

Astragalus membranaceus and oxaliplatin-induced neuropathy: pain relief and prevention of nervous tissue modifications

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Neurotoxicity is the limiting side effect of the anticancer agent oxaliplatin. A tangled panel of symptoms, sensory loss, paresthesia, dysesthesia, pain may be disabling for patients adversely affecting quality of life. Pharmacological treatments demonstrating a therapeutic effect on oxaliplatin's cumulative neurotoxicity are unsatisfactory and limited to symptomatic effects.

Astragalus membranaceus is an adaptogenic herb from the traditional Chinese medicine. Aimed to study the antineuropathic profile of this plant, a hydroalcoholic extract from selected roots of *A. membranaceus* was obtained and characterized. *A. membranaceus* extract was tested in a rat model of painful oxaliplatin-induced neuropathy (2.4 mgkg⁻¹ intraperitoneally, daily for 21 days). The extract was administered per os (300 mgkg⁻¹) once a day, starting from the first day of oxaliplatin injection until the 20th. On day 21 *A. membranaceus* extract treatment was able to significantly reduce oxaliplatin-dependent pain, when evaluated as an increase on suprathreshold stimulation (hyperalgesia-related measure) or as a decrease in pain threshold (allodynia-related measure). The extract strongly prevented the serious nephro- and hepato-toxicity induced by repeated treatment with the anticancer drug. In the nervous system the hydroalcoholic extract reduced the morphometric alterations induced by oxaliplatin in the dorsal root ganglia, and significantly prevented the changes in the activating transcription factor 3 and in the phosphorylated heavy chain of neurofilament expression levels both in nerves and ganglia. In the dorsal horn of the spinal cord and in pain related cerebral areas *A. membranaceus* extract prevented the oxaliplatin-induced increase of glial density.

The hydroalcoholic extract of *Astragalus membranaceus* relieves pain and promotes the rescue mechanisms that protect nervous tissue from the damages triggering chronic pain. A safe profile strongly suggests the usefulness of this natural product in oxaliplatin-induced neuropathy.

Keywords

Chemotherapy, neuropathic pain, microglia, astrocyte, nervous system.