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Short communication

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The Plasma Level of ALT Can Predict the Metabolic Rate of Arctigenin Derivative

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SUMMARY*. Alanine transaminase (ALT) and aspartate transaminase (AST) are important clinical biochemical parameters to indicate the health of liver organ. The present study aims to find the new role of ALT and AST to predict the metabolic behavior of drugs or drug candidates. Arctigenin derivative was selected as the representative drug candidate, and *in vitro* human liver microsomes (HLMs) incubation system was employed to determine the metabolism of arctigenin derivative. HLMs were prepared from paracancerous tissues surrounding liver tumors, and the HLMs incubation mixture (vol = 200 μL) contains the following components: 0.1 mg/mL of HLMs, 100 μM of arctigenin derivative, 5 mM of UDPGA, 50 μg/mg alamethicin, 50 mM of Tris-HCl buffer (pH = 7.4), and 20 mM of $MgCl_2$. The metabolic behavior was compared in HLMs incubation mixture with and without phase II co-factor UDPGA. In the HLMs incubation system without UDPGA, the substrate arctigenin derivative was eluted at 6.7 min. We did not observe any metabolite in this incubation system. In the contrast, both the substrate arctigenin derivative and its metabolite can be detected in HLMs incubation system with UDPGA. Furthermore, we found the linear correlation between the concentration of substrate and the formation of product. Therefore, we choosed 50 μM as the concentration of selected substrate. The metabolism of arctigenin derivative has good correlation with the activity of ALT (R^2 = 0.86). However, the activity of AST did not have good correlation with the metabolism of arctigenin derivative (R^2 = 0.079). In conclusion, if we tried to elucidate the metabolic behavior of arctigenin derivative, we just needed to take blood to determine the activity of ALT, because the activity of ALT has good correlation with the metabolism capability of arctigenin derivative.

RESUMEN. Alanina transaminasa (ALT) y aspartato transaminasa (AST) son importantes parámetros bioquímicos clínicos para indicar la salud del órgano hepático. El presente estudio tiene como objetivo encontrar el nuevo papel de ALT y AST para predecir el comportamiento metabólico de fármacos o fármacos candidatos. Se seleccionó el derivado de arctigenina como el candidato de fármaco representativo y se utilizó un sistema de incubación *in vitro* de microsomas hepáticos humanos (HLMs) para determinar el metabolismo del derivado de arctigenina. Se prepararon HLMs a partir de tejidos paracancerosos que rodean tumores hepáticos y la mezcla de incubación de HLMs (volumen = 200 μl) contiene los siguientes componentes: 0,1 mg/mL de HLMs, 100 μM de derivado de arctigenina, 5 mM de UDPGA, 50 μg/mg de alamethicina, 50 mM de tampón Tris-HCl (pH = 7,4), y 20 mM de $MgCl_2$. El comportamiento metabólico se comparó en la mezcla de incubación de HLMs con y sin el cofactor de fase II UDPGA. En el sistema de incubación de HLMs sin UDPGA, el derivado de arctigenina eluyó a los 6,7 min. No observamos ningún metabolito en este sistema de incubación. En contraste, tanto el derivado de arctigenina como su metabolito pueden detectarse en el sistema de incubación de HLMs con UDPGA. Más aún, se encontró una correlación lineal entre la concentración de sustrato y la formación del producto. Por lo tanto, se eligió 50 μM como la concentración de sustrato seleccionado. El metabolismo del derivado de arctigenina tiene una buena correlación con la actividad de ALT (R^2 = 0,86). Sin embargo, la actividad de AST no tuvo una buena correlación con el metabolismo del derivado de arctigenina (R^2 = 0,079). En conclusión, si intentamos dilucidar el comportamiento metabólico del derivado de arctigenina, sólo necesitamos tomar sangre para determinar la actividad de ALT, porque tiene una buena correlación con la capacidad de metabolismo del derivado de arctigenina.

KEY WORDS: ALT, arctigenin derivative, AST, glucuronidation.

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