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Preclinical Evaluation of Nerolidol Suspension and its Nano Lipid Carrier Against Cyclophosphamide-Induced Organ Toxicity in Swiss Albino Mice

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ABSTRACT

Background and Aim: Cyclophosphamide (CP) is a potent anticancer drug but its therapeutic application is often limited due to significant multi-organ damage. Increased oxidative stress, generation of inflammatory cytokines, and apoptotic proteins are considered as confounding factors in this pathological event. Nerolidol (NER) is a lipophilic bioactive molecule with potent antioxidant and anti-inflammatory properties but possess limitation of low solubility and low bioavailability. Therefore, in the current study, we aimed to mitigate CP-induced multi-organ damage by treating Swiss Albino mice with NER nanoformulation as an adjuvant therapeutic regimen.

Method: *In-silico* study, using Schrödinger software, was used to assess the binding affinity of NER with Nrf2 and NF-kB. In *in-vivo* study, NER 200-400 mg/kg p.o, NER-NLC 200 and fenofibrate 80 mg/kg, p.o were given from 1st day to 14th day. CP 200 mg/kg, i.p., was administered on the 7th day. After 24 h of the last dosing, neurobehavioral tests like spontaneous body alternation, passive avoidance and forced swim tests were performed. On completion of the study, mice were sacrificed, heart, liver, kidney, brain and spleen was removed and used for biochemical estimations, histopathology and immunohistochemical study.

Results: *In-silico* study showed significant binding of NER into the pocket domain of Nrf2 and NF-kB. *In-vivo* study showed protective effect of NER-NLC 200 and NER 400 against CP-induced multi-organ toxicity whereas NER 200 was found to be ineffective against these derailed biomarkers, histological and immunohistochemical attributes.

Conclusion: Findings of the study suggested that NER is a potential therapeutic molecule that can mitigate CP-induced multi-organ damage either at the dose of 400 mg/kg (suspension) or at the dose of 200 mg/kg (nanoformulation) via modulation of Nrf2 and NF-κB pathway.

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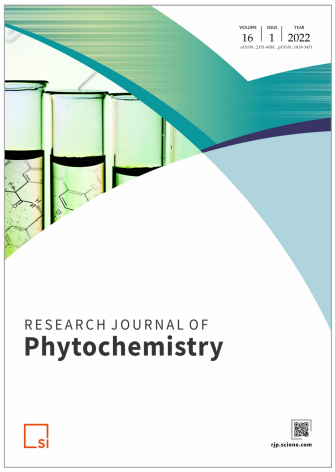

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