marked structural changes were observed by day 7, which intensified by days 14 and 21. These included disorganization and thinning of retinal layers, predominantly in the outer nuclear and ganglion cell layers, cytoplasmic vacuolization and nuclear pyknosis of photoreceptors, perivascular edema and narrowing of capillaries, proliferation of Müller glial cells and astrocytes, forming gliosis foci.

Reticulin staining revealed fragmentation and irregular arrangement of reticulin fibers, with reduced capillary density and microcirculatory disturbances. Succinic dehydrogenase (SDH) activity significantly decreased in the toxic hepatitis group compared with controls ($p < 0.05$), indicating mitochondrial dysfunction. Acid phosphatase (ACP) activity increased, particularly in ganglion cells and microglial elements, reflecting enhanced lysosomal activation and inflammatory response. Animals receiving hepatoprotective treatment (silymarin) showed partial preservation of retinal architecture compared with untreated hepatitis group. Notable improvements included better organization of retinal layers with reduced degeneration of photoreceptor and ganglion cells, restored reticulin network and improved capillary morphology, increased SDH activity approaching control values ($p < 0.05$), decreased ACP activity, indicating attenuation of inflammatory processes. All animals in the control group maintained normal activity, body weight, and intact ocular morphology. In the toxic hepatitis group, animals demonstrated lethargy, reduced food intake, and signs of hepatotoxicity (jaundice of mucous membranes, hepatomegaly). In control animals, the retina displayed well-preserved laminar organization with clear boundaries of all layers, normal vascular architecture, and absence of glial proliferation. These included disorganization and thinning of retinal layers, predominantly in the outer nuclear and ganglion cell layers, cytoplasmic vacuolization and nuclear pyknosis of photoreceptors, perivascular edema and narrowing of capillaries, proliferation of Müller glial cells and astrocytes, forming gliosis foci. Reticulin staining revealed fragmentation and irregular arrangement of reticulin fibers, with reduced capillary density and microcirculatory disturbances. Succinic dehydrogenase (SDH) activity significantly decreased in the toxic hepatitis group compared with controls ($p < 0.05$), indicating mitochondrial dysfunction. Acid phosphatase (ACP) activity increased, particularly in ganglion cells and microglial elements, reflecting enhanced lysosomal activation and inflammatory response. Animals receiving hepatoprotective treatment (silymarin) showed partial preservation of retinal architecture compared with untreated hepatitis group. Notable improvements included better organization of retinal layers with reduced degeneration of photoreceptor and ganglion cells, restored reticulin network and improved capillary morphology, increased SDH activity approaching control values ($p < 0.05$) decreased ACP activity, indicating attenuation of inflammatory processes. In experimental toxic hepatitis, the retina of the eyeballs revealed pronounced dystrophic and vascular changes affecting both the neurosensory elements and the pigment epithelium. Hematoxylin–eosin staining showed disruption of retinal layer architecture, dystrophic changes in the cells of the inner and outer nuclear layers,

cytoplasmic vacuolization, and pycnotic nuclear alterations with signs of karyorrhexis. The outer segments of photoreceptors underwent destruction, the nerve fiber layer became thinned, and ganglion cells exhibited signs of swelling and partial degeneration. With Schiff (PAS) staining, vascular changes were most prominent. Vessel walls demonstrated an intense PAS-positive reaction, indicating the accumulation of glycoproteins and hyaline-like masses. The vascular walls were thickened, and the capillary lumens were markedly narrowed. Perivascular findings included edema, loosening of connective tissue, and cellular infiltration. In the pigment epithelium and basal membranes, focal PAS-positive inclusions were observed, reflecting impaired metabolic processes. Thus, the study showed that toxic hepatitis induces a complex of microcirculatory disturbances and dystrophic changes in the retina. These processes manifest as vascular wall damage, photoreceptor degeneration, pigment epithelium destruction, and pronounced signs of hypoxia. The combination of these alterations confirms a direct relationship between systemic toxic liver injury and the morphological state of the visual analyzer.

## Conclusion

Histochemical analysis revealed decreased succinate dehydrogenase activity, indicating impaired mitochondrial metabolism, along with elevated acid phosphatase activity, reflecting enhanced lysosomal activity and inflammatory response. Parallel assessment of liver and retinal tissues confirmed a close biological relationship between hepatic injury and retinal pathology. Importantly, administration of a hepatoprotective agent attenuated degenerative changes, improved microcirculation, and restored enzymatic balance in retinal structures, supporting the therapeutic relevance of hepatoprotection not only for liver tissue but also for preservation of visual function. These findings provide a novel experimental basis for considering retinal alterations as an additional diagnostic marker of systemic toxicity in hepatic injury, and highlight the potential of hepatoprotective therapy in preventing secondary ocular complications of toxic hepatitis. The morphological study demonstrated that toxic hepatitis leads to pronounced vascular–dystrophic changes in the retina. The main manifestations include thickening and PAS-positive transformation of vascular walls, narrowing of their lumens, perivascular edema and infiltration, as well as photoreceptor destruction and pigment epithelium damage.

**References**

1. Avetisov E.S. Retinal Pathology: A Guide for Physicians. Moscow: Meditsina; 2016. 432 p.
2. Balabolkin M.I., Kvetnoy I.M. Morphological and Functional Changes in Metabolic Disorders. St. Petersburg: SpetsLit; 2018. 389 p.
3. Kovalevsky E.I., Churilov L.P. Histological Methods of Research in Medicine. St. Petersburg: Elbi-SPb; 2019. 287 p.
4. Nikolaev A.V., Shilova I.V. Morphological changes of the visual organ in systemic liver diseases. Archive of Pathology. 2020;82(4):42–48.
5. Sheveleva T.S., Egorova I.Yu. Pathomorphology of retinal vascular lesions in toxic conditions. Russian Ophthalmology Bulletin. 2021;137(3):56–63.
6. Bhutto I., Lutty G. Understanding age-related retinal diseases through the pathology of the human choroid and retina. Prog Retin Eye Res. 2012;31(4):303–316.
7. Cogan D.G., Kuwabara T. The retina in liver disease. Trans Am Ophthalmol Soc. 1959;57:142–155.
8. Cunha-Vaz J. Pathophysiology of retinal changes in diabetes and liver disorders. Acta Ophthalmol Scand. 2006;84(6):699–711.
9. Gass J.D.M. Stereoscopic Atlas of Macular Diseases. 5th ed. St. Louis: Mosby; 2012. 1069 p.
10. Hendrickson A., Djajadi H., Possin D. Histological evaluation of retinal responses in systemic intoxication models. Exp Eye Res. 2017;160:17–25.
11. Johnson R.N., Olson J.L. Retinal pathology in systemic toxic and metabolic disorders. Surv Ophthalmol. 2018;63(4):482–495.
12. Kaur C., Foulds W.S., Ling E.A. Blood–retinal barrier in hypoxic and ischemic conditions: basic concepts, clinical features and management. Prog Retin Eye Res. 2008;27(6):622–647.
13. Saari J.C. Retinoids and the visual cycle. Exp Eye Res. 2012;91(6):673–685.
14. Khidirova G.O. Morphofunctional changes of the visual organ in liver damage. World Scientific Research Journal. 2025;40(1):278–280.
15. Khidirova G.O. The influence of the liver on the functioning of vision. Journal of New Century Innovations. 2025;78(2).
16. Abdumutalova S.D. 17. Khidirova G.O. The role of electrolyte metabolism on cardiac tissue. Spectrum Journal of Innovation, Reforms and Development. 2025;40:5–9.

17. Khidirova G.O. Mechanisms of cardiovascular system changes depending on the state of mineral metabolism. Tashkent Medical Academy Medical Journal of Young Scientists. 2025;13(03).
18. Khidirova G.O. Morphofunctional characteristics of the main vessels of the cardiovascular system in hyperparathyroidism. Scientific and Practical Journal "Pediatrics." 2024;4.