Species-, sex-, and tissue-dependent metabolism of soy isoflavones in humans, rats and mice and its biological implications.

Sebastian T. Soukup, Sabine E. Kulling, The IsoCross Consortium

Department of Safety and Quality of Fruit and Vegetables, Max Rubner-Institut, Karlsruhe, Germany

Abstract

The potential beneficial or adverse health effects of soy isoflavones (IF) especially the impact on hormone-related breast cancer is controversially discussed. As the biotransformation of IF affects their estrogenic potency, our aim was to determine the metabolism of IF in a comprehensive manner including the phase II and microbial derived metabolite profile of daidzein and genistein.
Due to the broad spectrum of possible IF metabolites with different physicochemical properties (logP, pks, and chemical stability) and the complexity of the biological matrices to be investigated, particular attention was given to the method for metabolite quantification. We succeeded in developing a sensitive and robust UHPLC-MS/MS method including an automated SPE sample preparation.
IF metabolites were analyzed in blood and selected tissues of humans, rats and mice of both sexes after intake of defined soy extract. In blood of humans IF were mainly conjugated (>98%) with 7-glucuronide-4'-sulfates as major metabolites, independent of sex. In rats IF were also mainly present as conjugates (>96%), in females as 7-glucuronides whereas in males daidzein-disulfate and genistein-7-glucuronide-4'-sulfate predominated. In mice considerably higher amounts of aglycones (3-26%) were found. The main phase II metabolites in mice of both sexes were the 7-glucuronides and 7-sulfates. Qualitative and quantitative species differences were also found regarding the microbial derived metabolite profile of IF.
In conclusion, marked differences in the IF metabolite profile between humans, rats and mice were observed. These should be considered when applying findings of animal studies to humans, e.g., for benefit-risk assessment of IF.

EUROTOX 2016 - 52st European Congress of the European Societies of Toxicology
04-07 September 2016, Seville, Spain