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Effect of Verapamil on the Pharmacokinetics of Pinocembrin in Rats

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SUMMARY. **Pinocembrin and verapamil might be co-administrated due to their similar pharmacological activities. This study investigated the interaction between verapamil and pinocembrin in rats and clarified its potential mechanism. The pharmacokinetic profiles of oral administration of pinocembrin (50 mg/kg) in Sprague-Dawley rats, with or without pretreatment of verapamil (10 mg/kg/day for 7 days) were investigated. The effects of verapamil on the transport and metabolic stability of pinocembrin were also investigated using Caco-2 cell transwell model and rat liver microsomes. The results showed that verapamil could significantly increase the peak plasma concentration, and decrease the oral clearance of pinocembrin. The Caco-2 cell transwell experiments indicated that verapamil could decrease the efflux ratio and the intrinsic clearance rate of pinocembrin. Those results indicated that verapamil could increase the system exposure of pinocembrin through inhibiting the metabolism of pinocembrin or increasing its absorption.**

RESUMEN. La pinocembrina y el verapamilo pueden coadministrarse debido a sus actividades farmacológicas similares. Este estudio investigó la interacción entre el verapamilo y la pinocembrina en ratas y aclaró su mecanismo potencial. Se investigaron los perfiles farmacocinéticos de la administración oral de pinocembrina (50 mg/kg) en ratas Sprague-Dawley, con o sin pretratamiento de verapamilo (10 mg/kg/día durante 7 días). Los efectos del verapamilo sobre el transporte y la estabilidad metabólica de pinocembrina también se investigaron utilizando el modelo de transpocillos de células Caco-2 y microsomas de hígado de rata. Los resultados mostraron que el verapamilo podría aumentar significativamente la concentración plasmática máxima y disminuir el aclaramiento oral de pinocembrina. Los experimentos de transpocillos de células Caco-2 indicaron que el verapamilo podría disminuir la proporción de eflujo y la tasa de depuración intrínseca de pinocembrina. Esos resultados indicaron que el verapamilo podría aumentar la exposición del sistema a la pinocembrina al inhibir el metabolismo de la pinocembrina o aumentar su absorción.

KEY WORDS: drug-drug interaction *P-gp*, pharmacokinetics, pinocembrin, verapamil

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