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Mechanism Investigation for Piceatannol-Propofol Interaction

Lexiao JIN [1] #, Guowei WU [2] #, Zhenying ZHAO [3], Dongyue ZHENG [4] & Xiao CUI [5] *

[1] *Department of Anesthesiology, Critical Care and Pain, the Second Affiliated Hospital & Yuying Children's Hospital, Wenzhou Medical University, Wenzhou, China*
[2] *Children's Heart Center, Institute of Cardiovascular Development and Translational Medicine, Wenzhou Medical University, Wenzhou, China*
[3] *Department of Pharmacy, Tianjin Union Medicine Centre, Tianjin, China*
[4] *Department of Operating Room Nursing, The Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, China*
[5] *Department of Pharmacy, The Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, China*

***SUMMARY*. Piceatannol is an analog of resveratrol, and has been demonstrated to exhibit multiple biochemical and pharmacological activities, such as anti-inflammatory and anti-tumor activities. The recent study aims to determine the inhibition of piceatannol towards the glucuronidation of propofol using *in vitro* human liver microsomes (HLMs)-catalyzed glucuronidation of propofol. Piceatannol exhibits competitive inhibition towards propofol glucuronidation with the inhibition kinetic parameter (Ki) to be 15.1 μM. Furthermore, piceatannol was demonstrated to exert competitive inhibition towards the activity of UGT1A9 which is the catalytic enzyme of propofol glucuronidation, and the inhibition kinetic parameter (Ki) was 0.3 μM. Additionally, piceatannol was also demonstrated to exhibit strong inhibition on the activity of UGT1A3, indicating the potential influence of piceatannol on UGT1A3-catalyzed metabolism of drugs and some important endogenous substances (*e.g.,* bile acids, etc.). In conclusion, the present study demonstrated the influence of piceatannol towards the metabolism of propofol through inhibiting the activity of UGT1A3.**

RESUMEN. El piceatanol es un análogo del resveratrol y se ha demostrado que exhibe múltiples actividades bioquímicas y farmacológicas, entre ellas anti-inflamatorias y anti-tumorales. El presente estudio tiene como objetivo determinar la inhibición de piceatanol sobre la glucuronidación de propofol utilizando la glucuronidación de propofol catalizada por microsomas hepáticos humanos *in vitro* (VAM). El piceatanol exhibe inhibición competitiva hacia la glucuronidación de propofol con un parámetro cinético de inhibición (Ki) de 15,1 μM. Además, piceatannol demostró ejercer inhibición competitiva hacia la actividad de UGT1A9, enzima responsable de la glucuronidación de propofol, y el parámetro cinético de inhibición (Ki) fue de 0,3 μM. Piceatanol también demostró exhibir fuerte inhibición de la actividad de UGT1A3, indicando la influencia potencial de piceatanol sobre el metabolismo catalizado de fármacos por UGT1A3 y algunas importantes sustancias endógenas (por ejemplo, ácidos biliares, etc.). En conclusión, el presente estudio demostró la influencia de piceatanol hacia el metabolismo de propofol a través de la inhibición de la actividad de UGT1A3.

KEY WORDS: drug-drug interaction, piceatannol, propofol, UGT1A9.

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

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