

## Effect of *Centella asiatica* Formulation on the Pharmacokinetics of Amitriptyline in Rats: A Herb-Drug Interaction Study

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**SUMMARY.** This study evaluates the effect of *Centella asiatica* formulation on the pharmacokinetics of amitriptyline in rats. In this study, rats were randomly divided into two groups (n = 6 each) which were served as a control (amitriptyline alone) and treatment group (amitriptyline with *C. asiatica*), respectively. Rats were administered vehicle saline or *C. asiatica* (62.5 mg/kg, p.o. daily for 7 days), then administered a single amitriptyline dose (25 mg/kg, p.o.) on day 8. Plasma samples were analyzed for amitriptyline concentration using a developed and validated reversed-phase high-performance liquid chromatography (RP-HPLC) method. Pharmacokinetic parameters were calculated using non-compartmental analysis. The co-administration of *C. asiatica* with amitriptyline resulted in increased plasma maximum concentration ( $C_{max}$ ), area under the curve ( $AUC_{0-24}$ ) and elimination half-life ( $t_{1/2}$ ) by 14.34, 23, and 13.81%, respectively. The present study demonstrated that *C. asiatica* extract has the potential to alter the pharmacokinetics of amitriptyline by a significant reduction in amitriptyline clearance and an increase in its  $AUC$ ,  $C_{max}$  and  $t_{1/2}$ .

**RESUMEN.** Este estudio evalúa el efecto de la formulación de *Centella asiatica* sobre la farmacocinética de la amitriptilina en ratas. Las ratas se dividieron aleatoriamente en dos grupos (n = 6 cada uno) que sirvieron como control (amitriptilina sola) y grupo de tratamiento (amitriptilina con *C. asiatica*), respectivamente. A las ratas se les administró suero fisiológico o *C. asiatica* (62.5 mg/kg, p.o. diariamente durante 7 días), luego se les administró una dosis única de amitriptilina (25 mg/kg, p.o.) el día 8. Se analizaron las concentraciones plasmáticas de amitriptilina usando un método validado de cromatografía líquida de alta resolución en fase reversa (RP-HPLC). Los parámetros farmacocinéticos se calcularon usando análisis no compartimental. La administración conjunta de *C. asiatica* con amitriptilina resultó en un aumento de la concentración máxima en plasma ( $C_{m\acute{a}x}$ ), el área bajo la curva ( $AUC_{0-24}$ ) y la semivida de eliminación ( $t_{1/2}$ ) en un 14.34, 23 y 13.81%, respectivamente. El presente estudio demostró que el extracto de *C. asiatica* tiene el potencial de alterar la farmacocinética de la amitriptilina mediante una reducción significativa en la depuración de amitriptilina y un aumento en su  $AUC$ ,  $C_{m\acute{a}x}$  y  $t_{1/2}$ .

**KEY WORDS:** amitriptyline, bioavailability, *Centella asiatica*, CYP450, Gotu Kola, herbal drug interaction.

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