OMICS Group Conferences
Accelerating Scientific Discovery
3rd International Conference and Exhibition on
Metabolomics & Systems Biology
March 24-26, 2014 San Antonio, USA

# Study on pharmacokinetics and drug-drug interactions of naringin

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## Abstract

Naringin, a kind of dihydroxyflavones, widely exists in *Citrus* fruit. It displays antitussive, anti-inflammatory, neuroprotective, anti-atherosclerosis and other bioactivities. In this study, the bioavailability of total naringin, as an antitussive drug, in rats and dogs were determined to be 46.11% and 36.82%. Total naringin was also distributed in stomach, intestines, liver, kidney, lung and weasand, except brain, which provides the evidence of peripheral antitussive mechanism. The protein binding of naringin in human plasma showed moderate intension (72.14%-74.06%) compared to rats (83.30%-84.56%) and dogs (48.71%-51.33%), and displayed stronger of its aglycon naringenin (97.53%-100%). Eighteen and twenty-two metabolites were found in the plasma, bile, urine and feces of rats and dogs, and less metabolites were found in human liver microsomes. Multiple CYP450s have participated in the metabolism of naringin and naringenin in human liver microsomes, and multiple metabolites were produced via each pathway. In rat kidney, naringin existed as naringenin-glucuronic acid. Five major human isoforms of CYP450s with six selective reactions were applied to measure the inhibition by naringin and naringenin, including 1A2, 2C9, 2C19, 2D6, and 3A4/5. The $IC_{50}$s of the isoforms were at non-suppressed level except for 2C9 (29.6 and 38.2 μM for naringin and naringenin). The pregnane X receptor induced potential with the comparison to the positive control rifampin was measured to be 28.4 % for naringin and 16.5 % for naringenin. These evidentially showed that naringin absorbed and eliminated rapidly in organism, and interacted few with main CYP450s. Naringin has showed good druggability according to the experimental data.

## Biography

Weiwei Su, Ph.D., is Professor at Life Sciences School at Sun Yat-sen University, Ph.D candidate supervisor and Director of Guangzhou Quality R&D Center of Traditional Chinese Medicine. She has served as an editorial board member of repute. So far, her team has had 30 Chinese granted patents, one European patent and one Japanese patent, and been licensed for clinical studies of three new drugs with independent intellectual property right. Her research interests are in R&D of novel drugs from medicinal animals and plants in South China using biological activity screening and traditional Chinese Medicine (TCM) quality study and TCM fingerprint-pharmacodynamics combined researches.

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