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Determination and Pharmacokinetic Study of Avicularin in Rat Plasma by UPLC-MS/MS after Intravenous Administration

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***SUMMARY*. Avicularin (quercetin-3-alpha-L-arabinofuranoside) is a plant flavonoid and a quercetin glycoside. It has been reported to possess diverse pharmacological properties such as anti-inflammatory and anti-infectious effects. In this work, a sensitive and selective UPLC-MS/MS method was developed and full validated for determination of avicularin in rat plasma. Jaceosidin was used as the internal standard (IS), and protein precipitation by acetonitrile-methanol (9:1, v/v) was used to prepare samples. Chromatographic separation was achieved on a UPLC BEH C18 column (2.1 × 100 mm, 1.7 μm) with 0.1% formic acid and acetonitrile as the mobile phase with gradient elution. An electrospray ionization (ESI) source was applied and operated in positive ion mode; multiple reactions monitoring (MRM) mode was used for quantification. Calibration plots were linear throughout the range 2-500 ng/mL for avicularin in rat plasma. RSD of intra-day and inter-day precision were both less than 13%. The accuracy of the method was between 90.4 and 109.0%. Mean recoveries of avicularin in rat plasma ranged from 75.6 to 85.3%. The developed UPLC-MS/MS method was successfully applied to pharmacokinetic study of avicularin after intravenous administration of 2 mg/kg in rats. We found that avicularin was rapidly eliminated, the t1/2 was 0.8 ± 0.3 h and CL 55.3 ± 8.2 L/h/kg.**

RESUMEN. Avicularina (quercetina-3-alfa-L-arabinofuranósido) es un flavonoide y un glucósido de quercetina. Se ha informado que posee diversas propiedades farmacológicas, tales como efectos anti-inflamatorios y anti-infecciosos. En este trabajo fue desarrollado y validado un método de UPLC-MS/ S sensible y selectivo para la determinación de avicularina en plasma de rata. Se utilizó jaceosidina para el estándar interno (IS) y la precipitación de proteínas con metanol-acetonitrilo (9:1, v/v) se usó para preparar las muestras. La separación cromatográfica se consiguió en una columna de UPLC BEH C18 (2,1 × 100 mm, 1,7 μM) con ácido fórmico al 0,1% y acetonitrilo como fase móvil, con gradiente de elución. SE aplicó una fuente de ionización electrospray (ESI) operada en modo de iones positivos y se utilizó el modo de monitoreo de reacciones múltiples (MRM) para la cuantificación. Las curvas de calibración fueron lineales en todo el rango de 2-500 ng/mL para avicularina en plasma de rata. La precisión RSD de intra-día y entre días es < 13%. La precisión del método fue entre 90,4 y 109,0%. Las recuperaciones medias de avicularina en plasma de rata oscilaron entre 75,6 y 85,3%. El método UPLC-MS/MS desarrollado se aplicó con éxito para el estudio farmacocinético de avicularina después de la administración intravenosa de 2 mg/kg en ratas. Encontramos que avicularina se elimina rápidamente, el t1/2 fue de 0,8 ± 0,3 h y CL 55.3 ± 8.2 L h/kg.

KEY WORDS: avicularin, pharmacokinetics, rat plasma, UPLC-MS/MS.

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