Title: Screening of oxidative metabolism of flavonoid aglycones by liquid chromatography-mass spectrometry

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Abstract:
Background Cytochromes P450 are the most significant enzymes for drug metabolism. Flavonoids are common constituents of everyday diet that have been shown to have beneficial potential on human health. Flavonoids undergo substantial hepatic metabolism and the metabolites might significantly contribute to the effects of these dietary constituents as well as possible interactions with drugs.

Purpose The objective of this study was to establish rapid high performance liquid chromatography-mass spectrometry (HPLC-MS) method for screening of metabolic profile of the larger number of flavonoid aglycones using human liver microsomes as the source of cytochrome P450 enzymes.

Methods Cytochrome P450-mediated metabolism was monitored on a set of 30 flavonoid aglycones. The formation of metabolites was determined by HPLC-MS method employing diode-array detector and accurate mass quadrupole time-of-flight mass spectrometry (Q-TOF/MS) detector.

Results The formation of metabolites was observed in 11 out of 30 flavonoids, namely 3,7-dihydroxyflavone, 6-hydroxyflavone, 7-hydroxyflavone, acacetin, apigenin, flavone, galangin, kaempferol, naringenin, sakuranetin and tangeretin. The identification of metabolites was based on accurate molecular mass and retention time compared to standard. Hydroxylation and demethylation were major metabolic pathways observed.

Conclusion Screening of cytochrome P450-mediated metabolism of flavonoids by human liver microsomes was successfully carried out using HPLC-MS. This methodology proved to be fast and reliable for assessment of metabolic behaviour of flavonoids. It can be further utilized for monitoring metabolic reactions mediated by individual cytochromes P450.