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Study on pharmacokinetics and drug-drug interactions of naringin

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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 bynaringin and naringenin, including 1A2, 2C9, 2C19, 2D6, and 3A4/5. The IC_{50}s of the isoforms were atnon-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

Luodi Fan, Ph.D. candidate of Sun Yat-sen University,studiesbioactive natural products under Professor Weiwei Su who is a well-known expert in the field of Traditional Chinese Medicine fingerprint-pharmacodynamics combined research. His main area of research interest is in pharmacokinetic research of novel drugs, especially the drug-drug interactions between drugs and human Cytochrome P450s. Recently, Luodi Fan studied the metabolites, metabolic pathways and metabolic rate of novel drugs that metabolized by human Cytochrome P450s and Uridine diphosphate Glucuronyl Transferases, also thetransformation law of novel drugs in intestinal flora, and the mechanism of metabolic difference.

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