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Influence of Epigallocatechin-3-Gallate on Pharmacokinetics of Pristimerin in Rats and its Potential Mechanism

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SUMMARY. Pristimerin is a biological component isolated from the Chinese herbal plant *Tripterygium wilfordii* Hook which possesses numerous pharmacological activities. The aim of this study was to investigate the effects of epigallocatechin-3-gallate (EGCG) on the pharmacokinetics of pristimerin in rats. The pharmacokinetics of orally administered pristimerin with or without EGCG pretreatment were investigated. Additionally, the effects of EGCG on the absorption and metabolic stability of pristimerin were investigated using the Caco-2 cell transwell model and rat liver microsomes. The results indicated that when the rats were pretreated with EGCG, the C_{max} of pristimerin increased from 189.13 ng/mL to 277.53 ng/mL (46.7%), and the AUC_{0-t} increased by approximately 82.0%. A markedly higher transport of pristimerin across the Caco-2 cells was observed in the basolateral-to-apical direction and was abrogated in the presence of EGCG. These results indicated that *P-gp* might be involved in the absorption of pristimerin. Of note, the metabolic half-life of pristimerin was prolonged by the pretreatment with EGCG. In conclusion, EGCG could affect the pharmacokinetics of pristimerin, and it might work through increasing the absorption of pristimerin by inhibiting *P-gp,* or through slowing down the metabolism of pristimerin in the rat liver.

RESUMEN. La pristimerina es un componente biológico aislado de la hierba china *Tripterygium wilfordii* Hook, que posee numerosas actividades farmacológicas. El objetivo de este estudio fue investigar los efectos de la epigalocatequina-3-galato (EGCG) en la farmacocinética de pristimerina en ratas. Se investigó la farmacocinética de la pristimerina administrada por vía oral con o sin pretratamiento con EGCG. Además, se investigaron los efectos del EGCG en la absorción y la estabilidad metabólica de la pristimerina utilizando el modelo de transwell de células Caco-2 y los microsomas de hígado de rata. Los resultados indicaron que cuando las ratas fueron pretratadas con EGCG, la C_{max} de pristimerina aumentó de 189.13 ng/mL a 277.53 ng/mL (46.7%), y el AUC_{0-t} aumentó aproximadamente 82.0%. Se observó un transporte marcadamente superior de pristimerina a través de las células Caco-2 en dirección basolateral a apical y se anuló en presencia de EGCG. Estos resultados indicaron que la *P-gp* podría estar involucrada en la absorción de pristimerina. Es de destacar que la semivida metabólica de pristimerina se prolongó por el tratamiento previo con EGCG. En conclusión, el EGCG podría afectar la farmacocinética de la pristimerina y podría funcionar aumentando la absorción de la pristimerina mediante la inhibición de la *P-gp,* o al disminuir el metabolismo de la pristimerina en hígado de rata.

KEY WORDS: Pristimerin; Epigallocatechin-3-gallate; CYP450; Drug-drug interaction; *P-gp*.

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