Abstract

The use of food supplements containing natural chemopreventive compounds increased in recent years. Some of the most popular chemopreventive compounds are flavonoids. Due to their natural origin, flavonoids are generally accepted as safe compounds. They exert antioxidant, anti-cancer and anti-inflammatory properties. However, flavonoids should be considered as foreign compounds (xenobiotics). Flavonoids interact with many enzymes, among the most important belong cytochromes P450 (CYPs), key enzymes of the first phase of biotransformation of xenobiotics (e.g. drugs, carcinogens). CYPs catalyze reactions leading mainly to detoxification of xenobiotics. However, some CYPs are involved in the activation of carcinogens, particularly CYP1A1 and CYP1A2 activate e.g. heterocyclic amines. Flavonoids might enhance the activation of carcinogens via induction of these CYPs or stimulation of their activities and hence, increase the risk of a cancer development.

The thesis is focused on the influence of flavonoids and food carcinogens on the induction and activity of CYP1A1 and CYP1A2 in liver and small intestine of rats. For the purpose of this study, the small intestine was dissected into three parts: proximal (nearest to stomach), middle and distal. Western blotting was used for the evaluation of CYP induction. Activities of CYP1A1 and CYP1A2 were determined by using specific substrates 7-ethoxyresorufin and 7-methoxyresorufin, respectively.

Tested flavonoids (administered p.o.) myricetin, dihydromyricetin and food supplement Antistax containing flavonoids did not influence the induction and activity of CYP1A1 and CYP1A2 significantly neither in rat liver nor in the small intestine.

Next, the sequential p.o. exposure of animals to model chemopreventive compound β-naphthoflavone (known inducer of CYP1A family) and food carcinogen PhIP was carried out. Both compounds were administered also separately. In rat liver, the administration of PhIP 72 h after β-naphthoflavone caused slight decrease in the induction and activity of CYP1A1 in comparison with β-naphthoflavone administered separately. In small intestine, this decrease was not found. In the small intestine, the highest induction and activity of CYP1A1 after p.o. administration of β-naphthoflavone and β-naphthoflavone with PhIP was detected in the proximal part of the small intestine and decreased gradually towards the distal part.

In this thesis, the influence of i.p. administered carcinogen Sudan I on induction of CYP1A1 in rat small intestine was also examined. In all parts of the small intestine Sudan I induced CYP1A1 to the same extend.

(In Czech)

Key words: carcinogens, chemoprevention, cytochrome P450, flavonoids, Western blotting