Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **38** (12): 2440-7 (2019)

Received: September 1, 2019
Accepted: September 19, 2019

In vitro Inhibitory Effects of Aurantio-Obtusin on Human Liver Cytochrome P450 Enzymes

Hui SU [1,2], Yujie LI [1], Feng REN [1], Haitao JIANG [1] & Jianpei ZHAO [1] *

[1] *Department of General Surgery, Ningbo No. 2 Hospital, Ningbo 315000, Zhejiang Province, China*
[2] *Department of General Surgery, The First Affiliated Hospital of Jinan University, Guangzhou 510630, China*

SUMMARY*. Aurantio-obtusin is an anthraquinone compound and possesses numerous pharmacological activities. However, whether aurantio-obtusin affects the activity of human liver cytochrome P450 (CYP) enzymes remains unclear. In this study, the inhibitory effects of aurantio-obtusin on the eight human liver CYP isoforms (*i.e.,* 1A2, 3A4, 2A6, 2E1, 2D6, 2C9, 2C19, and 2C8) were investigated *in vitro* using human liver microsomes (HLMs). The results showed that aurantio-obtusin inhibited the activity of CYP1A2, 3A4, and 2E1, with IC_{50} values of 21.05, 13.57, and 16.12 μM, respectively, but that other CYP isoforms were not affected. Enzyme kinetic studies showed that aurantio-obtusin was not only a non-competitive inhibitor of CYP3A4, but also a competitive inhibitor of CYP1A2 and 2E1, with Ki values of 6.98, 9.52, and 8.32 μM, respectively. In addition, aurantio-obtusin is a time-dependent inhibitor for CYP3A4 with K_{inact}/K_I value of 0.051/11.87 $\mu M^{-1}min^{-1}$. The *in vitro* studies of aurantio-obtusin with CYP isoforms indicate that aurantio-obtusin has the potential to cause pharmacokinetic drug interactions with other co-administered drugs metabolized by CYP1A2, 3A4, and 2E1. Further clinical studies are needed to evaluate the significance of this interaction.

RESUMEN. Aurantio-obtusina es un compuesto de antraquinona y posee numerosas actividades farmacológicas. Sin embargo, aún no está claro si aurantio-obtusina afecta la actividad de las enzimas del citocromo P450 (CYP) del hígado humano. En este estudio, los efectos inhibitorios de la aurantio-obtusina en las ocho isoformas del CYP del hígado humano (es decir, 1A2, 3A4, 2A6, 2E1, 2D6, 2C9, 2C19 y 2C8) se investigaron *in vitro* utilizando microsomas hepáticos humanos (HLM). Los resultados mostraron que la aurantio-obtusina inhibió la actividad de CYP1A2, 3A4 y 2E1, con valores de CI50 de 21.05, 13.57 y 16.12 μM, respectivamente, pero que otras isoformas de CYP no se vieron afectadas. Los estudios cinéticos enzimáticos mostraron que la aurantio-obtusina no solo era un inhibidor no competitivo de CYP3A4, sino también un inhibidor competitivo de CYP1A2 y 2E1, con valores de Ki de 6.98, 9.52 y 8.32 μM, respectivamente. Además, la aurantio-obtusina es un inhibidor dependiente del tiempo para CYP3A4 con un valor de Kinact/KI de 0.051/11.87 $\mu M^{-1}min^{-1}$. Los estudios *in vitro* de aurantio-obtusina con isoformas de CYP indican que la aurantio-obtusina tiene el potencial de causar interacciones farmacocinéticas con otros fármacos administrados conjuntamente metabolizados por CYP1A2, 3A4 y 2E1. Se necesitan más estudios clínicos para evaluar la importancia de esta interacción.

KEY WORDS: aurantio-obtusin, CYP1A2, CYP3A4, CYP2E1, herb-drug interaction

* Author to whom correspondence should be addressed. *E-mail:* zai31068duo@163.com

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