Abstract

This thesis is focused on the study of glycosphingolipids in the rat liver in different types of cholestasis and the effect of oxidative stress on changes in the composition and localization of gangliosides.

First, it was necessary to optimize the immunochemical detection of glycosphingolipids. GM1 ganglioside was selected as a representative of a large glycolipid family. We found that minimum water content in the fixing solution was a key condition for fixation of histological sections. Optimized method of GM1 detection was subsequently used in *in vivo* experiments.

We have demonstrated that estrogen-induced cholestasis characterized by high concentrations of bile acids and increased oxidative stress caused changes in the synthesis and distribution of liver gangliosides. HMOX induction is associated with a reduction in oxidative stress level and accompanied by normalization in GSL content.

In experiments with obstructive cholestasis, we found that changes in the distribution and synthesis of gangliosides were not strictly specific to a particular type of cholestasis. We assume that it represents a general mechanism of hepatoprotection. We also confirmed the important role of bilirubin, product of HMOX reaction, in protection of hepatocytes against oxidative damage caused by high concentrations of bile acids in obstructive cholestasis.

The results of the thesis demonstrate that accumulated bile acids and increased oxidative stress in the liver result in changes in the synthesis and distribution of glycosphingolipids. These molecules play important role in hepatoprotection due to their physical-chemical properties. HMOX induction may reduce oxidative stress and affect metabolism of gangliosides.

Key words: GM1 ganglioside, Heme oxygenase, Cholestasis, Oxidative stress