Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **37** (8): 1621-6 (2018)

Received: May 17, 2018
Revised version: June 14, 2018
Accepted: June 15, 2018

Influence of Grapefruit Juice on Pharmacokinetics of Omeprazole in Rats

Yingbin DENG [1], Weijun WU [1], Yuetao YANG [1], Yuxin CHEN [2] * & Zhiyi WANG [1] *

[1] *Department of Emergency Medicine, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, No. 109, West Xueyuan Road, Wenzhou 325027, China*

[2] *Department of Hepatobiliary Surgery, Qilu Hospital, Shandong University, No. 107 WenhuaXi Road, Jinan, 250012, Shandong, China*

SUMMARY. This study investigates the food-drug interaction between grapefruit juice (GFJ) and omeprazole. The pharmacokinetics of orally administered omeprazole (2 mg/kg) with or without GFJ pretreatment were investigated in rats. Caco-2 cell transwell model and rat liver microsomes incubation systems were also used to support the *in vivo* pharmacokinetic data and investigate its potential mechanism. The results indicated that co-administration of GFJ could increase the systemic exposure of omeprazole significantly, including area under the curve (1060.93 ± 169.82 *vs.* 597.72 ± 148.06 ng.h/mL) and maximum plasma concentration (333.05 ± 28.67 vs. 226.96 ± 18.66 ng/mL). The area under the curve (183.91 ± 22.84 *vs.* 319.28 ± 16.64 ng·h/mL) and maximum plasma concentration (65.89 ± 7.28 *vs.* 98.71 ± 10.85 ng/mL) of 5-hydroxy-omeprazole (metabolite of omeprazole) decreased significantly with the pretreatment of GFJ. The apparent permeability of omeprazole across the Caco-2 cell transwell model increased significantly with the pretreatment of GFJ (from 2.28 ± 0.31 × 10^{-6} to 2.91 ± 0.44 × 10^{-6} cm/s), and the metabolic stability of omeprazole was also increased from 25.7 ± 6.8 to 46.1 ± 8.1 min with the pretreatment of GFJ ($p < 0.05$). In conclusion, GFJ could increase the systemic exposure of omeprazole in rats when GFJ and omeprazole was co-administered, and it might work mainly through increasing the absorption of omeprazole by inhibiting *P-gp,* or through slowing down the metabolism of omeprazole in rat liver by inhibiting the activity of CYP3A4.

RESUMEN. Este estudio investiga la interacción de alimentos y medicamentos entre el jugo de pomelo (GFJ) y el omeprazol. La farmacocinética de omeprazol administrado por vía oral (2 mg/kg) con o sin pretratamiento con GFJ se investigó en ratas. También se usaron los sistemas de incubación de células transgénicas Caco-2 y sistemas de incubación de microsomas hepáticos de rata para respaldar los datos farmacocinéticos *in vivo* e investigar su mecanismo potencial. Los resultados indicaron que la administración concomitante de GFJ podría aumentar significativamente la exposición sistémica de omeprazol, incluido el área debajo de la curva (1060.93 ± 169.82 vs. 597.72 ± 148.06 ng.h/mL) y la concentración plasmática máxima (333.05 ± 28.67 *vs*. 226.96 ± 18,66 ng/mL). El área bajo la curva (183.91 ± 22.84 *vs*. 319.28 ± 16.64 ng.h/mL) y la concentración plasmática máxima (65.89 ± 7.28 *vs*. 98.71 ± 10.85 ng/mL) de 5-hidroxi-omeprazol (metabolito de omeprazol) disminuyeron significativamente con el pretratamiento de GFJ. La aparente permeabilidad de omeprazol a través del modelo de transwell de células Caco-2 aumentó significativamente con el pretratamiento de GFJ (de 2,28 ± 0,31 × 10^{-6} a 2,91 ± 0,44 × 10^{-6} cm/s), y la estabilidad metabólica de omeprazol también aumentó de 25.7 ± 6.8 a 46.1 ± 8.1 min con el pretratamiento de GFJ ($p < 0.05$). En conclusión, GFJ podría aumentar la exposición sistémica de omeprazol en ratas cuando se administraron concomitantemente GFJ y omeprazol, y podría funcionar principalmente al aumentar la absorción de omeprazol al inhibir la *P-gp,* o al desacelerar el metabolismo del omeprazol en el hígado de rata al inhibir la actividad de CYP3A4.

KEY WORDS: CYP3A4, food-drug interaction, *P-gp*.

* Authors to whom correspondence should be addressed. *E-mails:* yx_chen002@163.com (Yuxin Chen); zy_wang09@163.com (Zhiyi Wang)

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