

Rapid Simultaneous Determination of Jujuboside A and Jujuboside B in Rats and its Pharmacokinetics by UPLC-MS/MS

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SUMMARY. An accurate and effective liquid chromatography and triple quadrupole mass spectrometry method were established and validated for the determination of jujuboside A (JuA) and jujuboside B (JuB) in rat plasma. Plasma samples were prepared by precipitating proteins with acetonitrile. The analytes were separated using a UPLC BEH C18 column (2.1 × 50 mm, 1.7 μm, Waters, USA) maintained at 40 °C. The mobile phase consisted of acetonitrile and water (containing 0.1% formic acid) and was set at a flow rate of 0.4 mL/min. Quantitative analysis was carried out in the multiple reaction monitoring (MRM) mode of m/z 1205.57→1073.48 for JuA; m/z 1043.54→911.45 for JuB and m/z 487.25→411.27 for polygalactic acid (internal standard, IS). Linear regression was performed using the least-squares method, the linearity of the obtained JuA and JuB were in the range of 10-10000 and 5-2000 ng/mL, while the lowest limit of quantification was 2 and 1, respectively. The mean recoveries of JuA and JuB from the plasma exceeded 75.08%. The intra-run and inter-run assay precisions were both less than 8.95%. The method was successfully applied to a pharmacokinetic study of JuA and JuB after a sublingual administration of 2 mg/kg in rats.

RESUMEN. Se estableció y validó un método preciso y efectivo de cromatografía líquida y espectrometría de masas de triple cuadrupolo para la determinación de jujubósido A (JuA) y jujubósido B (JuB) en plasma de rata. Las muestras de plasma se prepararon precipitando proteínas con acetonitrilo. Los analitos se separaron utilizando una columna UPLC BEH C18 (2.1 × 50 mm, 1.7 μm, Waters, EE. UU.) Mantenido a 40 °C. La fase móvil consistió en acetonitrilo y agua (que contenía ácido fórmico al 0,1%) y se ajustó a un caudal de 0,4 mL/min. El análisis cuantitativo se llevó a cabo en el modo de monitoreo de reacción múltiple (MRM) de m/z 1205.57→1073.48 para JuA; m/z 1043.54→911.45 para JuB y m/z 487.25→411.27 para ácido poligalácico (estándar interno, IS). La regresión lineal se realizó mediante el método de cuadrados mínimos, la linealidad de JuA y JuB obtenidas estaban en el rango de 10-10000 y 5-2000 ng/mL, mientras que el límite más bajo de cuantificación fue 2 y 1, respectivamente. Las recuperaciones medias de JuA y JuB del plasma superaron el 75.08%. Las precisiones de los ensayos intra- e inter-corridas fueron menores al 8.95%. El método se aplicó con éxito a un estudio farmacocinético de JuA y JuB después de una administración sublingual de 2 mg/kg a ratas.

KEY WORDS: jujuboside A, jujuboside B, pharmacokinetics, rat plasma, UPLC-MS/MS.

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