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Short communication

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Mechanism Analysis for Atractylenolide II-Zidovudine Interaction

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***SUMMARY*. Herb-drug interaction severely limits the clinical utilization of drugs and herbs. The present study aims to determine the inhibition of zidovudine glucuronidation by herbal ingredient atractylenolide II which is the major ingredient from atractylodes (*Atractylodes macrocephala* Koidz.). *In vitro* mechanism analysis and *in silico* prediction model were used to explain atractylenolide II-zidovudine interaction. The results showed the significant inhibition of atractylenolide II towards zidovudine glucuronidation. *In vitro* mechanism analysis showed that atractylenolide II strongly inhibited the activity of UDP-glucuronosyltransferase (UGT) 2B7 which is the major drug-metabolizing enzyme involved in the metabolism of zidovudine. The inhibition kinetic type belongs to be competitive, and the inhibition kinetic parameter (K_i) was calculated to be 11.0 uM. *in silico* docking method showed the high binding free energy between atractylenolide II and UGT2B7, which was attributed to high internal molecular energy and internal energy. In conclusion, high binding free energy between atractylenolide II and UGT2B7 contributed the strong competitive inhibition of atractylenolide II towards the activity of UGT2B7, which is the major reason for atractylenolide II-zidovudine interaction.**

RESUMEN. La interacción entre hierbas y drogas limita severamente la utilización clínica de ambas. El presente estudio tiene como objetivo determinar la inhibición de la glucuronidación de zidovudina por el ingrediente herbario atractylenolido II, que es el principal ingrediente de atractylodes (*Atractylodes macrocephala* Koidz.). El análisis del mecanismo *in vitro* y el modelo de predicción *in silico* se utilizaron para explicar la interacción atractylenolido II-zidovudina. Los resultados mostraron una inhibición significativa de atractylenolido II sobre la glucuronidación de zidovudina. El análisis del mecanismo *in vitro* mostró que atractylenolido II inhibió fuertemente la actividad de UDP-glucuronosiltransferasa (UGT) 2B7, que es la principal enzima que metaboliza fármacos involucrados en el metabolismo de zidovudina. La cinética de inhibición es de tipo competitivo y el parámetro cinético de inhibición (K_i) se calculó en 11,0 μM. El método de anclaje *in silico* mostró la alta energía libre de unión entre atractylenolido II y UGT2B7, que se atribuyó a la alta energía molecular interna y a la energía interna. En conclusión, la alta energía libre de unión entre atractylenolido II y UGT2B7 contribuye a la fuerte inhibición competitiva de atractylenolido II sobre la actividad de UGT2B7, que es la principal razón de la interacción entre atractylenolido II y zidovudina.

KEY WORDS: atractylenolide II, drug-drug interaction, herb-drug interaction, *in silico,* UDP-glucuronosyltransferase (UGT), 2B7zidovudine.

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