

Title : Effect of flavonol and its dimethoxy derivatives on paclitaxel-induced peripheral neuropathy in mice

Abstract

Background: Peripheral neuropathy is the dose limiting side effect of many anticancer drugs. Flavonoids exhibit good antinociceptive effect in animal models. Their efficacy against different types of nociception has been documented. The present study investigated the effect of flavonol (3-hydroxy flavone), 3',4'-dimethoxy flavonol, 6,3'-dimethoxy flavonol, 7,2'-dimethoxy flavonol and 7,3'-dimethoxy flavonol against paclitaxel-induced peripheral neuropathy in mice.

Methods: A single dose of paclitaxel (10 mg/kg, i.p.) was administered to induce peripheral neuropathy in mice and the manifestations of peripheral neuropathy such as tactile allodynia, cold allodynia and thermal hyperalgesia were assessed 24 h later by employing Von Frey hair aesthesiometer test, acetone bubble test and hot water tail immersion test, respectively. The test compounds were prepared as a suspension in 0.5% carboxymethyl cellulose and were administered s.c. in various doses (25, 50, 100 and 200 mg/kg). The above behavioral responses were assessed prior to and 30 min after drug treatment. In addition, the effect of test compounds on proinflammatory cytokines like tumor necrosis factor- α (TNF- α), interleukin-1-beta (IL-1 β) and free radicals was investigated by using suitable in vitro assays.

Results: A dose-dependent attenuation of tactile allodynia, cold allodynia and thermal hyperalgesia was evidenced in mice treated with flavonol derivatives. The test compounds inhibited TNF- α , IL-1 β and free radicals in a concentration-dependent manner.

Conclusions: These results revealed that flavonol and its dimethoxy derivatives ameliorated the manifestations of paclitaxel-induced peripheral neuropathy in mice. The inhibition of proinflammatory cytokines and free radicals could contribute to this beneficial effect.

Keywords: cold allodynia; dimethoxy flavonols; flavonol; free radicals; paclitaxel; peripheral neuropathy; tactile allodynia; thermal hyperalgesia; TNF- α

For more details : <https://www.degruyter.com/document/doi/10.1515/jbcpp-2016-0127/html>