Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **36** (6): 1088-91 (2017)

Received: February 21, 2017
Accepted: February 24, 2017

Vemurafenib Disrupted the Metabolism of Drugs Treating Chronic Obstructive Pulmonary Diseases (COPD)

Mayila ABUDOUKELIMU [1], Fang YAN [2], Li LEI [3] & Yang GUO * [3]

[1] *Department of respiratory, the sixth affiliated hospital of xinjiang medical university, Urmuqi City, Xinjiang 830002 China*
[2] *Department of respiratory, the first affiliated hospital of xinjiang medical university, Urmuqi, Xinjiang 830054 china*
[3] *Department of respiration, Changji peoples Hospital, Changji City, Xinjiang 831100 China*

***SUMMARY*. Both chronic obstructive pulmonary diseases (COPD) and cancers are severe diseases to threaten the health of people. Therefore, it is highly possible for patients to take co-administration of vemurafenib and many drugs used to treat COPD. Due to the large contribution of UDP-glucuronosyltransferase (UGT) 2B7 towards the metabolism of COPD treatment drugs, this study aims to determine the inhibition of vemurafenib on the activity of important drug-metabolizing enzyme (DME) UDP-glucuronosyltransferase (UGT) 2B7, trying to indicate the potential vemurafenib-COPD treatment drugs interaction. *In silico* docking method was used to dock vemurafenib into the activity cavity of UGT2B7 which crystal structure was constructed through homology modeling. The results showed that vemurafenib can be well docked into the activity cavity of UGT2B7, and the amino acids residues in the activity cavity of UGT2B7 were consisted of Trp6, Ala8, Trp13, Met14, Lys17, Ser36, Ser38, Ile51, His258, Cys259, Pro261, Gly287, Ser288, Arg315, Trp333, Ile334, Pro335, Gln336, His351, and Glu359. For the hydrogen bonds interaction, vemurafenib has 2.1 nm distance with the interaction amino acid. Vemurafenib formed hydrophobic interaction with the following amino acids: Ala8, Glu9, Tyr10, Met14, Ser35, Ser36, Ala37, Ser38, Pro55, Thr56, Ser285, Gly287, Arg315, Trp333, Ile334, and Gln336. The binding affinity was calculated to be -8.3 kcal/mol. In conclusion, this study demonstrated the strong interaction between vemurafenib and UGT2B7, indicating the potential drug-drug interaction between vemurafenib and drugs mainly undergoing UGT2B7-catalyzed metabolism.**

RESUMEN. Tanto la enfermedades pulmonares obstructivas crónica (EPOC) como el cáncer son enfermedades graves que amenazan la salud de las personas. Por lo tanto, es muy posible que los pacientes tomen vemurafenib coadministrado con fármacos usados para tratar la EPOC. Debido a la gran contribución de la UDP-glucuronosiltransferasa (UGT) 2B7 en el metabolismo de los fármacos de la EPOC, este estudio tiene como objetivo determinar la inhibición del vemurafenib sobre la actividad de la UDP-glucuronosiltransferasa (UGT) 2B7, tratando de indicar la interacción potencial de los fármacos de tratamiento con vemurafenib-EPOC. Se utilizó el método de acoplamiento *in silico* para atracar vemurafenib en la cavidad activa de UGT2B7, cuya estructura cristalina se construyó mediante modelado de homología. Los resultados mostraron que el vemurafenib puede estar bien acoplado a la cavidad de actividad de UGT2B7 y los residuos de aminoácidos en la cavidad de actividad de UGT2B7 estaban constituidos por Trp6, Ala8, Trp13, Met14, Lys17, Ser36, Ser38, Ile51, His258, Cys259, Pro261, Gly287, Ser288, Arg315, Trp333, Ile334, Pro335, Gln336, His351 y Glu359. Para la interacción de enlaces de hidrógeno, vemurafenib tiene una distancia de 2,1 nm con el aminoácido de interacción. El vemurafenib formó una interacción hidrófoba con los siguientes aminoácidos: Ala8, Glu9, Tyr10, Met14, Ser35, Ser36, Ala37, Ser38, Pro55, Thr56, Ser285, Gly287, Arg315, Trp333, Ile334 y Gln336. La afinidad de unión se calculó que era -8,3 kcal/mol. En conclusión, este estudio demostró la fuerte interacción entre vemurafenib y UGT2B7, lo que indica la posible interacción fármaco-fármaco entre vemurafenib y fármacos que sufren principalmente metabolismo catalizado por UGT2B7.

KEY WORDS: cancers, chronic obstructive pulmonary diseases (COPD), drug-drug interaction (DDI), UDP-glucuronosyltransferase (UGT) 2B7, vemurafenib.

* Author to whom correspondence should be addressed. *E-mail:* guoyang2046@sina.com

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