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Simultaneous Determination of Gastrodin and Rhynchophylline in Rat Plasma by UPLC-MS/MS: Application to Pharmacokinetic Interaction Study

Yanqu ZHOU, Junying WANG, Shipei FANG, Guangsheng QIAN & Chunmei FU *

Key Laboratory of Drug-Targeting and Drug Delivery System of the Education Ministry, Sichuan Engineering Laboratory for Plant-Sourced Drug and Sichuan Research Center for Drug Precision Industrial Technology, West China School of Pharmacy, Sichuan University, Chengdu, 610041 (P.R. China)

SUMMARY. **Traditional Chinese medicine Gastrodiae Rhizoma and Uncariae Ramulus Cum Uncis are often used in combination to treat cardiovascular disease or nervous system disease. Gastrodin and rhynchophylline are the main active ingredients of Gastrodiae Rhizoma and Uncariae Ramulus Cum Uncis respectively. In this paper, an UPLC-MS/MS method was developed and validated for simultaneous determination of gastrodin and rhynchophylline in rat plasma, and this method was applied to investigate pharmacokinetic interaction between two pure substances after oral administration. The current method was validated in selectivity, accuracy, precision, recovery, matrix effects as well as stability, and successfully applied to simultaneous quantification of rhynchophylline and gastrodin in rat plasma. The pharmacokinetic parameters were calculated after administrating two drugs either separately or together. The results show the absorption of rhynchophylline was increased, but metabolism was decreased obviously after co-administration. The pharmacokinetic parameters of gastrodin have no significant difference between single-dose administration and co-administration. The current study is valuable for understanding drug-drug interaction of Gastrodin and rhynchophylline, and the rationality of prescription compatibility of Tianma-Gouteng herb pair.**

RESUMEN. La medicina tradicional china Gastrodiae Rhizoma y Uncariae Ramulus Cum Uncis a menudo se usan en combinación para tratar enfermedades cardiovasculares o enfermedades del sistema nervioso. Gastrodina y rhynchophyllina son los principales ingredientes activos de Gastrodiae Rhizoma y Uncariae Ramulus Cum Uncis, respectivamente. En este artículo, se desarrolló y validó un método UPLC-MS/MS para la determinación simultánea de gastrodina y rhynchophyllina en plasma de rata, y este método se aplicó para investigar la interacción farmacocinética entre dos sustancias puras después de la administración oral. El método actual fue validado en selectividad, exactitud, precisión, recuperación, efectos de matriz y estabilidad, y se aplicó con éxito a la cuantificación simultánea de rhynchophyllina y gastrodina en plasma de rata. Los parámetros farmacocinéticos se calcularon después de administrar dos fármacos por separado o juntos. Los resultados muestran que la absorción de rhynchophyllina aumentó, pero el metabolismo disminuyó obviamente después de la administración conjunta. Los parámetros farmacocinéticos de gastrodina no presentan diferencias significativas entre la administración de una dosis única y la administración conjunta. El estudio actual es valioso para comprender la interacción farmacológica de gastrodina y rhynchophyllina, y la racionalidad de la compatibilidad de prescripción del par de hierbas Tianma-Gouteng.

KEY WORDS: drug-drug interaction, gastrodin, pharmacokinetics, rhynchophylline, UPLC-MS/MS

* Author to whom correspondence should be addressed. *E-mail:* fuchunmei@scu.edu.cn

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