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## The effects of alpha-pinene on inflammatory responses and oxidative stress in the formalin test

Kaveh Rahimi <sup>1</sup>, Mohammad Zalaghi <sup>2</sup>, Elahe Ggazi Shehznizad <sup>2</sup>, Ghazal Salari <sup>2</sup>,  
Fatemeh Baghdezfoli <sup>2</sup>, Akram Ebrahimifar <sup>3</sup>

Affiliations

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### Abstract

Alpha-pinene ( $\alpha$ -pinene), an essential oil that falls under the category of monoterpenes, has various advantages. This research delves into the potential benefits of  $\alpha$ -pinene in alleviating nociception caused by the formalin test and the molecular mechanisms involved. Alpha-pinene (1, 5, or 10 mg/kg/day, i.p.) was administrated for 7 days before the formalin test. Observations of nociceptive behaviors were made during the formalin test. We examined the levels of TNF- $\alpha$  and IL-1 $\beta$ , as well as the expression of COX-1 in the spinal cord. Additionally, we evaluated the levels of TNF- $\alpha$ , IL-1 $\beta$ , SOD, GSH, CAT, and MDA in the skin of the hind paw that received a formalin injection. The peripheral injection of formalin triggered nociceptive behaviors, which was notably diminished by  $\alpha$ -pinene 5 or 10 mg/kg. The biochemical evaluation revealed that  $\alpha$ -pinene significantly moderated the evaluation in TNF- $\alpha$  and IL-1 $\beta$  in the spinal cord induced by formalin injection. Additionally, it was found that  $\alpha$ -pinene had a decreasing effect on the expression of COX-1 protein in the spinal cord. Also,  $\alpha$ -pinene 5 or 10 mg/kg caused a decrease of TNF- $\alpha$ , IL-1 $\beta$ , and MDA and an increase of SOD, GSH, and CAT at the formalin injection site. The study discovered that doses of 5 or 10 mg/ml of  $\alpha$ -pinene can effectively relieve nociceptive response in the formalin test. Alpha-pinene pretreatment reduced the presence of pro-inflammatory cytokines. It also improved the oxidative stress condition by enhancing antioxidant factors and reducing oxidant factors.

**Keywords:** Alpha-pinene; Formalin test; Oxidative stress; Pro-inflammatory cytokines.

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