Inhibition of spinal neuroinflammation contributes to the analgesic effects of PSZ and WCK compounds in a rat model of peripheral neuropathy

Pei-Jyuan Li (李佩娟)[1], Shi-Ying Huang (黃世英)[2], Han-Chun Hung (洪翰君)[3] , Ping-Jyun Sung (宋秉鈞)[4], Zhi-Hong Wen (溫志宏)[1]

[1]Department of Marine Biotechnology and Resources, National Sun Yat-sen University, Kaohsiung, Taiwan; [2]Center for Neuroscience, National Sun Yat-sen University, Kaohsiung, Taiwan; [3]Doctoral Degree Program in Marine Biotechnology, National Sun Yat-sen University and Academia Sinica, Kaohsiung , Taiwan; [4]Taiwan Coral Research Center, National Museum of Marine Biology and Aquarium, Pingtung, Taiwan

Recently, natural marine compounds have been considered to havepotential for use in the development of novel antiinflammatory drugs. Chronic central nervous system (CNS) neuroinflammation, a sustained inflammatory state within the CNS, can lead to the development of sustained neuropathic pain, characterized by hyperalgesia and allodynia. Current clinical therapies such as the use of opioids and other analgesics are still ineffective in alleviating neuropathic pain. Therefore, a new therapeutic lead compound is necessary for the clinical treatment of neuropathic pain. Through preliminary screening, we previously found that marine-derived compounds, PSZ and WCK, produced *in vitro* antiinflammatory effects. In the present study, to characterize the potential antinociceptive properties of PSZ and WCK, we evaluated PSZ and WCK in a rat model of chronic constriction injury (CCI), a well-established model of neuropathic pain. Our *in vivo* data support the hypothesis that PSZ and WCK serves as an analgesic compound for neuropathy. First, in CCI rats, intrathecal (i.t.) injection of PSZ and WCK significantly inhibited both established thermal hyperalgesia and mechanical allodynia in a dose-dependent manner. Second, i.t. administration of PSZ and WCK once daily significantly attenuated the development of thermal hyperalgesia and mechanical allodynia in CCI rats without obvious behavioral side effects. Third, a spinal immunohistofluorescence assay indicated that i.t. injection of PSZ and WCK significantly inhibited CCI-induced activation of microglia and astrocytes, increased proinflammatory mediators, and upregulated the phosphorylation of p38 in the lumbar spinal cord. Our results suggest that PSZ and WCK can reduce neuropathic pain behaviors by inhibiting spinal neuroinflammatory processes. In summary, we demonstrated that PSZ and WCK, marine-derived compounds, has potential antinociceptive properties for the future treatment of neuropathic pain.