

INFLUENCE OF NIFEDIPINE, NITRENDIPINE AND VERAPAMIL AT LOW CONCENTRATION ON ANTIPYRINE METABOLISM EXAMINED BY EXTRACORPOREAL RAT LIVER PERFUSION

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An increase in calcium ion concentration in the cytoplasm due to the influence of various toxic agents causes disturbances in the structure and function of hepatocytes, leading to their damage and even death. Calcium ions enter the cell mostly through calcium channels, therefore, it has been suggested that calcium channel inhibitors (CCI) could protect hepatocytes from the action of toxic substances.

The present study investigated the effect of the selected CCI (nifedipine, nitrendipine and verapamil) on liver function, measured by the efficiency of oxidation reaction, in this case by determination of the rate of antipyrine metabolism. The experiment was carried out using the method of extracorporeal liver perfusion (ELP).

None of the studied CCI applied at a concentration of 50 $\mu\text{mol/l}$ increased the rate of antipyrine metabolism over the whole period of ELP. However, supplementation of perfusion fluid with nifedipine, nitrendipine or verapamil at a concentration of 20 $\mu\text{mol/l}$ considerably improved metabolic liver efficiency during the second hour of perfusion, i.e. at the time, when large number of hepatocytes started to perish, which could indicate protective action of the tested CCI. However, the CCI-induced acceleration of antipyrine metabolism was not a result of their influence on calcium channels, since these drugs block calcium channels, when given at the concentrations as high as 100–400 $\mu\text{mol/l}$. Moreover, it seems that facilitation of antipyrine metabolism during ELP was not due to their action on microsomal enzymes because CCI were administered at very low concentrations, besides, they are metabolic inhibitors, and not inducers. The present experiment suggests that low concentrations of CCI can exert hepatoprotective effect. However, confirmation of this conclusion requires further studies using other experimental methods.

Key words: *nifedipine, nitrendipine, verapamil, antipyrine metabolism, extracorporeal liver perfusion*

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