

## Analgesic and Anti-inflammatory Effects of Neriifolin in Rats with Spinal Nerve Ligation-Induced Neuropathic Pain

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**SUMMARY.** Neriifolin is a cardenolide glycoside abundant in seeds, such as *Thevetia ahouai* and *Thevetia neriifolia*, and has been reported to possess anti-inflammatory properties. The present study aimed to investigate the analgesic potential of neriifolin in L5 spinal nerve ligation (SNL) induced peripheral neuropathic pain. Different doses of neriifolin or saline were administered intrathecally once daily for 11 consecutive days. Pain arousal was assessed on day one prior and 7-14 days after surgery in terms of mechanical withdrawal threshold and thermal withdrawal latency. Astrocytic and microglial activation and release of inflammatory mediators were determined on the final day 14 after surgery. The results demonstrated that neriifolin attenuated the mechanical allodynia and thermal hyperalgesia induced by SNL. Furthermore, Neriifolin significantly inhibited SNL-induced activation of glial cells (astrocytes and microglia). Moreover, the unregulated expression of inflammatory mediators in neuropathic pain was significantly inhibited by neriifolin. Our findings suggested that repeated administration of neriifolin may alleviate neuropathic pain, possibly through inhibiting neuroinflammation.

**RESUMEN.** La neriifolina es un glucósido cardenólido abundante en semillas, como *Thevetia ahouai* y *Thevetia neriifolia*, y se ha informado que posee propiedades antiinflamatorias. El presente estudio tuvo como objetivo investigar el potencial analgésico de la neriifolina en el dolor neuropático periférico inducido por la ligadura del nervio espinal L5 (SNL). Se administraron diferentes dosis de neriifolina o solución salina por vía intratecal una vez al día durante 11 días consecutivos. La activación del dolor se evaluó el día uno antes y entre 7 y 14 días después de la cirugía en términos de umbral de retirada mecánica y latencia de retirada térmica. La activación astrocítica y microglial y la liberación de mediadores inflamatorios se determinaron el último día 14 después de la cirugía. Los resultados demostraron que la neriifolina atenuó la alodinia mecánica y la hiperalgesia térmica inducidas por SNL. Además, la neriifolina inhibió significativamente la activación inducida por SNL de las células gliales (astrocitos y microglia). Además, la neriifolina inhibió significativamente la expresión no regulada de mediadores inflamatorios en el dolor neuropático. Nuestros hallazgos sugirieron que la administración repetida de neriifolina puede aliviar el dolor neuropático, posiblemente mediante la inhibición de la neuroinflamación.

**KEY WORDS:** neriifolin, neuroinflammation, spinal nerve ligation.

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