ABSTRACT

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Title of diploma thesis: Metabolism and transport of 6-prenylnaringenin *in vitro*

Prenylflavonoids constitute a group of plant secondary metabolites with various positive effects on human health. Hops (*Humulus lupulus* L.) represent a rich source of prenylflavonoids including 6-prenylnaringenin (6-PN). Recently, 6-PN has been found to possess various biological effects including analgesic, antiproliferative, and estrogen-modulating activity. Despite its potential to be used as a nutraceutical, the pharmacokinetic properties of 6-PN are still unknown. This thesis had therefore two objectives. The first objective was to determine the hepatic and intestinal metabolism of 6-PN in humans as well as its hepatic metabolism in rats and mice *in vitro* using precision-cut tissue slices (PCTS). Samples were analyzed using UHPLC-MS/MS. 6-PN was efficiently metabolized predominantly into phase II metabolites with four glucuronides and four sulfates identified in the studied PCTS. For the first time, a novel metabolite of 6-PN formed as a result of concurrent glucuronidation and sulfation has been identified, which has not yet been described for other structurally similar hop prenylflavonoids. Sulfation occurred at higher rate in human intestinal (jejunum) PCTS compared to human liver PCTS. As for the interspecies differences, 6-PN was metabolized into two major glucuronides in rodent PCTS but only one major glucuronide in human PCTS. The second objective was to determine whether 6-PN is a substrate of the efflux transporter ABCB1. Human PCTS prepared from jejunum were incubated with or without the inhibitor of ABCB1, and the extent of 6-PN accumulation was then compared using UHPLC-MS/MS. The presence of the inhibitor had no effect on the accumulation of 6-PN in PCTS; therefore, 6-PN is probably not a substrate of ABCB1 transporter. This study provides new insights into the hepatic and intestinal metabolism of 6-PN in humans, as well as interspecies differences regarding its biotransformation. Furthermore, it provides new knowledge regarding the intestinal transport of 6-PN.