Phytomedicine. 2019 Feb;53:37-42. doi: 10.1016/j.phymed.2018.09.027. Epub 2018 Sep 4.

Gastroprotective effect of limonene in rats: Influence on oxidative stress, inflammation and gene expression.

de Souza MC[1], Vieira AJ[1], Beserra FP[1], Pellizzon CH[1], Nóbrega RH[1], Rozza AL[2].

Author information

Abstract

BACKGROUND: In an increasing search for natural products that may heal the ulcers and avoid its recurrence, limonene appears as a promising candidate.

HYPOTHESIS/PURPOSE: The present study aimed to investigate the protective effect of limonene in ethanol-induced gastric ulcers, in addition, to investigate the involvement of antioxidant and anti-inflammatory activities, besides the modulation of gene expression.

STUDY DESIGN: Male Wistar rats were orally treated with vehicle (8% tween 80), carbenoxolone (100 mg/kg) or limonene (25, 50 or 100 mg/kg) and then orally received ethanol to induce gastric ulcers formation.

METHODS: The activity of myeloperoxidase (MPO) was measured. Levels of glutathione (GSH) and activities of glutathione peroxidase (GPx), glutathione reductase (GR) and superoxide dismutase (SOD) were measured. We investigated the anti-inflammatory effect of limonene measuring the levels of pro-inflammatory cytokines tumor necrosis factor-a (TNF-a), interleukin-6 (IL-6), interleukin-1β (IL-1β) and anti-inflammatory cytokine interleukin-10 (IL-10) by ELISA. Additionally, we investigate through real-time PCR (qPCR) the gene expression of nuclear factor-kappa B (Nf-κb), Gpx, Il-1β, Mpo, and Il-10.

RESULTS: Our results showed that limonene 50 mg/kg was the lowest effective dose, offering 93% of reduction in gastric ulcer area compared with the vehicle. There was an increase in mucus production and higher preservation of gastric mucosa integrity after treatment with limonene.There was a reduction in the MPO activity, a biomarker of neutrophils infiltration, and an increase in GPx activity, suggesting an antioxidant effect. Limonene displayed anti-inflammatory activity through decreasing the levels of TNF-a, IL-6, and IL-1β and increasing the level of IL-10. Limonene could down-regulate the expression of Nf-κb, Il-1β, and Mpo and up-regulate the expression of Gpx.

CONCLUSION: Our results demonstrate that oral treatment with limonene exerts gastroprotection through local mucosal defense mechanisms, such as increasing the mucus production, modulation of the oxidative stress and inflammatory response and inhibition of Nf-κb expression.

KEYWORDS: Antioxidant; Gastric ulcer; Gene expression; Inflammation; Limonene; qPCR

PMID: 30668410 DOI: 10.1016/j.phymed.2018.09.027