Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **37** (3): 514-7 (2018)

Received: January 29, 2018
Accepted: February 6, 2018

Clinical Ginkgolide A-Ear-Nose-Throat (ENT) Diseases Treatment Drugs Interaction Based on the Inhibition of Phase II Drug-Metabolizing Enzymes (DMEs)

Jian-Ping CUI [1 #], Rui-Yu LI [2 # *& Yue LI [3]

[1] *Xingtai Medical College, Xingtai, 054000, China*
[2] *Institute of integrated traditional Chinese and Western medicine, The Second Affiliated Hospital of Xingtai Medical College, Xingtai, 054000, China*
[3] *Department of Psychology, Chengde Medical College, ChengDe. Hebei 067000 China*

***SUMMARY*. UDP-glucuronosyltransferases (UGTs) catalyze the glucuronidation of ear-nose-throat (ENT) diseases treatment drugs, and the inhibition of UGT isoforms by co-administered drugs might significantly increase the plasma exposure of drugs. This study aims to investigate the inhibition of ginkgolide A (GA) on one of the most important UGT isoforms, UGT1A1. *In silico* docking method was used. Chemical structure of GA was drawn using chemdraw software, and homology modeling was utilized to construct the crystal structure of UGT1A1. The chemical structure of GA can be well docked into the activity cavity of UGT1A1, and the binding free energy was calculated to be -6.41 kcal/mol. The amino acids residues in the activity cavity of UGT1A1 binding with GA contained Gly-12, Ser-13, Trp-15, Leu-16, Asp-45, Ala-47, Phe-48, Leu-51, Gln-82, Arg-83, Ser-284, Met-285, and Trp-329. Within these amino acids, the amino acids residues GLy-12, Arg-83, and Ser-284 formed hydrogen bonds with GA. For the hydrophobic interaction, the involved amino acids residues contained Ser-13, Trp-15, Leu-16, Ala-47, Phe-48, Leu-51, and Gln-82. These results showed that both hydrogen bonds and hydrophobic interaction contributed the strong inhibition of GA on the activity of UGT1A1, indicating the strong drug-drug interaction (DDI) between GA and clinical drugs mainly undergoing UGT1A1-catalyzed metabolism.**

RESUMEN. Las UDP-glucuronosiltransferasas (UGT) catalizan la glucuronidación de fármacos utilizados en el tratamiento de enfermedades de oído, nariz y garganta (ENT) y la inhibición de isoformas de UGT por fármacos coadministrados podría aumentar significativamente la exposición plasmática de fármacos. Este estudio tiene como objetivo investigar la inhibición de ginkgólido A (GA) en una de las isoformas UGT más importantes, UGT1A1. Se utilizó el método de acoplamiento *in silico*. La estructura química de GA se dibujó usando un programa de quimiotaxis y se utilizó un modelo de homología para construir la estructura cristalina de UGT1A1. La estructura química de GA puede acoplarse bien en la cavidad de actividad de UGT1A1 y la energía libre de unión se calculó en -6,41 kcal/mol. Los residuos de aminoácidos en la cavidad de actividad de unión de UGT1A1 con GA contenían Gly-12, Ser-13, Trp-15, Leu-16, Asp-45, Ala-47, Phe-48, Leu-51, Gln-82, Arg-83, Ser-284, Met-285 y Trp-329. Dentro de estos aminoácidos, los residuos de aminoácidos GLy-12, Arg-83 y Ser-284 formaron enlaces de hidrógeno con GA. Para la interacción hidrofóbica, los residuos de aminoácidos implicados contenían Ser-13, Trp-15, Leu-16, Ala-47, Phe-48, Leu-51 y Gln-82. Estos resultados mostraron que tanto los enlaces de hidrógeno como la interacción hidrofóbica contribuyeron a la fuerte inhibición de GA sobre la actividad de UGT1A1, lo que indica la fuerte interacción fármaco-fármaco (DDI) entre GA y fármacos clínicos que principalmente experimentan metabolismo catalizado por UGT1A1.

KEY WORDS: drug-drug interaction, ear-nose-throat (ENT) diseases, enzyme inhibition, UDP-glucuronosyltransferase (UGT) 1A1.

# These two authors equally contributed to this work.
* Author to whom correspondence should be addressed. *E-mail:* zianbian323@163.com

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