



In vitro Study on the Effect of Agrimoniin on the Activity of Cytochrome P450 Enzymes

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SUMMARY. The effect of agrimoniin on the activity of cytochrome P450 (CYP450) enzymes would induce drug-drug interaction, which leads to adverse effects or even failure of therapy. Agrimoniin was incubated with eight human liver CYP isoforms in pooled human liver microsomes. The enzyme kinetics and time-dependent study were performed to obtain kinetic parameters and characteristics *in vitro*. Agrimoniin significantly inhibited the activity of CYP1A2, 2D6, and 3A4 in a dose-dependent manner with IC₅₀ values of 6.26, 9.35, and 8.30 μ M, respectively. Agrimoniin served as a non-competitive inhibitor of CYP3A4 and a competitive inhibitor of CYP1A2 and 2D6. Moreover, the incubation time was found to play a vital role in the inhibition of CYP3A4. *In vitro* inhibitory effect of agrimoniin on the activity of CYP1A2, 2A6, and 3A4 was reported in this study. The potential drug-drug interactions between agrimoniin and drugs metabolized by CYP1A2, 2D6, and 3A4 should be paid special attention.

RESUMEN. El efecto de la agrimonina sobre la actividad de las enzimas del citocromo P450 (CYP450) induciría la interacción fármaco-fármaco, lo que conduce a efectos adversos o incluso al fracaso de la terapia. Se incubó agrimoniina con ocho isoformas CYP de hígado humano en microsomas de hígado humano agrupados. La cinética enzimática y el estudio dependiente del tiempo se realizaron para obtener parámetros cinéticos y características *in vitro*. Agrimoniina inhibió significativamente la actividad de CYP1A2, 2D6 y 3A4 de una manera dependiente de la dosis con valores de CI₅₀ de 6.26, 9.35 y 8.30 μ M, respectivamente. Agrimonina sirvió como un inhibidor no competitivo de CYP3A4 y un inhibidor competitivo de CYP1A2 y 2D6. Además, se descubrió que el tiempo de incubación juega un papel vital en la inhibición de CYP3A4. En este estudio se informó el efecto inhibitorio *in vitro* de la agrimonina sobre la actividad de CYP1A2, 2A6 y 3A4. Se debe prestar especial atención a las posibles interacciones fármaco-fármaco entre la agrimonina y los fármacos metabolizados por CYP1A2, 2D6 y 3A4.

KEY WORDS: agrimoniin; CYP1A2; CYP2D6; CYP3A4; drug-drug interaction

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