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PATHOMORPHOLOGICAL CHANGES IN RATS WITH EXPERIMENTAL MODELS OF CHRONIC VIRAL HEPATITIS

The study was performed as a part of research work “Immunochemical cofactors and genetic predictors of development of diseases associated with persisting and latent infections” (state registration number 0110U006145).

ABSTRACT. Background. The research was focused on progressive excessive formation of connective tissue subsequently leading to architectural changes of the liver tissue. Justification of drug choices is based on their possibility to modulate regression of fibrosis and resorption of connective tissue. **Objective.** To study the anti-fibrotic properties of pharmaceuticals Arginine glutamate (Glutargin) and complex drug Cytoflavin in the liver of rats with the experimental model of induced chronic hepatitis. **Methods.** Experimental studies have been conducted on adult male Wistar rats. Chronic hepatitis was induced in laboratory animals by Nikolenko V.U. et al. (2006). The model is based on toxic damage of hepatocytes with carbon tetrachloride and formation of autoimmune response. Ant-fibrotic effect of Arginine glutamate and combined metabolic drug Cytoflavin were studied. Histological specimens were stained with haematoxylin, eosin, alcian blue (sialylated glycocalyx of cells) and picrofuchsin by Van Gieson (to identify the connective tissue of the liver), histochemical PAS-reaction with Schiff's reagent to detect glycogen. **Results and conclusion.** The article studied pathological changes in rats with experimental model of chronic viral hepatitis during treatment with pathogenetic drugs, namely, Arginine glutamate (hepatoprotector Glutargin) and metabolic product (combination drug) Cytoflavin to study their impact on the process of fibrogenesis in the liver. **Conclusion.** In animal model of induced chronic hepatitis the greatest clinical efficacy was shown for Arginine glutamate, its application showed greater slowdown in the processes of fibrosis comparing with Cytoflavin.

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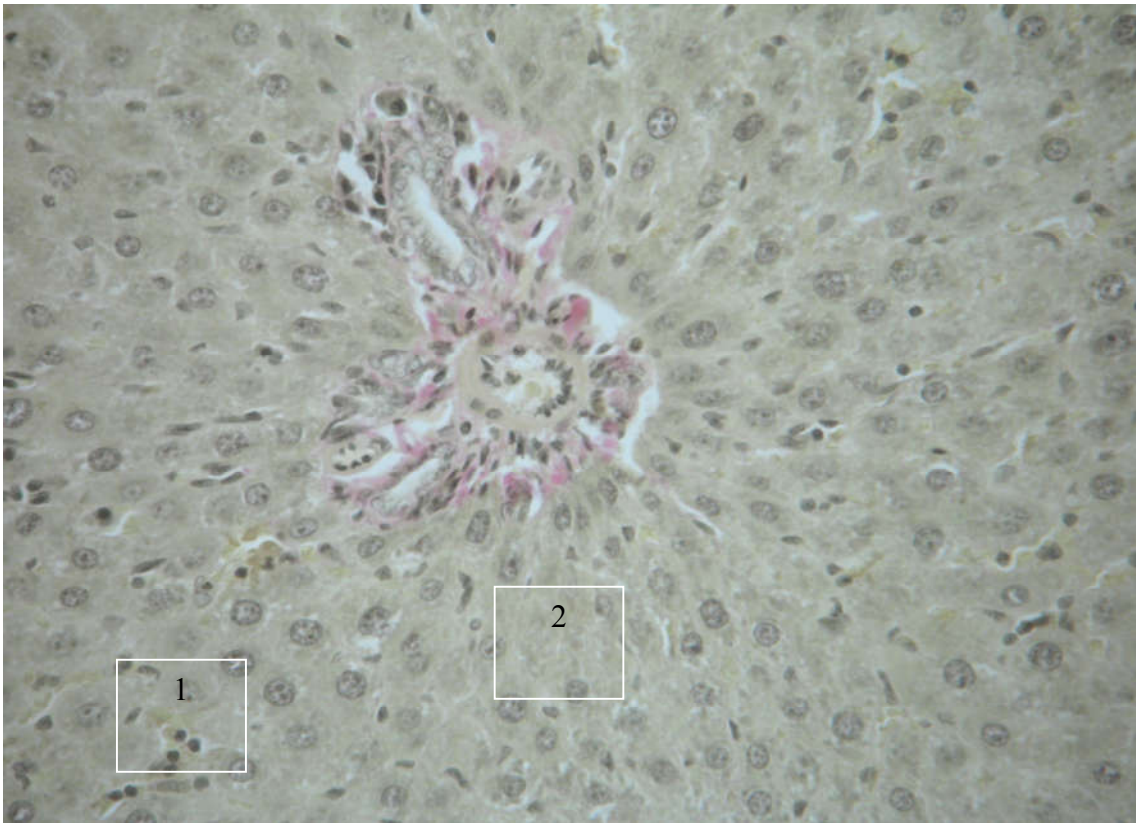


Fig. 1. Morphological changes in group 2 rat. Lymphocytic infiltration, fibrous cords, cytoplasmic protein dystrophy, necrosis; 1 – lymphoid infiltration; 2 – cytoplasmic protein dystrophy, 'empty' cytoplasm, necrosis. Van Gieson stain. ×400.

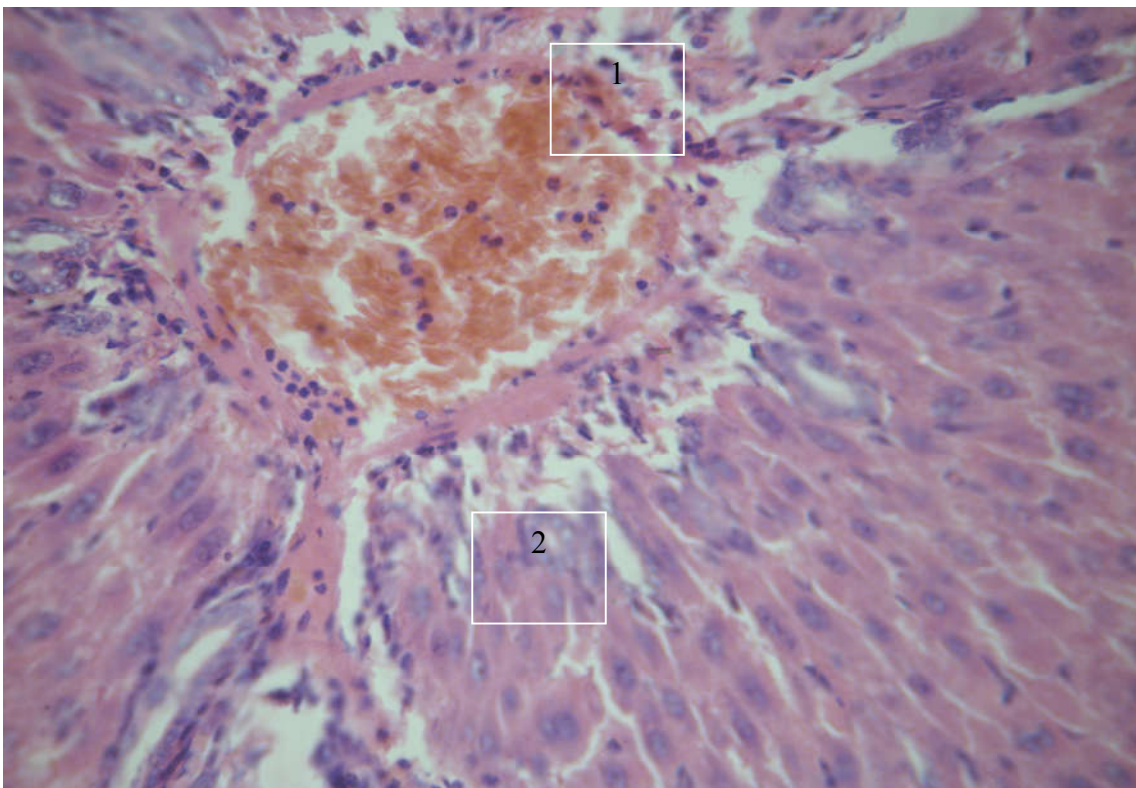


Fig. 2. Morphological changes in group 2 rat. Lymphocytic infiltration, central vein fibrosis, fibrous cords, cytoplasmic protein dystrophy, necrosis, ductular proliferation; 1 – lymphoid infiltration; 2 – ductular proliferation. Hematoxylin&Eosin stain. ×400.

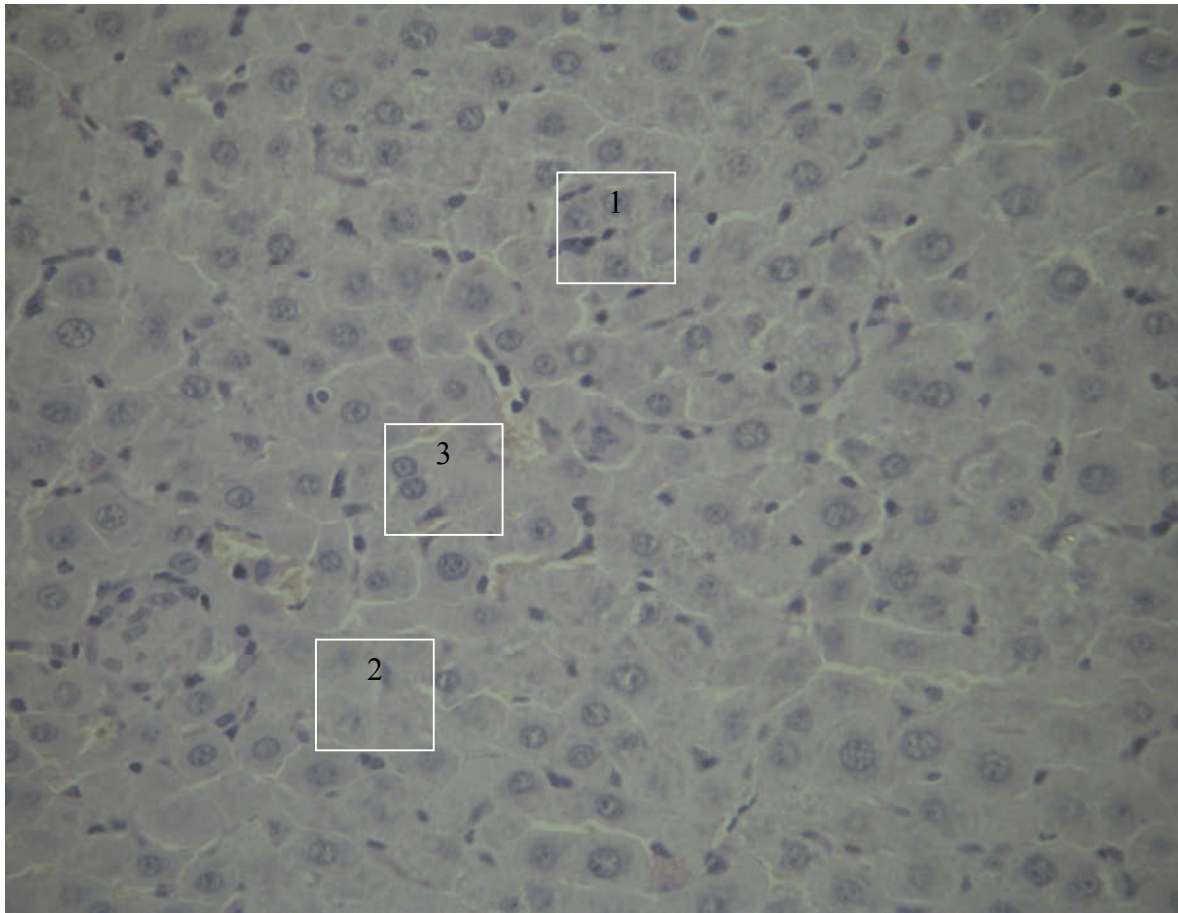


Fig. 3. Morphological changes in group 3 rat receiving L-Arginine L-glutamate. Lymphocytic infiltration, cytoplasmic protein dystrophy, 'empty' cytoplasm; 1 — lymphoid infiltration; 2 — cytoplasmic protein dystrophy, 'empty' cytoplasm; 3 — binuclear hepatocytes. Periodic acid-Schiff stain. $\times 400$.

References

1. EASL Recommendations on Treatment of Hepatitis C. *J Hepatol.* 2015;63:199-236. At: <http://www.easl.eu/medias/cpg/HEPC-2015/Full-report.pdf>.
2. Bataller R, Brenner DA. Hepatic stellate cells as a target for the treatment of liver fibrosis. *Semin Liver Dis.* 2001;21:437-51. PMID: 11586471.
3. Serov VV, Shehter AB. [Connective tissue (functional morphology and general pathology)] Moscow: Meditsina; 1981. 312 p. Russian.
4. Fedorchenko SV. [Chronic HCV-infection: monograph]. Kyiv: Medytsyna; 2010. 272 p. Ukrainian.
5. Friedman SL, Maher JJ, Bissell DM. Mechanisms and therapy of hepatic fibrosis: report of the AASLD Single Topic Basic Research Conference. *Hepatology.* 2000;32(6):1403-8. PMID: 11093750.

6. Afdhal NH, Nunes D. Evaluation of liver fibrosis: a concise review. *Am J Gastroenterol.* 2004;99(6):1160-74. PMID: 15180741.
7. Malyi VP, Zvyaginceva TD, Titovskii SP. [HCV infection (acute and chronic): clinical, pathogenetic and therapeutic aspects]. Kyiv; 2005. 292 p. Russian.
8. Sherlock S, Duli G, authors. [Diseases of the liver and biliary tract] [translated from English]. Moscow: GEOTAR-Meditsina; 2002. 864 p. Russian.
9. Desmet VJ. Histological classification of chronic hepatitis. *Acta Gastroenterol Belgica.* 1997;60(4):259-67.
10. Shevchenko OP, Suremenko MS, Svyatenko TV, Bila-Popovich GS, Striga VA. [Infection with viral hepatitis B and C among patients with different pathologies in risk groups and the general population in the Dnipropetrovsk region]. *Dermatovenerologiya, Kosmetologiya, Seksopatologiya.* 2007;(1-4):144-8. Ukrainian.
11. Andreichin MA., Drizhak VI, Ryabokon OV, Kopcha VS. [Viral hepatitis and liver cancer] Ternopil: TDMU; 2010. 188 p. Ukrainian.
12. Pavlov ChS. [The principles of diagnosis and treatment approaches to fibrosis and cirrhosis of liver]. *Ross Med Zh.* 2007;9(1):11-5. Russian.
13. Arthur MJ. Reversibility of liver fibrosis and cirrhosis following treatment for hepatitis C. *Gastroenterology.* 2002 May;122(5):1525-8.. PMID: 11984538.
14. Kobrin TI, Telegin DE. [Predicting effectiveness of antiviral therapy in patients with chronic hepatitis C]. *Infektsiini hvoroby.* 2010;(2):69-79. Ukrainian.
15. Pawlotsky JM. Hepatitis C treatment: the data flood goes on – an update from the liver meeting 2014. *Gastroenterology.* 2015 Mar;148(3):468-79. doi: 10.1053/j.gastro.2015.01.002. PMID: 25576860.
16. Serpaggi J, Carnot F, Nalpas B, Canioni D, Guéchet J, Lebray P, Vallet-Pichard A, Fontaine H, Bedossa P, Pol S. Direct and indirect evidence for the reversibility of cirrhosis. *Hum Pathol.* 2006 Dec;37(12):1519-26. PMID: 16997354.
17. Brenner DA. Reversibility of Liver Fibrosis. *Gastroenterol Hepatol.* 2013;9(11):737-9. PMID: PMC3995196.
18. Shevchenko OP, Pokrova OD, Bila-Popovich GS. [Treatment of viral hepatitis on a background of uremia]. *Dermatovenerologiya, Kosmetologiya, Seksopatologiya.* 2006;(3-4):174-7. Ukrainian.
19. Fadeenko GD, Kushnir IE', Chernova VM, Solomenceva TA [et al.]. [Application of glutargin of patients with liver cirrhosis]. In: [Collected works of scientific-practic. conf. "Glutargin - new principles of pharmacotherapy of liver disease"; 2003; Kharkiv, Ukraine]. Kharkiv; 2003. p.58-9.
20. Gubergric NB. [Chronic hepatitis and cirrhosis of the liver. Modern classification, diagnostics and treatment: a training manual]. 3rd ed., rev. and enl. Kyiv: ZAO Vipol; 2010. 328 p. Russian.

21. Matyash VI. [Evaluation of the effectiveness glutargin in Integrated viral therapy hepatitis]. In: [Application of the new Ukrainian Glutargin drug in clinical practice: A guide for practitioners; 2003; Kharkiv and Lugansk, Ukraine]. Kharkiv, Lugansk; 2003. p. 44-50. Russian.
22. Golubovska OA, editor. [Infectious diseases: textbook]. Kyiv: Medytsyna; 2012. 728 p. Ukrainian.
23. Shostakovich-Koretska LR, Andreeva IA, Shevchenko OP. [Cabinet of infectious diseases: the structure, functions and organization of work: study guide]. Dnepropetrovsk; 2013. 175 p. Ukrainian.
24. Nakamura T, Sakata R, Ueno T, Sata M, Ueno H. Inhibition of transforming growth factor beta prevents progression of liver fibrosis and enhances hepatocyte regeneration in dimethylnitrosamine-treated rats. *Hepatology*. 2000 Aug;32(2):247-55. PMID: 10915731.
25. Ikejima K, Honda H, Yoshikawa M, Hirose M, Kitamura T, Takei Y, Sato N. Leptin augments inflammatory and profibrogenic responses in the murine liver induced by hepatotoxic chemicals. *Hepatology*. 2001;34(2):288-297. PMID: 11481614.
26. Shevchenko OP, Fomenko OZ, Shevcova AI, Ushakova GO. [Changes of matrix metalloproteinase activity and glycosaminoglycans in conditions of chronic hepatitis induced in rats]. *Odessa medical journal*. 2009;(6):31-3. Ukrainian.
27. Babak OYa. [Application of the new drug glutargin in gastroenterology]. *Suchasna gastroenterologiya*. 2003;2(12):85-9. Russian.
28. Baranova IP, Zykova OA, Konnova OA. [Viral hepatitis A: cytoflavin metabolic therapy: A guide for doctors]. Penza; 2006. 18 p. Russian.
29. Shevchenko OP, Suremenko MS, BilaPopovich GS. [Glutargin efficacy in treatment of patients with cirrhosis]. *Naukovyi visnyk Uzhgorodskogo universytetu. Series: Medicine*. 2009;36:35-7. Ukrainian.
30. Sukhanov DS. [Application of cytoflavin therapy for medicinal liver lesions in patients with pulmonary tuberculosis] In: [Proceedings of XIII Russian National Congress "Human and medicine"; 2006; Moscow, Russia]. Moscow; 2006. p. 297. Russian.
31. Nikolenko VYu, Nikolenko Yul, Nikolenko OYu; inventors; Horkyi Donetsk State Medical University, assignee. Method for simulating chronic hepatitis type "C". Ukrainian patent UA 15752. 2006 Jul 17. Int Cl. G09B 23/28. Ukrainian.
32. Shevchenko OP. [Study of glutargin antyfibrotic action in experimental models of chronic hepatitis C] In: [Liver disease in clinical practice: materials scientific-practic. conf. with intern. participation; 2009; Kharkiv, Ukraine]. Kharkiv; 2009. p.191-2. Ukrainian.

33. Shevchenko OP, Fomenko OZ. [The cytoflavin impact on liver regeneration and contents of the extracellular matrix in experimental hepatitis in rats]. In: [Current issues of pharmaceutical and medical science and practice 2011: All-Ukrainian scientific-practic. conf. with Intern. participation 'Modern aspects of medicine and pharmacy-2011'; Zaporizhzhia, Ukraine]. Zaporizhzhya; 2011. Vol. 24, part 2. p. 18. Ukrainian.