

ABSTRACT

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Title of diploma thesis: Effect of prenylated flavonoids on biotransformation enzymes *in vitro*

Prenylated flavonoids xanthohumol (XH), isoxanthohumol (IXH), 6-prenylnaringenin (6PN) and 8-prenylnaringenin (8PN) are flavanones and chalcones occurring in hops and their characteristic feature is prenyl chain on A ring. As these substances, present in beer and dietary supplements, are foreign compounds for organism, they can affect drug-metabolizing enzymes, including carbonyl reducing enzymes. The aim of our study was to find out, whether XH, IXH, 6PN, and 8PN have any impact on cytosolic carbonyl reductase 1 (CBR1) and aldo-keto reductase 1C subfamily (AKR1C). Viability test revealed that prenylated flavonoids in lower concentrations do not affect or even increase the viability of primary rat hepatocytes, but higher concentrations are toxic. AKR1C activity was increased in 8PN treated hepatocytes, the activity of CBR1 was significantly increased in IXH and 8PN treated samples. An increase in expression of AKR1C3 in IXH and 6PN treated samples, and decrease in XH and 8PN samples was observed. Expression of CBR1 was at the detection limit. Using qRT-PCR was found that XH caused significant increase in gene expression of *Cbr1*, and significant decrease in *Akr1c14* expression in rat hepatocytes. In cytosolic exposure study, the activities of tested enzymes were decreased in all samples in all concentrations, except 6PN (100 μ M), activity of CBR1 was also decreased in all samples treated with prenylated flavonoids with the exception of 6PN (10 and 100 μ M) and 8PN (10 and 50 μ M). Based on the results, prenylated flavonoids XH, IXH, 6PN and 8PN do affect the viability of hepatocytes, the activity of CBR1 and AKR1C subfamily, gene expression of enzymes is significantly affected only by XH.