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Short communication

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Gomisin J Affects the Therapeutic Role of Irinotecan towards Glioma through Alteration of its Therapeutic Index

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***SUMMARY*. The potential drug-drug interaction between gomisin J and irinotecan was predicted through determining the inhibition of gomisin J towards SN-38 glucuronidation. *In vitro* recombinant UGT1A1 catalyzed SN-38 glucuronidation was used to determine the inhibition capability of gomisin J. At 2 μM of SN-38, the glucuronidation activity of SN-38 was inhibited by 18.5, 41.9, 67.1, and 74.6% by 20, 40, 80, and 100 μM of gomisin J, respectively. In Lineweaver-Burk plot, the intersection point was located in the vertical axis, indicating the competitive inhibition of gomisin J towards the glucuronidation of SN-38. The inhibition kinetic parameter (K_i) was calculated to be 19.8 μM. All these data indicated the potential drug-drug interaction between gomisin J and irinotecan. Additionally, SN-38 glucuronidation is a probe reaction for UGT1A1. Therefore, gomisin J might induce drug-drug interaction with the clinical drugs mainly undergoing UGT1A1-catalyzed glucuronidation.**

RESUMEN. La posible interacción fármaco-fármaco entre gomisina J e irinotecán se predijo mediante la determinación de la inhibición de la gomisina J sobre la glucuronidación de SN-38. La glucuronidación de SN-38 catalizada *in vitro* por UGT1A1 recombinante se utilizó para determinar la capacidad de inhibición de gomisina J. En una concentración 2 μM de SN-38, la actividad de glucuronidación de SN-38 fue inhibida por 18.5, 41.9, 67.1, y 74.6% por 20, 40, 80 y 100 μM de gomisina J, respectivamente. En el diagram de Lineweaver-Burk, el punto de intersección se encuentra en el eje vertical, indicando la inhibición competitiva de gomisina J sobre la glucuronidación de SN-38. El parámetro cinético de inhibición (K_i) se calculó en 19,8 μM. Todos estos datos indican el potencial de interacción farmacológica entre gomisina J e irinotecán. Además, la glucuronidación de SN-38 es una reacción sonda para UGT1A1. Por lo tanto, gomisina J podría inducir interacciones farmacológicas con los fármacos que sufren principalmente glucuronidación catalizada por UGT1A1.

KEY WORDS: Irinotecan, Glioma, Gomisin J.

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