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RESEARCH COMMUNICATION

Nerolidol protects the liver against cyclophosphamide-induced hepatic inflammation, apoptosis, and fibrosis via modulation of Nrf2, NF-κB p65, and caspase-3 signaling molecules in Swiss albino mice

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Abstract

Cyclophosphamide (CP)-induced hepatotoxic manifestations are major concern for patients undergoing chemotherapy, which often limit its therapeutic utility. Nerolidol (NER) is a natural bioactive molecule having potent gonadoprotective, neuroprotective, and cardioprotective properties but has not been explored for its hepatoprotective effect and underlying mechanism. Therefore, in the current study hepatoprotective potential of nerolidol was studied in CP-induced hepatic oxidative stress, inflammation, apoptosis, and fibrosis via modulation of Nrf2, NF-κB p65, caspase-3, TGF-β1, and associated biochemical status in Swiss albino mice. NER (200, 400 mg/kg, p.o) and fenofibrate (FF) 80 mg/kg, p.o. were administered from first to fourteenth day and CP was administered at the dose of 200 mg/kg, i.p on seventh day. On fifteenth day, animals were sacrificed and estimation of oxidative stress, inflammation, apoptosis, fibrosis, histopathology (H E and MT staining), and immunohistochemistry was performed in the liver tissue. Administration of NER effectively normalized the elevated level of hepatic injury markers (alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase), marker of oxidative stress that is, malondialdehyde, inflammatory cytokines (TNF-α, IL-6, IL-1β, and IL-10), NF-κB p65, apoptotic marker (cleaved caspase 3) and increased the level of Nrf2 and antioxidant enzymes (superoxide dismutase, CAT, and glutathione). Treatment with NER further reduced the structural damage of hepatocytes and markers of hepatic fibrosis such as TGF-β1, hyaluronic acid, 4-hydroxyproline and collagen-rich stained area, estimated by MT staining. Findings of the current study showed that nerolidol exhibited potent antioxidant, anti-inflammatory, anti-apoptotic, and anti-fibrotic potential and thus acted as hepatoprotective agent. Present study represents novel mechanism of nerolidol against CP-induced hepatotoxicity. However, further studies are needed to use nerolidol as an adjuvant in chemotherapeutically treated patients.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.