Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **38** (6): 1235-40 (2019)

Received: February 17, 2019
Revised version: April 5, 2019
Accepted: April 7, 2019

Effects of Astragaloside IV on the Pharmacokinetics of Triptolide in Rats

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***SUMMARY*. Radix astragali and triptolide are might used together for treatment of diseases in China clinics. This study investigates the effects of astragaloside IV (AS-IV, the main components of Radix astragali) on the pharmacokinetics of triptolide in rats. The pharmacokinetics of orally administered triptolide (1 mg/kg) with or without AS-IV pretreatment (100 mg/kg/day for 7 days) were investigated. The plasma concentration of triptolide was determined using LC-MS/MS method, and the pharmacokinetics profiles were calculated and compared. Caco-2 cell transwell model was also used to investigate the effects of AS-IV on the transport pf triptolide. The results showed that when the rats were pretreated with AS-IV, the maximum concentration (C_{max}) of triptolide decreased from 211.98 to 183.35 ng/mL ($P < 0.05$), and the area under the concentration-time curve from zero to infinity ($AUC_{0\text{-}inf}$) also decreased from 2210.23 to 1721.35 μg·h/L ($P < 0.05$). The oral clearance of triptolide increased significantly from 4.56 to 5.90 L/h/kg ($P < 0.05$). The Caco-2 cell transwell experiments indicated that AS-IV could increase the efflux ratio of triptolide from 2.28 to 3.21 through inducing the activity of *P-gp*. In conclusion, these results indicated that AS-IV could affect the pharmacokinetics of triptolide, possibly by decreasing the systemic exposure of triptolide by inducing the activity of *P-gp*.**

RESUMEN. Radix astragali y triptólido pueden usarse juntas para el tratamiento de enfermedades en las clínicas de China. Este estudio investiga los efectos del astragaloside IV (AS-IV, los componentes principales de Radix astragali) en la farmacocinética de triptólido en ratas. Se investigó la farmacocinética de triptólido administrado por vía oral (1 mg/kg) con o sin pretratamiento con AS-IV (100 mg/kg/día durante 7 días). La concentración plasmática de triptólido se determinó utilizando LC-MS/MS y se calcularon y compararon los perfiles farmacocinéticos. El modelo de transwell de células Caco-2 también se utilizó para investigar los efectos de AS-IV en el transporte de triptólido. Los resultados mostraron que cuando las ratas fueron tratadas previamente con AS-IV, la concentración máxima (C_{max}) de triptólido disminuyó de 211.98 a 183.35 ng/mL ($P < 0.05$), y el área bajo la curva de concentración-tiempo de cero a infinito ($AUC_{0\text{-}inf}$) también disminuyó de 2210.23 a 1721.35 μg·h/L ($P < 0.05$). El aclaramiento oral de triptólido aumentó significativamente de 4.56 a 5.90 L/h/kg ($P < 0.05$). Los experimentos de transwell de células Caco-2 indicaron que AS-IV podría aumentar la relación de flujo de salida de triptólido de 2.28 a 3.21 a través de la inducción de la actividad de *P-gp*. En conclusión, estos resultados indicaron que AS-IV podría afectar la farmacocinética de triptólido, posiblemente al disminuir la exposición sistémica de triptólido al inducir la actividad de *P-gp*.

KEY WORDS: Caco-2 cell, drug-drug interaction, *P-gp,* Radix astragali, triptolide.

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