Summary

Liver mitochondria play a crucial role in intermediary metabolism and main metabolic pathways. We evaluated the pharmacological effect on liver mitochondria *in vitro* using two novel anticancer drugs: 3-bromopyruvate and α-tocopheryl succinate. Metabolic influence on liver mitochondria was performed *in vivo* by high fat and high cholesterol diet.

Toxicity of both drugs was evaluated in cell cultures of hepatocytes isolated from rat and mouse liver. The effect of anticancer drugs on liver mitochondrial functions *in vitro* was studied on suspensions of isolated liver mitochondria, tissue homogenate and permeabilized hepatocytes. Mitochondrial respiration was measured using high-resolution respirometry.

3-bromopyruvate caused morphological and functional damage of primary rat and mouse hepatocytes in cell cultures; this toxic effect was accompanied by an increase of reactive oxygen species production and mitochondrial dysfunction. 3-bromopyruvate decreased the oxygen consumption of mitochondria energized by substrates for complex I and complex II. α-Tocopheryl succinate caused a decrease of succinate-dependent respiration in all experimental models both in coupled and in uncoupled states. The most pronounced effect of α-tocopheryl succinate was apparent in isolated mitochondria and the least pronounced effect was observed in permeabilized hepatocytes.

High fat and high cholesterol diet caused changes of liver mitochondrial functions which were dependent on duration of the treatment. The maximal capacity of oxidative phosphorylation was increased after three weeks of the experiment, but followed by a decline after 6 weeks and later in comparison to normal diet controls. The oxidation of Krebs cycle substrates was significantly inhibited after 12 and more weeks of high fat diet feeding. On the other hand β-oxidation of fatty acids was increased already after one week of high fat diet feeding. The capacity of fatty acids oxidation returned to control level after 24 weeks of experimental diet.