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Rapid and sensitive LC-MS/MS method for the determination of auraptene in rat plasma and its application in a pharmacokinetic and bioavailability study in rats

X.D. Ye[1]*, H. Ouyang[1,2]*, L.Y. Zhong[1], T.E. Li[1], X.Y. Rao[1], Y.L. Feng[2] and W.L. Yang[1]

[1]Jiangxi University of Traditional Chinese Medicine, Nanchang, China
[2]State Key Laboratory of Innovative Drug and Efficient Energy-Saving Pharmaceutical Equipment, Nanchang, China

*These authors contributed equally to this study.
Corresponding authors: Y.L. Feng / W.L. Yang
E-mail: fengyulin2003@126.com / yangwuliang@163.com

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ABSTRACT. A simple, sensitive and specific liquid chromatography-tandem mass spectrometry method was developed and validated for the determination of auraptene, a constituent isolated from Fructus aurantii with potential to combat Alzheimer's disease, in rat plasma. Rat plasma samples were pretreated by protein precipitation with methanol. The analytes were separated by a Waters Sun Fire C18 column (50 mm x 2 mm, 5 μm) and eluted with 1:1000 methanol and formic acid/water (v/v) mobile phase with a flow rate of 0.5 mL/min. Multiple reaction monitoring was used to monitor the transition of the deprotonated auraptene molecule with an m/z of 299.3 $[M+H]^+$, to the product ion with an m/z of 162.9 $[M+H]^+$. Progesterone, with an m/z of 315.2→ 96.9 was used as an internal standard. The limits of detection and of quantification of auraptene in the rat plasma were 1 and 5 ng/mL,

respectively. The method was linear in the concentration range of 20-2000 ng/mL with coefficient correlation of 0.9956. After auraptene (100 mg/kg, *p.o.*) administration, the maximum plasma concentration and the time taken to reach maximum concentration were 1719.5 ± 384.3 g/mL and 108.0 ± 25.3 min, respectively. The elimination half-life was 108.0 ± 25.3 for auraptene (100 mg/kg, *p.o.*) and 3.0 ± 0 min for auraptene (2 mg/kg, *i.v.*). The oral bioavailability was about 8.5%.

Key words: Auraptene; LC-MS/MS; Pharmacokinetics; Bioavailability; Rat

