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Efficacy of Lithospermi radix water extracts for the attenuation of oxaliplatin-induced neurotoxicity

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Oxaliplatin can induce peripheral neuropathy (OXIPN) as an adverse side effect in cancer patients. Until now, no effective, preventive or therapeutic drug has been developed; therefore, the dose-limiting factor of OXIPN is still an obstacle in the use of oxaliplatin to treat cancer patients. In our previous pilot study, we tried to find effective materials to relieve oxaliplatin-mediated neurotoxicity using a library of medicinal herb extracts that have been traditionally used. We screened extracts with biological activities to relieve oxaliplatin-mediated neurotoxicity using in vitro cell-based assays which employed the nerve growth factor (NGF)-induced neurite growth from rat pheochromocytoma PC12 cells, and found that the aqueous extract of Lithospermi radix (WLR) could effectively recover the cells from the neurotoxicity of oxaliplatin. The neuroprotective potential of WLR was further confirmed by measuring the changes in nociceptive sensitivities to external mechanical stimuli in neuropathic animals induced by oxaliplatin. Oxaliplatin treatment induced neurotoxicity in NGF-induced differentiated PC12 cells based on the morphological observations which included reduced lengths and branching numbers of neurites. Co-treatment of WLR recovered the differentiated PC12 cells from the neurotoxicity of oxaliplatin. In a chronic OXIPN animal model, administration of oxaliplatin i.p. induced enhanced nociceptive sensitivity to mechanical stimuli along with spinal activation of microglias and astrocytes and loss of intraepidermal nerve fibers in footpads, which is remarkably suppressed by oral administration of WLR. In conclusion, we demonstrated that WLR can attenuate oxaliplatin-induced neurotoxicity in both in vitro and in vivo experimental models. Therefore, WLR could be considered as a good starting material to develop a novel therapeutic agent targeting OXIPN. Image

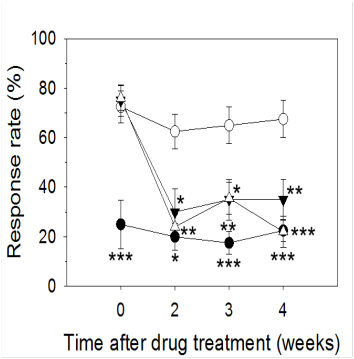

Figure. Progressive time course effect of daily administration of WLR on the nociceptive behavior of animals subjected to oxaliplatin-induced neurotoxicity. The data represent the combined results of the oxaliplatin plus vehicle (0.5% CMC, open circles, n=8), plus WLR (250 mg/kg, closed triangles, n=8), or plus amifostine (100 mg/kg, open triangles, n=10) mice. Only the vehicle (0.9% saline and 0.5% CMC)-treated mice (closed circles, n=8) were also included in parallel as a normal control group. *p<0.05, **p<0.01, ***p<0.001 vs. saline-treated control group.

Biography

Jin-Mu Yi has his expertise in evaluation of anti-cancer and anti-CIPN activity using in vitro and in vivo model.

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