Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **36** (3): 599-602 (2017)

Short communication

Received: November 12, 2016
Accepted: November 17, 2016

Anti-Cancer Drug Vemurafenib Showed Strong Inhibition on the Activity of Drug-Metabolizing Enzymes

Zhao-qiang ZHANG [1], Yun-hua GAO [1] *, Lian-Suo ZHAI [2], Ming LI [3], Ji-Shan ZHAO [1], Shu-Yan ZHANG [4], Jie SHEN [4]

[1] *Department of Pharmacy,* [2] *Department of Orthopaedics, Jiyang County People's Hospital, Shandong Province, 251400, China*
[3] *Department of Pharmacy, Jinan Vocational College of Nursing, Jinan Shandong, 250000, China*
[4] *Hebi Polytechnic, No. 5, Chaoge Road, Hebi, Henan Province, 458030, China*

SUMMARY*. Melanoma is a malignant tumour of melanocytes, and vemurafenib is an efficient drug clinically used to treat melanoma under the trade name Zelboraf. This study aims to determine the inhibition potential of vemurafenib on the activity of carboxylesterase 1 (CES1) and carboxylesterase 2 (CES2). *In vitro* human liver microsomes (HLMs)-catalyzed hydrolysis metabolism of 2-(2-benzoyl-3-methoxyphenyl) benzothiazole (BMBT) to form its hydrolysis metabolite 2-(2-hydroxy-3-methoxyphenyl) benzothiazole (HMBT) was used to investigate the inhibition of vemurafenib on the activity of CES1, and *in vitro* human liver microsomes (HLMs)-catalyzed hydrolysis metabolism of fluorescein diacetate (FD) to fluorescein was used to investigate the inhibition of vemurafenib on the activity of CES2. The results showed that 100 μM of vemurafenib did not show significant inhibition on the activity of CES1. In the contrast, 100 μM of vemurafenib showed significant inhibition on the activity of CES2 ($p < 0.001$). For the inhibition of vemurafenib on the activity of CES2, the half concentration inhibiting 50% activity of CES2 was calculated, and the results showed that the IC50 value of vemurafenib's inhibition on CES2 was calculated to be 25.1 μM. In conclusion, drug-drug interaction might exist between vemurafenib and clinical drugs mainly undergoing CES2-catalyzed hydrolysis metabolism.

RESUMEN. El melanoma es un tumor maligno de los melanocitos y vemurafenib es un fármaco eficaz utilizado clínicamente para tratar el melanoma con el nombre comercial de Zelboraf. Este estudio tiene como objetivo determinar la inhibición potencial de vemurafenib sobre la actividad de carboxylesterasa 1 (CES1) y carboxylesterasa 2 (CES2). Se utilizaron microsomas de hígado humano (HLMs) *in vitro,* que catalizan el metabolismo de hidrólisis de 2-(2-benzoil-3-metoxifenil) benzotiazol (BMBT) para formar su metabolito 2-(2-hidroxi-3-metoxifenil) benzotiazol (HMBT), para investigar la inhibición de vemurafenib sobre la actividad de CES1. También se usaron HLMs *in vitro* para investigar el metabolismo de hidrólisis catalizada de diacetato de fluoresceína (FDA) a fluoresceína para estudiar la inhibición de vemurafenib sobre la actividad de CES2. Los resultados mostraron que 100 μM de vemurafenib no ejercen inhibición significativa de la actividad de CES1. En contraste, 100 μM de vemurafenib mostró una inhibición significativa ($p < 0{,}001$) sobre la actividad de CES2. Para la inhibición de vemurafenib sobre la actividad de CES2 se calculó la concentración lque inhibe la actividad de 50% de CES2 y los resultados mostraron que el valor de IC50 de la inhibición de vemurafenib sobre CES2 era 25,1 μM. En conclusión, podría existir una interacción fármaco-fármaco entre vemurafenib y medicamentos principalmente sometidos a metabolismo de hidrólisis catalizada por CES2.

KEY WORDS: carboxylesterases (CES), drug-drug interaction (DDI), inhibition kinetics, *in vitro* incubation system, melanoma, vemurafenib.

* Author to whom correspondence should be addressed. *E-mail:* gaowanxia888@163.com

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