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Simultaneous Determination of Melatonin and its Active Metabolite in Rat Plasma by LC-MS/MS: Application to Pharmacokinetic Study

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***SUMMARY*. A selective liquid chromatographic–mass spectrometric method (LC-MS/MS) has been established and validated for simultaneous determination of melatonin and its active metabolite in human plasma. Plasma samples were extracted by one step protein precipitation procedure and separated on a Acquity BEH C18 column (2.1 × 50 mm, 1.7 m particle size), with acetonitrile-0.1% formic acid solution as mobile phase at flow rate of 0.4 mL/min. The linear range was 1-500 ng/mL for melatonin and 0.1-50.0 ng/mL for its active metabolite, with lower limit of quantitation of 1 ng/mL and 0.1 ng/mL, respectively. Intra- and inter day precision and accuracy met the requirements, with the extraction recoveries 90.99-94.49% and 86.01-94.32% for the two analytes, respectively. The validated method was successfully applied to a pharmacokinetic study of melatonin and its active metabolite in rat after oral administration and intravenous of melatonin.**

RESUMEN. Se ha establecido y validado un método selectiva de cromatografía líquida y espectrometría de masas (LC-MS/MS) para la determinación simultánea de melatonina y su metabolito activo en plasma humano. Las muestras de plasma se extrajeron mediante un procedimiento de precipitación de proteínas en un solo paso y se separaron en una columna Acquity BEH C18 (2,1 × 50 mm, tamaño de partícula 1,7 m), con solución de acetonitrilo-0,1% de ácido fórmico como fase móvil a una velocidad de flujo de 0,4 mL/min. El rango fue lineal de 1-500 ng/mL para melatonina y 0.1-50.0 ng/mL para su metabolito activo, con un límite inferior de cuantificación de 1 y 0.1 ng/mL, respectivamente. La precisión y exactitud intra- e interdía cumplieron los requisitos, con las recuperaciones de extracción de 90.99-94.49% y 86.01-94.32% para los dos analitos, respectivamente. El método validado se aplicó con éxito a un estudio farmacocinético de melatonina y su metabolito activo en ratas después de la administración oral e intravenosa de melatonina.

KEY WORDS: 6-hydroxymelatonin, melatonin, pharmacokinetic, UPLC-MS/MS.

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