Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **37** (9): 1870-6 (2018)

Received: July 1, 2018
Revised version: July 20, 2018
Accepted: July 21, 2018

Effects of Quercetin on the Pharmacokinetics of Puerarin in Rats

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***SUMMARY*. Puerarin has been reported to possess a wide range of pharmacological activities. This study investigates the effects of quercetin on the pharmacokinetics of puerarin in rats. The pharmacokinetics of orally administered puerarin (50 mg/kg) with or without quercetin pretreatment (20 mg/kg/day for 7 days) were investigated. The plasma concentration of puerarin was determined using LC-MS/MS method. The pharmacokinetics profiles were calculated and compared. Additionally, a Caco-2 cell transwell model was used to investigate the potential mechanism of quercetin's effects on the pharmacokinetics of puerarin. The results showed that when the rats were pretreated with quercetin, the maximum concentration (C_{max}) of puerarin increased from 420.15 ± 76.35 to 683.7 ± 82.72 ng/mL, and the area under the concentration-time curve from zero to infinity ($AUC_{0\text{-}inf}$) also increased from 2096.69 ± 325.61 to 3687.35 ± 521.25 μg·h/L. The Caco-2 cell transwell experiments indicated that quercetin could decrease the efflux ratio of puerarin from 1.88 to 1.42. In conclusion, these results indicated that quercetin could affect the pharmacokinetics of puerarin, possibly by increasing the systemic exposure of puerarin by inhibiting the activity of *P-gp*.**

RESUMEN. Se ha informado que puerarina posee una amplia gama de actividades farmacológicas. Este estudio investiga los efectos de la queretana en la farmacocinética de puerarina en ratas. Se investigó la farmacocinética de puerarina administrado por vía oral (50 mg/kg) con o sin pretratamiento con quercetina (20 mg/kg.día durante 7 días). La concentración plasmática de puerarina se determinó mediante el método LC-MS/MS. Los perfiles farmacocinéticos se calcularon y compararon. Además, se utilizó un modelo de transwell de células Caco-2 para investigar el mecanismo potencial de los efectos de quercetina en la farmacocinética de puerarina. Los resultados mostraron que cuando las ratas fueron pretratadas con quercetina, la concentración máxima (C_{max}) de puerarin aumentó de 420.15 ± 76.35 a 683.7 ± 82.72 ng/mL, y el área bajo la curva de concentración-tiempo de cero a infinito ($AUC_{0\text{-}inf}$) también aumentó de 2096.69 ± 325.61 a 3687.35 ± 521.25 μg h/L. Los experimentos de translocación de células Caco-2 indicaron que la quercetina podría disminuir la relación de eflujo de puerarin de 1.88 a 1.42. En conclusión, estos resultados indicaron que la quercetina podría afectar la farmacocinética de puerarin, posiblemente al aumentar la exposición sistémica de puerarin al inhibir la actividad de *P-gp*.

KEY WORDS: Caco-2 cell, LC-MS/MS, *P-gp*.

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ISSN 0326 2383 (printed ed.)
ISSN 2362-3853 (on line ed.)