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Determination and Pharmacokinetics Study of Luteolin, Kaempferol and Quercetin of *Botrychium ternatum* in Rat Plasma by UPLC-MS/MS

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***SUMMARY. Botrychium ternatum* was commonly used for the treatment of lung diseases according to the theory of Traditional Chinese Medicine (TCM). An ultra-liquid chromatography tandem mass spectrometry (UPLC–MS/MS) method was developed for the simultaneous determination of three main components in *Botrychium ternatum* decoction: luteolin, kaempferol, and quercetin in rat plasma, using cynaroside as an internal standard (IS). The samples were chromatographed on a CORTECS UPLC C18 column (2.1 × 50 mm, 1.6 μm) by a mobile phase consisting of acetonitrile and water (0.1% formic acid) at a flow rate of 0.4 mL/min. The protonated ions of analytes were detected in negative ionization in multiple reaction monitoring mode (MRM). The ions of target fragment were 284.98→133.03 m/z for luteolin, 284.97→92.94 m/z for kaempferol, 301.12→151.05 m/z for quercetina, and 447.05→284.96 m/z for IS. The linear calibration curve of the concentration range were 0.5 to 100 ng/mL for luteolin, 0.2-50 ng/mL for kaempferol, and 1-250 ng/mL for quercetin, with a LLOQ (lower limit of quantification) of 0.2 ng/mL for quercetin and 0.2 ng/mL for luteolin and kaempferol. RSD of inter-day and intra-day precision were both no more than 9.77% with the accuracy ranged from 95.54 to 106.05%. The average recovery of luteolin, kaempferol, and quercetin ranged from 89.53 to 114.02%. The developed and validated method was perfectly used in the pharmacokinetic study of *Botrychium ternatum* decoction after oral administration in rats.**

RESUMEN. Botrychium ternatum se usaba comúnmente para el tratamiento de enfermedades pulmonares de acuerdo con la teoría de la Medicina Tradicional China (MTC). Se desarrolló un método de espectrometría de masas en tándem de cromatografía ultra líquida (UPLC-MS/MS) para la determinación simultánea de tres componentes principales en la decocción de *Botrychium ternatum:* luteolina, kaempferol y quercetina en plasma de rata, utilizando cinarósido como estándar interno (IS). Las muestras se cromatografiaron en una columna CORTECS UPLC C18 (2,1 × 50 mm, 1,6 μm) mediante una fase móvil que consta de acetonitrilo y agua (ácido fórmico al 0,1%) a un caudal de 0,4 mL/min. Los iones protonados de analitos se detectaron en ionización negativa en modo de monitoreo de reacción múltiple (MRM). Los iones del fragmento diana fueron 284.98→133.03 m/z para luteolina, 284.97→92.94 m/z para kaempferol, 301.12→151.05 m/z para quercetina y 447.05→284.96 m/z para IS. La curva de calibración lineal del rango de concentración fue de 0.5 a 100 ng/mL para luteolina, 0.2-50 ng/mL para kaempferol y 1-250 ng/mL para quercetina, con un LLOQ (límite inferior de cuantificación) de 0.2 ng/mL para quercetina y 0.2 ng/mL para luteolina y kaempferol. La RSD de precisión entre días y días no fue superior al 9,77%, con una precisión del 95,54 al 106,05%. La recuperación promedio de luteolina, kaempferol y quercetina varió de 89.53 a 114.02%. El método desarrollado y validado se utilizó perfectamente en el estudio farmacocinético de la decocción de *Botrychium ternatum* después de la administración oral en ratas.

KEY WORDS: Botrychium ternatum, pharmacokinetic study,UPLC-MS/MS.

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