Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **37** (7): 1392-8 (2018)

Received: May 1, 2018
Revised version: May 22, 2018
Accepted: May 23, 2018

Development of an UPLC-MS/MS Validated Method for Determination and Pharmacokinetic Study of Neratinib in Rat Plasma

Peng HUANG[1,#], Ailian HUA[2,#], Shizhong WANG[2], Quan ZHOU[2], Shuanghu WANG[2], Yunfang ZHOU[2,*] & Lixian LIU[2,*]

[1] *Department of Pharmacy, The Third Affiliated Hospital of Wenzhou Medical University, Wenzhou 325200, China*
[2] *Department of Pharmacy, The People's Hospital of Lishui, Lishui 323000, China*

SUMMARY. **Neratinib is an oral and pan-tyrosine kinase inhibitor that utilizes epidermal growth factor receptor-1/epidermal growth factor receptor-2 (EGFR/HER2) tyrosine kinase ATP binding sites of some of the characteristics of strong selectivity. In present study, an accurate and selective ultra performance liquid chromatography with triple quadrupole mass spectrometer (UPLC-MS/MS) method has been established and validated to determine neratinib in rat plasma. Protein precipitation with acetonitrile was selected for sample processing. A CORTECS BEH C18 column was used to separate the analytes kept at 40 °C. The mobile phase was consist of acetonitrile and water (0.1% formic acid), the flow rate of which was 0.4 mL/min. The analytes were quantified by multiple reaction monitoring (MRM) mode with positive electrospray ionization, while the target fragment ions were m/z 557.3→112.15 for neratinib and m/z 486.19→112.1 for afatinib (IS). The calibration curve gained good linearity for neratinib at the range of 10-5000 ng/mL. The intra-run and inter-run precisions variations were both ≤ 7.55%. The recovery of neratinib from plasma was better than 77.78%. This validated method was applied to the pharmacokinetic study of neratinib at the oral and intravenou dosage of 10 and 2 mg/kg.**

RESUMEN. Neratinib es un inhibidor de la pan-tirosina quinasa oral que utiliza sitios de unión del receptor ATP de la tirosina quinasa del receptor del factor de crecimiento epidérmico/receptor del factor de crecimiento epidérmico-2 (EGFR/HER2) de algunas características de fuerte selectividad. En el presente estudio se ha establecido y validado una método de cromatografía líquida de alta resolución preciso y selectivo usando un espectrómetro de masas de triple cuadrupolo (UPLC-MS/MS) para determinar neratinib en plasma de rata. La precipitación de proteínas con acetonitrilo se seleccionó para el procesamiento de la muestra. Se utilizó una columna CORTECS BEH C18 para separar los analitos mantenidos a 40 °C. La fase móvil consistía en acetonitrilo y agua (ácido fórmico al 0,1%), cuyo caudal era 0,4 mL/min. Los analitos se cuantificaron mediante el modo de monitorización de reacción múltiple (MRM) con ionización por electrospray positiva, mientras que los iones del fragmento objetivo fueron m/z 557.3→112.15 para neratinib y m/z 486.19→112.1 para afatinib (IS). La curva de calibración obtuvo una buena linealidad para neratinib en el rango de 10-5000 ng/mL. Las variaciones de precisiones intracorrientes e intercorrientes fueron ambas ≤ 7,55%. La recuperación de neratinib del plasma fue mejor que 77.78%. Este método validado se aplicó al estudio farmacocinético de neratinib en dosis oral e intravenosa de 10 y 2 mg/kg.

KEY WORDS: neratinib, pharmacokinetics, rat, UPLC-MS/M.

# These authors contributed equally to this work.
* Author to whom correspondence should be addressed. *E-mail:* zyf2808@126.com (Yunfang Zhou), lsliulx@163.com (Lixian Liu).

ISSN 0326 2383 (printed ed.)
ISSN 2362-3853 (on line ed.)