Determination of Pharmacokinetics of Chrysin and Its Conjugates in FVB Wild-Type and Bcrp1 Knockout Mice Using a Validated LC-MS/MS Method

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Purpose
The purpose of this study was to develop a sensitive and reproducible UPLC-MS/MS method to simultaneously quantify chrysin and its phase II metabolites, and to determine its pharmacokinetics in FVB wild-type and Bcrp(-/-) mice.

Methods
A Waters Ultra performance liquid chromatography (UPLC) system coupled with an ESI-triple quadrupole mass spectrometer (QTRAP5500; AB Sciex, Foster City, California) was used for the analysis in blood by MRM (Multiple Reaction Monitoring) method in the negative ion mode. An oral gavage of chrysin dispersed in oral suspension vehicle was given to wild-type and Bcrp (-/-) mice at dose of 20mg/kg. Blood samples at different time points were collected and analyzed by LC-MS/MS.

Results
The lower limit of quantitation (LLOQ) was 1.48, 1.70, and 0.5nM for chrysin, C-7-G, and C-7-S respectively. The validated method was successfully applied for pharmacokinetic study of chrysin in wild-type and Bcrp(-/-) FVB mouse after oral administration (20mg/kg). The AUC values for chrysin, C-7-G, and C-7-S was (0.06 ± 0.04), (2.00±0.82), and (1.32±0.42) h µM in wild-type mice and (0.11±0.08), (2.83±3.03), and (2.62±3.31) h µM in Bcrp(-/-) mice.

Conclusion
A sensitive and reliable UPLC-MS/MS method for determination of chrysin and its phase II metabolites in blood was developed and validated. This method was successfully applied for pharmacokinetic studies in mice. Our studies have shown BCRP might not be a critical efflux transporter for phase II disposition of chrysin, or other transporters were overexpressed as a compensation for the knockout of Bcrp.