ABSTRACT

Charles University in Prague  
Fac. of Pharmacy in Hradec Králové  
Dept. of Biochemical Sciences

Julius-Maximilians-University Würzburg  
Institute of Pharmacy and Food Chemistry  
Dept. of Pharmaceutical Chemistry

Candidate: Jana Čejchanová
Supervisor: PharmDr. Iva Boušová, Ph.D.  
PD Dr. Matthias Unger

Title of diploma thesis: Inhibition of Drug Glucuronidation by Extracts and Constituents of St. John's wort (Hypericum perforatum) and Thyme (Thymus vulgaris)

The issue of herb-drug interactions is discussed in last years more than ever before due to all over the world increasing popularity of herbal drugs. Whereas the awareness of herbal drugs interactions with cytochrome P450 is quite broad, the issue of their interaction with UDP-glucuronosyltransferase (UGT) enzymes, one of the main participants of the second phase metabolism in humans, is still full of questions.

This work is focused on medicinal herbs St. John's wort (Hypericum perforatum) and thyme (Thymus vulgaris) and their impact on glucuronidation in the in vitro studies. The HPLC method for fractionation of herbal extracts was developed. The inhibitory activity of herbal extracts, individual fractions, and selected constituents on UGT was studied in human liver and/or human intestinal microsomes using model substrate TFMU (4-trifluoromethylumbelliferone). Products of these inhibition assays (TFMU glucuronides) were analyzed by RP-HPLC with fluorescence and UV detection as well as by LC/MS/MS. The residual UGT activity was calculated.

St John’s wort (SJW) and thyme extracts, as well as biflavones of SJW and flavonoid isorhamnetin exerted significant concentration-dependent UGT inhibitory activity, which was in all performed assays more pronounced in human intestinal than in human liver microsomes. The inhibitory activity of some fractions was also high. Based on the data obtained, it seems likely that mainly naphthodianthrones and phloroglucinols of SJW and flavonoids of thyme may contribute to UGT inhibition. This work showed that SJW, thyme, and some of their constituents are able to significantly inhibit glucuronidation reactions. Further studies are necessary to evaluate the clinical importance of this observation.