

ABSTRACT

Charles University in Prague

Faculty of Pharmacy in Hradec Králové

Department of Biochemical Sciences

Candidate: Marie Volková

Supervisor: Doc. RNDr. Lenka Skálová, Ph.D.

Title of diploma thesis: Modulatory effects of Quercetin and Rutin on the activity and expression of cytochrome P4501A in the intestinal cells

Flavonoids originate as the secondary metabolites of plants and they are daily consumed in fruits and vegetables. They show the antioxidant, antiinflammatory, anticarcinogenic and other healthy effects. A potential anticarcinogenic effect is mediated by the strong antioxidant activity, but it can also include an inhibition of xenobiotica - metabolizing enzymes to the carcinogenic compounds.

This work has examined the potential inhibition effect of the flavonoids Rutin and Quercetin on an activity and expression of cytochrome P4501A (CYP1A) in the intestinal cells. Quercetin is the most abundant flavonoid and Rutin is its most abundant glycosidic form. CYP1A is responsible for an activation of many pre - carcinogenic ingested substances. The study was conducted on the intestinal cell line HCT-8. CYP1A's enzymatic activity was measured by EROD/MROD activity; quantity of CYP1A's protein was set by Western blotting.

Quercetin at the concentration of 1 μ M caused slightly increased EROD/MROD activity but higher concentration of Quercetin decreased EROD/MROD activity substantially. During a synchronous application with model inducers CYP1A (Methylcholantren, MCH; β -naftoflavon, β -NF), Quercetin significantly reduced induction of EROD/MROD activity mediated by MCH or β -NF. Quercetin also inhibited EROD/MROD activity in those cells where CYP1A had been induced by exposure with MCH or β -NF in advance. Rutin's effect, on the other hand, was substantially weaker and virtually insignificant in all conducted experiments.

Quercetin contained in food can partially reduce the activation of the pre-carcinogenics in the intestinal cells.