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Inhibition Potential of Andrographolide Derivative on the Activity of Intestinal UDP-Glucuronosyltransferases (UGTs) Isoforms

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SUMMARY. **Andrographolide is the major active component isolated from Andrographis paniculata, and has been reported to exert multiple biochemical and pharmacological activities. Many andrographolide derivatives are being developed to get more efficient therapeutic agents. This study aims to determine the effect of andrographolide derivative on the activity of intestinal UDP-glucuronosyltransferase (UGT) isoforms, including UGT1A7, UGT1A8, and UGT1A10. In vitro UGT incubation system was used, and 100 μM of andrographolide derivative was used to initially screen the inhibition potential. 100 μM of andrographolide showed no inhibition on the activity of UGT1A7. However, 100 μM of andrographolide showed significant inhibition on the activity of UGT1A8 and UGT1A10. Furthermore, inhibition kinetic type determination showed that the intersection point was located in the vertical axis of Lineweaver-Burk plot for the inhibition of andrographolide derivative on UGT1A8 and UGT1A10, indicating the competitive inhibition of andrographolide derivative on UGT1A8 and UGT1A10. The fitting equation for the second plot was *y = 0.2491x + 3.0706 and y = 1.7256x + 37.245* for the inhibition of andrographolide derivative on UGT1A8 and UGT1A10. Based on the fitting equations, the inhibition kinetic parameters (Ki) were calculated to be 12.3 and 21.6 μM, respectively. In conclusion, the inhibition of andrographolide derivative on intestinal UGT isoforms was demonstrated in this study.**

RESUMEN. Andrografólido es el principal compuesto activo aislado de Andrographis paniculata y se ha informado que ejerce múltiples actividades bioquímicas y farmacológicas. Muchos derivados del andrografólido se están desarrollando para obtener agentes terapéuticos más eficaces. Este estudio tiene como objetivo determinar el efecto de un derivado de andrografólido sobre la actividad de las isoformas de la UDP-glucuronosyltransferasa (UGT) intestinal, incluyendo UGT1A7, UGT1A8 y UGT1A10. En el sistema de incubación in vitro se utilizaron UGT y derivado de andrografólido 100 μM para rastrear inicialmente el potencial de inhibición. Andrografólido 100 μM no mostró inhibición de la actividad de UGT1A7, pero sí una inhibición significativa de la actividad de UGT1A8 y UGT1A10. Además, la inhibición de tipo cinético mostró que la determinación del punto de intersección se encuentra en el eje vertical de la representación de Lineweaver-Burk para la inhibición del derivado de andrografólido sobre UGT1A8 y UGT1A10, lo que indica inhibición competitiva. La ecuación de ajuste para el segundo gráfico fue *y = 0.2491x + 3,0706 e y = 1.7256x + 37.245* para la inhibición del derivado de andrografólido sobre UGT1A8 y UGT1A10. Con base en las ecuaciones de ajuste, los parámetros cinéticos de inhibición (Ki) se calcularon en 12,3 y 21,6 μM, respectivamente. En conclusión, en este estudio se demostró la inhibición del derivado de andrografólido sobre las isoformas de UGT intestinales.

KEY WORDS: andrographolide derivatives, enzyme inhibition, intestinal UDP-glucuronosyltransferases (UGTs).

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