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Pharmacokinetic Study of Lithospermoside in Rat Plasma by Ultra-Performance Liquid Chromatography Coupled with Tandem Mass Spectrometry

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***SUMMARY*. Lithospermoside, considered as the major active cyanogenic glycoside, possessed potential anti-tumor, antioxidant and anti-inflammatory activity. In our work, a sensitive and selective UPLC-MS/MS method for determination of lithospermoside in rat plasma was developed. Oxypaeoniflorin was used as internal standard, protein precipitation by acetonitrile was used for plasma sample treatment. UPLC separation was achieved on a C18 with 0.1% formic acid and acetonitrile as the mobile phase with gradient elution. Multiple reactions monitoring mode was used for quantification, m/z 330.1→168.0 for lithospermoside, and m/z 519.1→219.1 for internal standard. Calibration plots were linear throughout the range 50-10000 ng/mL. The recoveries ranged from 73.6 to 78.6%. RSD of intra-day and inter-day precision were less than 10%. The accuracy was between 97.4 and 105.7%. The method was successfully applied to pharmacokinetic study of lithospermoside after intravenous and oral administration in rats for the first time. The bioavailability of lithospermoside was found to be 55.1%.**

RESUMEN. El litospermósido, considerado el principal glicósido cianogénico activo, posee una actividad potencial antitumoral, antioxidante y antiinflamatoria. En nuestro trabajo se desarrolló un método de UPLC-MS/MS sensible y selectivo para la determinación de litospermósido en plasma de rata. Oxypaeoniflorina se usó como patrón interno y la precipitación de proteínas con acetonitrilo se usó para el tratamiento de muestras de plasma. La separación de UPLC se logró en una columna C18 con ácido fórmico al 0,1% y acetonitrilo como la fase móvil con elución en gradiente. Se usó el modo de monitoreo de reacciones múltiples para la cuantificación, m/z 330.1→168.0 para litospermósido, y m/z 519.1→219.1 para el estándar interno. Los diagramas de calibración fueron lineales en todo el rango 50-10000 ng/mL. Las recuperaciones variaron de 73.6 a 78.6%. La DSR de precisión intradía e interdía fue inferior al 10%. La precisión estaba entre 97.4 y 105.7%. El método se aplicó con éxito al estudio farmacocinético de litospermósido después de la administración intravenosa y oral en ratas por primera vez. La biodisponibilidad de litospermósido fue del 55.1%.

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

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