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Inhibition Potential of Demethylzeylasteral Towards the Glucuronidation of 7-Ethyl-10-Hydroxy-Camptothecin (SN-38)

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***SUMMARY*. 7-Ethyl-10-hydroxy-camptothecin (SN-38) is the active metabolite of irinotecan which has been approved to treat cancer. The toxicity of irinotecan has been regarded to be highly related with the exposure of SN-38 in the intestine. The present study aims to determine the inhibition of demethylzeylasteral towards the glucuronidation elimination reaction of SN-38 using *in vitro* recombinant UGT1A1 and human intestinal microsomal (HIM) incubation system. The results showed that demethylzeylasteral exerted dose-dependent inhibition towards both recombinant UGT1A1 and HIMs-catalyzed glucuronidation of SN-38. The inhibition type belongs to be noncompetitive inhibition and competitive inhibition type for the inhibition of demethylzeylasteral towards SN-38 glucuronidation in recombinant UGT1A1 and HIM incubation system, as demonstrated by Dixon plot. All these results indicate the potential elevation of irinotecan's toxicity when co-administered with demethylzeylasteral-containing herbs.**

RESUMEN. La 7-etil-10-hidroxi-camptotecina (SN-38) es el metabolito activo del irinotecán, que ha sido aprobado para tratar el cáncer. La toxicidad del irinotecán ha sido considerada como altamente relacionada con la exposición de SN-38 en el intestino. El presente estudio tiene como objetivo determinar la inhibición de demetilzeylasteral sobre la reacción de glucuronidación de SN-38 utilizando UGT1A1 recombinante *in vitro* y un sistema de incubación microsomal intestinal humana (HIM). Los resultados mostraron que el demetilzeylasteral ejerce una inhibición dosis-dependiente tanto hacia UGT1A1 recombinante como a la glucuronidación HIM de SN-38. El tipo de inhibición es no competitiva y el tipo de inhibición competitiva corresponde a la inhibición de demetilzeylasteral hacia SN-38 en la glucuronidación de UGT1A1 recombinante y en el sistema de incubación HIM, como lo demuestra el esquema de Dixon. Todos estos resultados indican la elevación del potencial de toxicidad de irinotecán al administrarse conjuntamente con hierbas que contengan demetilzeylasteral.

KEY WORDS: Demethylzeylasteral, Irinotecan, Glucuronidation, 7-ethyl-10-hydroxy-camptothecin (SN-38)

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