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Determination of Flumatininb in Rat Plasma by UPLC-MS/MS: Application to a Pharmacokinetic Study

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***SUMMARY*. An accurate and validated liquid chromatography method with triple quadrupole mass spectrometer has been developed for detecting flumatinib in rat plasma. A reversed-phase CORTECS BEH C18 column kept at 40 °C was used. Acetonitrile and water (0.01% formic acid) was used as mobile phase, pumped at a flow rate of 0.4 mL/min. Samples were prepared by precipitating protein with acetonitrile. The analytes were detected using a Waters triple quadrupole mass spectrometer with positive electrospray ionization in multiple reaction monitoring (MRM) mode for target fragment ions m/z 563.22→58.22 for flumatinib and m/z 557.3→112.15 for neratinib(IS). Good linearity for flumatinib was gained with concentration ranges of 1-1000 ng/mL and 0.1 ng/mL for the lower limit of quantification in this assay. Mean recovery of flumatinib from plasma was better than 86.6%. This validated method applied to a pharmacokinetic study of flumatinib after oral (10 mg/kg) or intravenous (5 mg/kg) administration in rats was performed successfully.**

RESUMEN. Se ha desarrollado un método de cromatografía líquida con espectrometría de masas de triple cuadrupolo preciso y validado para detectar flumatinib en plasma de rata. Se usó una columna de CORTECS BEH C18 de fase inversa mantenida a 40 ºC con acetonitrilo y agua (ácido fórmico al 0,01%) como fase móvil, bombeada a un caudal de 0,4 mL/min. Las muestras se prepararon precipitando las proteínas con acetonitrilo. Los analitos se detectaron utilizando un espectrómetro de masas de triple cuadrupolo Waters con ionización positiva por electrospray en modo de monitorización de reacción múltiple (MRM) para los fragmentos de iones m/z 563,22→58,22 para flumatinib y m/z 557,3→112,15 para neratinib (IS). En este ensayo se obtuvo una buena linealidad para el flumatinib con rangos de concentración de 1-1000 ng/mL y 0,1 ng/mL para el límite inferior de cuantificación. La recuperación media del flumatinib del plasma fue superior al 86,6%. El método validado se llevó a cabo con éxito aplicado a un estudio farmacocinético después de la administración oral (10 mg/kg) o intravenosa (5 mg/kg) de flumatinib en ratas.

KEY WORDS: flumatinib, pharmacokinetics, rat, UPLC-ESI-MS/MS.

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