Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense*)
Lat. Am. J. Pharm. **41** (8): 1677-83 (2022)

Received: May 6, 2022
Accepted: July 2, 2022

In Vitro Human Cytochrome P450 Isozymes (CYPs) Inhibition of Epifriedelanol on CYP2C9, CYP2E1 and CYP3A4

Jie YU [1 #], Fengxian ZOU [2 # *] & Lifang ZHAO [2]

[1] *Pilot National Laboratory for Marine Science and Technology (Qingdao), Shandong, Qingdao, 266200 China*

[2] *SGS-CSTC Standards Technical Services (Qingdao) Co., Ltd., Shandong, Qingdao, 266200 China*

SUMMARY. **Epifriedelanol is the main ingredient of expectorant in *Aster tataricus* and was newly found with diverse pharmacological activities. *In vitro* CYP450 inhibition of epifriedelanol was evaluated using human liver microsomes (HLMs) to understand their drug-drug interaction potential. CYP450 isoform-specific substrates of CYP1A2, CYP3A4, CYP2A6, CYP2E1, CYP2D6, CYP2C9, CYP2C19, and CYP2C8 were incubated in HLMs with or without epifriedelanol. Preliminary CYP450 inhibition (IC_{50}) data were generated for each of these isoforms. The type of inhibition and estimation of the inhibition constants (K_i) of CYP3A4, CYP2E1, and CYP2C9 were determined. Epifriedelanol was inhibitors of CYP3A4, CYP2E1, and CYP2C9, with IC_{50} of 66.13, 24.77, and 9.31 µM, respectively. Epifriedelanol exhibited competitive inhibition of CYP2E1 and CYP2C9 activity and the K_i were found to be 11.41 and 4.518 µM, respectively. Epifriedelanol exhibited non-competitive and time-dependent inhibition of CYP3A4 activity, and the K_I was found to be 30.30 Mm, K_I/K_{inact} was 33.65/0.108 µM/min. Epifriedelanol may lead to significant clinical adverse drug interactions upon coadministration of drugs that are substantially metabolized by CYP3A4, CYP2E1, or CYP2C9.**

RESUMEN. Epifriedelanol es el ingrediente principal del expectorante en Aster tataricus y se descubrió recientemente con diversas actividades farmacológicas. La inhibición *in vitro* de CYP450 de epifriedelanol se evaluó utilizando microsomas hepáticos humanos (HLM) para comprender su potencial de interacción farmacológica. Los sustratos específicos de la isoforma CYP450 de CYP1A2, CYP3A4, CYP2A6, CYP2E1, CYP2D6, CYP2C9, CYP2C19 y CYP2C8 se incubaron en HLM con o sin epifriedelanol. Se generaron datos preliminares de inhibición de CYP450 (IC_{50}) para cada una de estas isoformas. Se determinó el tipo de inhibición y estimación de las constantes de inhibición (*Ki*) de CYP3A4, CYP2E1 y CYP2C9. Epifriedelanol fue inhibidor de CYP3A4, CYP2E1 y CYP2C9, con IC_{50} de 66,13, 24,77 y 9,31 µM, respectivamente. El epifriedelanol mostró una inhibición competitiva de la actividad de CYP2E1 y CYP2C9 y se encontró que la *Ki* era de 11,41 y 4,518 µM, respectivamente. El epifriedelanol exhibió una inhibición no competitiva y dependiente del tiempo de la actividad de CYP3A4, y se encontró que la *Ki* era de 30,30 Mm, la *KI*/*Kinact* era de 33,65/0,108 µM/min. El epifriedelanol puede dar lugar a interacciones farmacológicas adversas clínicas significativas tras la coadministración de fármacos que son metabolizados sustancialmente por CYP3A4, CYP2E1 o CYP2C9.

KEY WORDS: CYP2C9, CYP2E1, CYP3A4, herb-drug interaction.

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

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