Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **38** (5): 855-9 (2019)

Received: November 16, 2018
Accepted: February 5, 2019

Herb-Drug Pharmacokinetic Interaction between Tetrandrine (Tet) and Icotinib in Rats

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***SUMMARY*. To investigate the effects of tetrandrine (Tet) on the pharmacokinetics of icotinib, twelve male rats were randomly divided into two groups (n = 6). Experimental group and control group were pretreated with Tet or saline once a day by oral administration for 10 days in a row. Then, icotinib (35mg/kg) were given to all rats orally on the 11th day. Blood samples were collected from the tail vein and the plasma concentrations of icotinib were detected by Ultra Performance Liquid Chromatography-tandem Mass spectrometric (UPLC) method. The pharmacokinetic parameters of cortisol in the experimental group and contral group were: 10.3 ± 3.9 and 7.3 ± 2.7 h for $t_{1/2z}$; 1.4 ± 0.5 and 0.7 ± 0.2 L/h/kg for CL/F; 26873.8 ± 8439.7 and 55472.6 ± 18997.9 μg/L·h for AUC(0-t); 27069.4 ± 8609.9 and 55563.5 ± 18987.1 μg/L·h for $AUC_{(0-\infty)}$; (6379.4 ± 1230.5) and 11612.9 ± 3125.7 h for C_{max}; 1.6 ± 0.4 and 0.7 ± 1.0 h for T_{max}, respectively. Those results indicated that the Tet can induce icotinib metabolism significantly in rats, which may be related to its induction effect on CYP450.**

RESUMEN. Para investigar los efectos de la tetrandrina (Tet) en la farmacocinética de icotinib, doce ratas macho se dividieron aleatoriamente en dos grupos (n = 6). El grupo experimental y el grupo de control se pretrataron con Tet o solución salina una vez al día mediante administración oral durante 10 días seguidos. Luego, se administró icotinib (35 mg/kg) a todas las ratas por vía oral el día 11º. Las muestras de sangre se tomaron de la vena de la cola y las concentraciones plasmáticas de icotinib se detectaron mediante el método de espectrometría de masas en tándem con cromatografía líquida de ultra performance (UPLC). Los parámetros farmacocinéticos del cortisol en el grupo experimental y el grupo contral fueron: 10.3 ± 3.9 y 7.3 ± 2.7 h para $t_{1/2z}$, 1.4 ± 0.5 y 0.7 ± 0.2 L/h/kg para CL/F, 26873.8 ± 8439.7 y 55472.6 ± 18997.9 μg/L para AUC (0-t), 27069.4 ± 8609.9 y 55563.5 ± 1 8987.1 μg/L para $AUC_{(0-\infty)}$, 6379.4 ± 1230.5 y 11612.9 ± 3125.7 h para C_{max} y 1.6 ± 0.4 y 0.7 ± 1.0 h para T_{max}, respectivamente. Esos resultados indicaron que el Tet puede inducir el metabolismo de icotinib significativamente en ratas, lo que puede estar relacionado con su efecto de inducción en CYP450.

KEY WORDS: icotinib, pharmacokinetics, tetrandrine, UPLC-MS/MS.

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