Life Sci, 236, 116867 2019 Nov 1

Nerolidol Ameliorates Cyclophosphamide-Induced Oxidative Stress, Neuroinflammation and Cognitive Dysfunction: Plausible Role of Nrf2 and NF- κB

Ashif Iqubal [1], Sumit Sharma [1], Abul Kalam Najmi [1], Mansoor Ali Syed [2], Javed Ali [3], M Mumtaz Alam [4], Syed Ehtaishamul Haque [5]

Affiliations Expand

PMID: 31520598 DOI: 10.1016/j.lfs.2019.116867

Abstract

Aim: Cyclophosphamide (CP) is a potent anticancer and immunosuppressant drug. Studies have shown significant oxidative stress and cognitive impairment but neuroinflammatory and histological aberrations with its administration is underexplored. Nerolidol (NER) is a lipophilic bioactive molecule with antioxidant mmatory properties but it has not been explored for neuroprotective potential in nifestations. Therefore, in the present study, we aimed to evaluate the neuropro potential of NER in CP-induced neuroinflammation and associated comorbid conditions like cognitive dysfunctions.

Materials and method: In-silico study using Schrödinger software was used to assess the binding affinity of NER with Nrf2. In the In vivo study, NER 200 and 400 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 test were performed. On completion of study, mice were sacrificed, hippocampus and cortex were removed for biochemical estimations, histopathology and immunohistochemistry of p65 NF- κB and Nrf2.

Key findings: In-silico study showed significant binding of NER into the pocket domain of Nrf2. In-vivo study showed protective effect of NER against CP-induced neuroinflammation, oxidative stress, cognitive impairment and structural abnormalities in the hippocampus and cortex regions.

Significance: Findings of the study suggested that NER is a potential therapeutic molecule which can mitigate CP-induced neurotoxic manifestations via Nrf2 and NF-κB pathway. However, more detailed studies are needed to explicate the mechanism underlying its neuroprotective effect.

Keywords: Cresyl Violet staining; Hippocampus; Molecular docking; Neurotoxicity; Sesquiterpene.

Supplementation of Lycopene Attenuates Oxidative Stress Induced Neuroinflammation and Cognitive Impairment via Nrf2/NF-κB Transcriptional Pathway

B Zhao et al. Food Chem Toxicol 109 (Pt 1), 505-516. Nov 2017. PMID 28974442.

Oxidative stress, considered as a major culprit in brain aging, triggers cognitive and memory impairment. Lycopene (LYC), a carotenoid pigment, possesses potent antioxida ...

Neuroinflammation and Endoplasmic Reticulum Stress Are Coregulated by cyclo(His-Pro) to Prevent LPS Neurotoxicity

I Bellezza et al. Int J Biochem Cell Biol 51, 159-69. Jun 2014. PMID 24699213.

Many neurological and neurodegenerative diseases are associated with oxidative stress and glial inflammation, all related to endoplasmic reticulum stress. Cyclo(His-Pro) ...

Olea Europaea Leaf Extract Up-Regulates Nrf2/ARE/HO-1 Signaling and Attenuates Cyclophosphamide-Induced Oxidative Stress, Inflammation and Apoptosis in Rat Kidney

HAS ALHaithloul et al. Biomed Pharmacother 111, 676-685. Mar 2019. PMID 30611992.

Olive leaf extract (OLE) has potential health benefits and protects against cytotoxicity in different organs. However, nothing has yet been reported on its potential to p ...

Molecular Mechanisms of Neurotoxicity Induced by Polymyxins and Chemoprevention

C Dai et al. ACS Chem Neurosci 10 (1), 120-131. 2019. PMID 30362702. - *Review*

Neurotoxicity is one major unwanted side-effects associated with polymyxin (i.e., colistin and polymyxin B) therapy. Clinically, colistin neurotoxicity is characterized b ...

Molecular Mechanisms in Cognitive Frailty: Potential Therapeutic Targets for Oxygen-Ozone Treatment

C Scassellati et al. Mech Ageing Dev 186, 111210. Mar 2020. PMID 31982474. - *Review*

In the last decade, cognitive frailty has gained great attention from the scientific community. It is characterized by high inflammation and oxidant state, endocrine and ...

Show more similar articles | See all similar articles

MeSH terms

Animals
Cognitive Dysfunction / chemically induced
Cognitive Dysfunction / metabolism
Cognitive Dysfunction / pathology
Cognitive Dysfunction / prevention & control
Cyclophosphamide / toxicity
Gene Expression Regulation
Hippocampus / drug effects
Hippocampus / metabolism
Immunosuppressive Agents / toxicity
Inflammation / chemically induced
Inflammation / metabolism
Inflammation / pathology
Inflammation / prevention & control
Male
Mice
NF-E2-Related Factor 2 / genetics
NF-E2-Related Factor 2 / metabolism
NF-kappa B / genetics
NF-kappa B / metabolism
Neuroprotective Agents
Neurotoxicity Syndromes / etiology
Neurotoxicity Syndromes / metabolism
Neurotoxicity Syndromes / pathology
Neurotoxicity Syndromes / prevention & control
Oxidative Stress / drug effects
Sesquiterpenes / pharmacology
Signal Transduction

Substances

Immunosuppressive Agents
NF-E2-Related Factor 2
NF-kappa B
Neuroprotective Agents
Nfe2l2 protein, mouse
Sesquiterpenes
Cyclophosphamide
nerolidol

LinkOut - more resources

Full Text Sources
Elsevier Science
Ovid Technologies, Inc.

Miscellaneous
Hazardous Substances Data Bank
NCI CPTAC Assay Portal

Search result 8 of 190 for **[(nerolidol[Text Word]) AND (metabolize[Text Word])] OR [(nerolidol[Text Word]) AND (metabolism[Text Word])]**

Previous result

The impact of sesquiterpenes β-caryophyllene oxide and trans-**nerolidol** on xenobiotic-metabolizing enzymes in mice in vivo.
Lněničková K, et al. Xenobiotica 2018.
In our in vivo study, we followed up the effect of p.o. administration of two sesquiterpenes β-caryophyllene oxide (CAO) and trans-**nerolidol** (NER) on various xenobiotic-metabolizing enzymes in mice liver and small intestine. 2. ...

Next result

Nerolidol and Farnesol Inhibit Some Cytochrome P450 Activities but Did Not Affect Other Xenobiotic-Metabolizing Enzymes in Rat and Human Hepatic Subcellular Fractions.
Špičáková A, et al. Molecules 2017.
The aim of our study was to test and compare the potential inhibitory effect of acyclic sesquiterpenes, trans-**nerolidol**, cis-**nerolidol** and farnesol, on the activities of the main xenobiotic-metabolizing enzymes in rat and human liver in vitro. ...The results indicate that acyclic sesquiterpenes might affect CYP1A, CYP2B and CYP3A mediated **metabolism** of concurrently

administered drugs and other xenobiotics. ...