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Pharmacokinetics of Hesperidin and its Hepatic, Gastric and Intestinal First-pass Effects in Rats

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***SUMMARY*. The aims of this study are to investigate the pharmacokinetics and its hepatic, gastric and intestinal first-pass effects of hesperidin (HP) in rats. A rapid and sensitive ultra-high performance liquid chromatographic method with vitexin-2"-*O*-rhamnoside as the internal standard (IS) was firstly developed and validated to investigate the pharmacokinetics of HP. Secondly, the hepatic, gastric and intestinal first-pass effect models were established to investigate the reasons of the low bioavailability of HP and the results indicated that the intestinal first-pass effect was remarkable to be 61.31%. Finally, verapamil and borneol being as the inhibitors of CYP3A and P-gp, bile salt being as the absorption enhancer, were respectively administrated with HP together in order to improve the bioavailability of HP, and the results indicated that the bile salt groups remarkably improved the bioavailability of HP via inhibiting the intestinal first-pass effect.**

RESUMEN. Los objetivos de este estudio son investigar la farmacocinética y sus efectos de primer paso hepático, gástrico e intestinal de la hesperidina (HP) en ratas. En primer lugar, se desarrolló y validó un método de cromatografía líquida rápida y sensible de ultra alto rendimiento con vitexina-2 "-*O*-ramnósido como estándar interno (IS) para investigar la farmacocinética de HP. En segundo lugar, los modelos de efecto de primer paso hepático, gástrico e intestinal se establecieron para investigar los motivos de la baja biodisponibilidad de HP y los resultados indicaron que el efecto de primer paso intestinal fue notable en un 61,31%. Finalmente, verapamilo y borneol como inhibidores de CYP3A y P-gp, siendo la sal biliar como potenciador de la absorción, se administraron con HP, respectivamente, para mejorar la biodisponibilidad de HP; los resultados indicaron que los grupos de sal biliar mejoraron notablemente la biodisponibilidad de HP mediante la inhibición del efecto de primer paso intestinal.

KEY WORDS: bioavailability, first-pass effect, hesperidin, pharmacokinetics.

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