ABSTRACT

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Title of a rigorous work: **The influence of flavonoids on the metabolism of xenobiotics**

Flavonoids are wide spread plant secondary metabolites with the protective effect against the cancer. One of the protective mechanisms of action is the modulation of the biotransformation enzymes. Xenobiotics - heterocyclic aromatic amines are presumably carcinogenic compounds generated during the ordinary cooking of meat and fish. The first metabolic step of the heterocyclic aromatic amines is the procarcinogen activation to the active *N*-hydroxy metabolites by cytochrome P4501A2 (CYP1A2). It would be desirable if the flavonoids in the appropriate manner modulate the enzymatic activity to eliminate the undesirable effects of the heterocyclic aromatic amines.

The aim of this study was to investigate the influence of the rutin and quercetin flavonoids and heterocyclic aromatic amines 2-amino-3-methylimidazo[4,5-*f*]quinoline (IQ) and 2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline (MeIQx) on CYP1A activity in the cell line LS174T and HCT-8. Rutin, quercetin, IQ and MeIQx were not toxic for cells up to the concentration of 50 μM. Quercetin was cytotoxic in higher concentrations. Quercetin is more toxic for the cell line LS174T in lower concentrations than for the cell line HCT-8.

Neither the 7-ethoxyresorufin-*O*-dealkylation (EROD) test nor the 7-methoxyresorufin-*O*-dealkylation (MROD) test affected CYP1A activity by the concentrations up to 50 μM of rutin, quercetin and MeIQx in the cell lines LS174T and HCT-8. IQ increased the amount of resorufin in the EROD test 1,6-times comparing to the control and 1,2-times in the MROD test comparing to the control in the cell line LS174T. EROD and MROD tests in the cell line HCT-8 were not influenced by those compounds.

Even if no effect of interference of flavonoids and heterocyclic aromatic amines on the CYP1A activity in the selected cell lines was detected, those compounds can interfere during the metabolism inside the organism in phase 1 or 2 of biotransformation or on a different pharmacokinetic level.