

ABSTRACT

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Title of thesis: Inhibition study of human membrane-bound carbonyl reductase.

Carbonyl reductases are an important group of enzymes that participate in metabolism of both endogenous substances also xenobiotics. Potential anticancer drug oracin is one of such xenobiotics that is metabolised by various carbonyl reductases to two enantiomers of dihydrooracin. The new human microsomal carbonyl reductase also takes part in biotransformation of oracin. This enzyme was recently purified on Department of biochemical sciences (Faculty of Pharmacy in Hradec Králové). The aim of this study was to find some inhibitors of the new enzyme and distinguish it in terms of inhibitors from another microsomal carbonyl reductase 11 β -hydroxysteroid dehydrogenase 1.

Flavonoids are substances produced by plants, they have a different both positive and also negative effect on human organism. One of such effect is inhibition effect on diverse enzymes. Carbonyl reductases also fall in this group. It has been described inhibitory effect of different flavonoids on carbonyl reductases.

Inhibition study of the new human micorosomal carbonylreductase was made with a group of flavonoids. The strongest inhibitor from the group of substances was quercetin and further apigenin, silibinin, luteolin, chlorogenic acid and rutin. Effect of quercetin and also 18 β -glycyrrhetic acid (an inhibitor of 11 β -hydroxysteroid dehydrogenase 1) on biotransformation of oracin in whole human liver micorosomal fraction was also determined.