Antineuroinflammatory and Analgesic Effects of a Marine-Derived Peptide, WPL, in Chronic-Constriction-Injury-Induced Neuropathic Rats

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Neuropathic pain occurs as a consequence of damage to peripheral nerves or the central nervous system (CNS) and is often refractory to opioids and other analgesics. Neuropathic pain is characterized by thermal hyperalgesia and mechanical allodynia, which are well documented in chronic constriction injury (CCI), a commonly used neuropathic animal model. In neuropathic animal models, glial cells in the CNS, specifically microglia and astrocytes, are reported to modulate neuropathic pain by releasing inflammatory cytokines. The therapeutic effects of current clinical treatment are still inadequate for patients with neuropathic pain. Therefore, research on novel treatments for neuropathic pain remains necessary. In recent years, marine-derived compounds have been identified as potential sources for new drug development. By using an *in vitro* screening system in our laboratory, we observed that a marine-derived peptide, WPL, exhibited antiinflammatory effects. In the present study, we investigated the *in vivo* antiinflammatory effects of WPL in a CCI rat model. Intrathecal (i.t.) administration of WPL produced a significant dose-dependent inhibition of the established thermal hyperalgesia and mechanical allodynia in CCI rats. Moreover, i.t. injection of WPL once daily prevented CCI-induced development of thermal hyperalgesia and mechanical allodynia, and the rats treated with i.t. WPL exhibited normal locomotor function. To characterize the antineuroinflammatory effects of WPL in neuropathic rats, we analyzed the lumbar enlargement of spinal tissue by using a spinal immunohistofluorescence method. I.t. administration of WPL markedly inhibited CCI-induced microglial and astrocyte activation and the upregulation of the proinflammatory mediators in the spinal cord, indicating that antineuroinflammatory effects are involved in the analgesic effects of WPL in peripheral neuropathy. The present study presents a marine-derived peptide that can disrupt glial cell activation and reduce inflammation. WPL may be a potent therapeutic agent for neuroinflammatory diseases, especially neuropathic pain.