

SUMMARY

Contribution to the study of the etiology and clinical significance of hepatic steatosis in the experiment

The aim of this dissertation thesis is to elucidate and describe the influence of ursolic acid and its hepatoprotective effects on liver tissue after partial hepatectomy and the effects of this acid on lipid metabolism. It includes studies of the early phase of liver regeneration in rats with induced hepatic steatosis.

The first part of the dissertation is focused on the study of liver regeneration after partial hepatectomy in rats with nutritionally induced hepatic steatosis using three experimental diets. To assess the liver regeneration, two rat models were selected, a healthy Wistar-type rat and a rat with high basal cholesterolemia, the so-called Prague hereditary hypercholesterolemic rat (PHHC). The standard model of non-alcoholic fatty liver disease (NAFLD), achieved by feeding both rat types on a high-cholesterol diet and an orotic acid diet for four weeks, confirmed the development of hepatic steatosis without signs of inflammation, necrosis or fibrotic changes. The methionine-choline deficient diet did not induce steatosis in the histological examination, although disruption of VLDL particle synthesis was found. Based on the incorporation of ^3H -thymidine into hepatocyte's DNA, the course of liver regeneration was slowed down in experiments with the high-cholesterol diet and with the orotic acid diet. The orotic acid model did not work well for the study of liver regeneration, due to the severe damage of the rat's liver parenchyma even before the partial hepatectomy and this operation was incompatible with survival of the rats. Comparison of the regeneration rate after partial hepatectomy between Wistar rats and PHHC rats by DNA synthesis assessment at 18 and 24 hours shows a delay in the onset of regeneration in hypercholesterolemic rats. That indicates possible complications for patients with simple steatosis undergoing liver transplantation or liver tissue resection.

The second topic was focused on liver regeneration influenced by the administration of various forms of ursolic acid, which were prepared exclusively from natural sources without the use of chemical solvents. Ursolic acid is known for its hepatoprotective effects but its low bioavailability is a major complication of its wider use. The hypolipidemic effects of ursolic acid were found after only 7 days of application in rats on a high-fat diet as significant reduction of cholesterol and triacylglycerol concentrations. At the same time, a supplementation with ursolic acid has been shown to stimulate DNA synthesis with lower enzymatic activity of ALT and AST after invasive surgery. Finally, the positive effects of ursolic acid on liver tissue before partial hepatectomy were found and suggested ursolic acid as a substance with hepatoprotective effects.