and shift of NADH/NAD^+ ratio to NADH. The lower content of cytochrome b_5 - electron acceptor in NADH-dependent microsomal electron-transfering chain (Archakov, 1975) may contribute into the slower rate of NADH oxidation in those animals.

The higher hypnotic effect of ethanol can also indicate the higher behavioural sensitivity of these animals to alcohol. It is interesting that it is associated with higher sensitivity of hepatocytes to ethanol-induced injury.

Thus, the results of our study indicate that the initial individual specificity of the biochemical processes in rat liver play an important role in the sensitivity to hepatotoxic effect of ethanol. A more active alcohol dehydrogenase and lipid peroxidation system, low antioxidant potential, low UDP-glucuronyl transferase and glutathione S-transferase activities, low cytochrome b_5 content and low rate of NADH oxidation predispose to the alcohol-induced liver damage.

The proposed animal model and approach can be used in the finding of new biomarkers of the sensitivity to the hepatotoxic effect of ethanol (predisposition to the alcohol-induced liver damage) as well as biomarkers of the initial sensitivity to other hepatotoxins.

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References

1. Abakumov, G.Z., Novitzky, G.K., Legon'kova, L.F. Role of the lipid peroxidation in the pathogenesis of virus hepatiti... Voprosy meditsinskoi khimii. - 1982. - N 6. P. 30-32.
2. Afifi A., Eisen C. Statistical analyses. Approach with the usi... of C. – Moscow, 1982.
3. Albano, E., Clot, P., Morimoto, M., Tomasi, ... Ingelman-Sundberg, M., French, S.W. Role of cytochrome P450 2E... dependent formation of hydroxyethyl free radical in the develop... of liver damage in rats intragastrically fed with ethanol. // Hepat... logy. - 1... 6. - N 23. - P. 155-163.
4. Archakov, A.I.(1975) Microsomal ...idation. N...ka, Moscow.
5. Buege, J.A., Aust, S.D. // In: Methods in ...nzymology. - Academic Press, New York, 1978. - V... 52. - P. ...6-312.
6. Dallner, G. Studies on the structural and enzymic organization of the membraneous elements of liver microsomes. // Acta Pathologica Microbiologica. - 196... - N 66. - ...94.
7. Day, C. P., Yeaman, S. ... The biochemistry of alcohol-induced fatty liver. // Biochem... et Biophysica Acta. - 1994. - N 1215. - P. 33 – 48.
8. Gatautus, V. J., Kar... L., Pearson, H. Separation of plasma carotenoids and guantit... of ... carotene using HPLC. // Clinica Chimica Acta. - 1987. - ... 166. - P. 19... – 206.
9. G...imo... K., ...orolyova, L.A., Brusov, O.S., Olfer'ev, V.D., Anto...enko, V.D., Panenko, L.F. Fermentativnye mekhanismy torm...henia perekisnogo okislenia v raslichnykh otdelakh golovnogo mozga krys. // Voprosy meditsinskoi khimii. - 1976. - N 22. - P. 89-94.
10. ...ette, J. R., Brodie, B. B., La Du, B. N. The oxidation of drugs by liver microsomes on the role of TPNH and oxygen. // Journal of Pharmacology and Experimental Therapeuties. - 1957. - N 119. - P. 532 – 540.
11. Habig, W. H., Pabst, M. I., Jakoby, W. B. Glutathione-S – transferases – the first enzymatic step in mercapturic acid formation. // Journal of Biological Chemistry. - 1974. - N 249. - P. 7130 – 7139.
12. Higgins, G. M., Anderson, R. M. Experimental pathology of the liver. I. Restoration of the liver of the white rat following partial surgical removal.//Archives of Pathology. - 1931. - N 12. - P. 186 - 202.
13. Ishak, K. G., Zimmerman, H. J., Ray, M. B. Alcoholic liver disease: pathologic, pathogenetic and clinical aspects. // Alcoholism: Clinical and Experimental Research. - 1991. - N 15. - P. 45 – 66.
14. Isselbaher, K. J. Enzymatic mechanisms of hormone metabolism. II. Mechanism of hormonal glucuronide formation. // Recent Progress Hormone Research. - 1956. N 12. - P. 134 - 143.
15. Karuzina, I.I., Archakov, A.I. Purification of the microsomal fraction of the liver and characteristics of its oxidation system.// In: Sovremennye metody v biokhimii / pod obshchei redaktsiei V.K.Orekhovicha. - Meditsina, Moscow. - 1977. - P. 42 - 78.
16. Kato, R., Gillette, R. Effect of starvation on NADPH – dependent enzymes in liver microsomes of male and female rats. // Journal of Pharmacology and Experimental Therapeutics. - 1965. - N 50. - P. 279 – 284.
17. Kawase, T., Kato, S., Lieber, S. C. Lipid peroxidation and antioxidant defence systems in rat liver after chronol ethanol feeding. // Hepatology. 1989. - N 10. - P. 815 – 821.
18. Kolb, V. G., Kamyshnikov, V. S. // Handbook on clinical chemistry. - Minsk, 1982. - P. 111 – 121.
19. Koroliuk, M.A., Ivanova, L.I., Maiorova, I.G., Toch... V.E. Method of the catalase activity determination. // Laborator... delo. - 1... 8. - N 1. - P. 16-19.
20. Kostiuk, V.A., Potapovich, A.I., Kovalyov... V. Simple and sensitive method of SOD activity determination, ... the reaction of cvertesin oxidation. // Voprosy me...tsinskoi khimii. - 1990. - N 2. - P. 88-91.
21. Kostiuk, V.A., Potapovich, A.I., ...unets, E.F. Spectrophotometric method of conjugated diens determination. // Voprosy meditsinskoi khimii. - 1984. - N 4. - P. ...127.
22. Lauterberg, B. H., Bilzer M. Mechanisms of acetaldehyde hepatotoxicity. // Journal of Hepatology. - 1988. - N 7. - P. 384-390.
23. Lieber, C. S. Alcohol and the liver: 1994 update. // Gastroenterology. - 1994. - N 106. - P. 1085 – 1105.
24. Lieber, C. S. Hepatic and other medical disorders of alcoholism: From pathogenesis to treatment. // Journal Studies of Alcoholism. - 1998. N 59. P. – 5.
25. Lieber, C. S. Microsomal ethanol-oxidazing system (MEOS): the first 30 years (1... – 1998)-a review. // Alcoholism: Clinical and Experimental Research. - 1999. - N 23. - P. 991 – 1007.
26. Lieber, S. S. and DeCarli, L. M. Hepatotoxicity of ethanol. // Journal of Hepatology. 1991. - N 12. - P. 394 – 401.
27. Lindros, K. O. Alcoholic liver disease: pathobiological aspects. // Journal of Hepatology. - 1995. - N 23. - P. 7 – 15.
28. Lipsrst, C.L.,Mimnaugh, E.G., Reagan, R.J. Drug metabolism by microsomes from extrahepatic organs of rat and rabbit prepared by calcium aggregation. // Life Sciences. - 1975. - N 17. - P. 813 – 818.
29. Mezey, E. Alcoholic liver disease. // Progres Liver Diseases. - 1982. - N 7. - P. 555 – 572.
30. Moin, V.M. Simple and sensitive method of glutathione activity determination in erythrocyte. // Laboratornoe delo. - 1986. - N 12. - P. 724-727.
31. Nordmann R., Ribiere C., Rouach H. Implication of free radical mechanisms in ethanol-induced cellular injury. // Free Radical Biology & Medicine. - 1992. - N 12. - P. 219 – 240.
32. Omura, T., Sato, R. (1964) The carbon monooxide-binoling pigment of liver microsomes. 2. Solubization, purification and properties
33. Pron'ko, P.S., Kus'mich, A.B., Zimatkin, S.M. Acetaldehyde concentration in blood of rats following alcohol intoxication and action of inhibitors. // Voprosy narkologii. - 1993. - N 3. - P. 40-42.
34. Pron'ko, P.S., Tarasov, Yu.A., Shishkin, S.N., Ostrovsky, Yu.M. Correlation of circade rhythms and endogenous ethanol and 11-oxicortikosterone levels in the rat body. // Vesti AN BSSR. Seriya biologicheskikh nauk. - 1987. - N 2. - P. 79-82.
35. Sedlak, J., Lindsay, R. H. Estimation of total proteinbound and nonprotein sulfhydryl group in tissue with Ellman's reagent. // Analytical Biochemistry. - 1968. - N 25. - P. 192 – 205.
36. Sherlock, Sh., Doolie, J. Liver and bile vessels diseases. - Moscow, 1999. - P. 440 – 462.
37. Simpson, K. J. Pathogenesis of alcoholic hepatic steatosis. // Addiction Biology. - 1996. - N 1. - P. 363 – 370.
38. Strominger, J. L., Maxweell, E. S., Axelrod, J., Kalckop, K. M. Enzymatic formation of uridine diphosphoglucuronic acid. // Journal of Bioloical. Chemistry. - 1957. - N 224. - P. 79 – 90.
39. Taylor, S. L. Sensitive fluorimetric method for tissul tocopherol analysis. // Lipids. - 1976. - N 11. - P. 350 – 358.
40. Tottmar, S. O. C., Petterson, H., Kiessling, K. H. // Biochemical Journal. - 1973. - N 135. - P. 577 – 586.
41. Urbakh, V. Yu. Statistical analyses in biological and medical studies. - Moscow, 1975.
42. Wight, D. G. D. Atlas of liver pathology.-2nd ed., Kluwer Acad. Publisher. - Dordrecht/Boston/London, 1993.
43. Zimatkin, S. M., Pronko, P. S., Grinevich, V. P. Alcohol action on liver: dose dependence and morpho-biochemical correlation's. //Casopis lekaru Ceskych. - 1997. - N 136. - P. 598 – 602.