## Abstract

Flavonoids are natural compounds commonly ingested in herbs and vegetables. They are believed to have a positive impact on human organism, in particular by their antioxidant, hepatoprotective and anti-cancer effects. In these days, it is possible to consume high concentrations of these compounds in form of dietary supplements. However it is not clear, whether flavonoids in such unnaturally high concentrations are still beneficial or rather harmful. It has already been proven, that flavonoids can influence the activity of biotransformation enzymes and interfere e.g. with the process of carcinogenesis and drug metabolism. For that reason it is important to investigate the impact of an increased intake of flavonoids.

The aim of this thesis was to investigate the influence of dihydromyricetin (a potential drug to cure alcohol use disorder) and its structurally similar flavonoid myricetin on the activity of enzymes, cytochrome P450 2E1 (CYP2E1) and N-acetyltransferases 1 and 2 (NAT1/2). The research included the determination of the impact of a premedication by these flavonoids on the expression and activity of CYP2E1 and NAT1/2. The inhibition capacity of myricetin and dihydromyricetin towards the activity of CYP2E1 and NAT1/2 was also investigated.

After the flavonoid premedication of rats the expression of CYP2E1 at its protein level did not differ from that of untreated control. The activity of CYP2E1 wasn't inhibited in an observed range of flavonoid concentrations (less than 0.1 mM).

An increase of the expression or the activity of NAT1/2 wasn't detected in isolated hepatic and intestinal cytosols of premedicated rats. Only in a proximal part of a small intestine the activity of NAT2 was decreased (more than 80%) after the myricetin premedication. The both flavonoids were proven to be inhibitors of human recombinant NAT. $IC_{50}$ were determined as 3.5 μM and 3.7 μM for myricetin towards NAT1 and NAT2 respectively, and 8.5 μM and 8.9 μM for dihydromyricetin towards NAT1 and NAT2.

Neither dihydromyricetin nor myricetin influenced the activity of CYP2E1, whereas both flavonoids are inhibitors of NAT.



**Key words**: Cytochromes P450, N-acetyltransferases, Metabolism, Induction