

Validated UPLC-MS/MS Method for the Determination of Arctiin and Arctigenin in Rat Plasma: Application to a Pharmacokinetic Study

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SUMMARY. An accurate and validated liquid chromatography method and a triple quadrupole mass spectrometry method were developed and validated for the determination of arctiin and arctigenin in rat plasma. Plasma samples were prepared by precipitating protein 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) with a gradient elution pumped at a flow rate of 0.4 mL/min. The analytes were detected with positive electrospray ionization in multiple reaction monitoring (MRM) mode for target fragment ions m/z 557.07→395.04 for arctiin, m/z 373.06→136.07 for arctigenin and m/z 610.1→302.98 for rutin (IS). Good linearity was achieved to quantify the concentration ranges of 50-5000 ng/mL for arctiin and 10-1000 ng/mL for arctigenin in rat plasma. The mean recoveries of arctiin and arctigenin from the plasma exceeded 75.58%. The intra-run and inter-run assay precisions were both less than 8.2%. The method was successfully applied to a pharmacokinetic study of arctiin and arctigenin after a sublingual administration of 5 mg/kg in rats.

RESUMEN. Se desarrolló y validó un método preciso de cromatografía líquida y un método de espectrometría de masas de triple cuadrupolo para la determinación de arctiina y arctigenina en plasma de rata. Se prepararon muestras de plasma precipitando las proteínas con acetonitrilo. Los analitos se separaron usando una columna UPLC BEH C18 (2,1 × 50 mm, 1,7 μm, Waters, EE.UU.) mantenida a 40 °C. La fase móvil consistió en acetonitrilo y agua (que contenía ácido fórmico al 0,1%) con una elución de gradiente bombeada a un caudal de 0,4 mL/min. Los analitos se detectaron con ionización positiva por electrospay en modo de monitorización de reacción múltiple (MRM) para los iones fragmentos diana m/z 557,07→395,04 para arctiina, m/z 373,06→136,07 para arctigenina y m/z 610,1→302,98 para rutina (IS). Se logró una buena linealidad para cuantificar los rangos de concentración de 50-5000 ng/mL para arctiina y 10-1000 ng/mL para arctigenina en plasma de rata. Las recuperaciones medias de arctiina y arctigenina del plasma superaron el 75,58%. Las precisiones de ensayo intra-corrida e inter-corrida fueron ambas inferiores al 8,2%. El método se aplicó con éxito a un estudio farmacocinético de arctiina y arctigenina después de una administración sublingual de 5 mg/kg en ratas.

KEY WORDS: arctiin, arctigenin, pharmacokinetics, rat plasma, UPLC-ESI-MS/MS.

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