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## **ACCEPTED MANUSCRIPT**

# High hepatic exposure of furanocoumarins in Radix Angelica dahuricae is associated with transporter mediated active uptake

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#### **ABSTRACT:**

#### Ethnopharmacological relevance

Radix Angelica dahuricae (RAD), the roots of Angelica dahurica (Hoffm.) Benth. & Hook.f. ex Franch. & Sav, is a well-known traditional Chinese medicine (TCM) and has been used for centuries to treat headaches, toothaches, nose congestion, abscesses, furunculoses, and acne. This herb is also one of frequently reported TCMs showing the herb-drug interaction potential. Furanocoumarins are main bioactive components of *RAD*.

## Aim of the study

This study is designed to characterize the tissue distribution profiles of furanocoumarins after oral administration of RAD extract in rats and to explore the mechanism underlying the high hepatic exposure of the major furanocoumarins.

#### Materials and methods

The tissue distribution of nine furanocoumarins was determined in rats after an oral dose of 0.46 g/kg RAD extract using high performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Unbound fractions (f<sub>u</sub>) of major furanocoumarins, including imperatorin (IM), isoimperatorin (IIM), bergapten (BER) and oxypeucedanin hydrate (OXYH), were measured in rat plasma and selected tissue homogenates (liver, kidney, lung and brain) with Rapid Equilibrium

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