Original Article

Anti-inflammatory and antinociceptive activity of vanillin

Abstract

Objective: Vanillin is known to have antimutagenic, anti-invasive, and metastatic suppression potential. Antinociceptive property in acetic acid and antioxidant and hepatoprotective properties in carbon tetrachloridetreated rats have also been demonstrated. Objective of this study is to evaluate the anti-inflammatory and antinociceptive activity of vanillin. **Materials and Methods:** The drugs and fine chemicals were purchased from Sigma Aldrich, Ranbaxy, India and MS Pharmaceuticals, India. Experimental Rats were assigned to groups of six animals each and anti-inflammatory activity was evaluated using carrageenan induced rat paw aedema and anti-nocicetion was done using tail flick method. Carrageenan-induced paw edema was used to evaluate pre and post anti-inflammatory activity and tail flick method was used in the evaluation of antinociceptive activity. Two-way analysis of variance (ANOVA) followed by Student's t-test was used for statistical analysis in both the studies. **Results:** There was significant decrease in the paw volume at 50 and 100 mg/kg doses of vanillin when compared with control group. Meanwhile, an increase in percentage maximum possible effect (MPE) was seen by same doses of vanillin. **Conclusion:** It has been concluded from the findings that vanillin possesses the anti-inflammatory and antinociceptive effect by virtue of its antihistaminic and central analgesic activity, respectively.

Key words:
Anti-inflammatory, antinociceptive, paw edema, vanillin

Introduction

Vanillin is a fine, white to slightly yellow crystal, usually needle-like, having a pleasant odor and taste suggestive of vanilla.[1] Vanillin (4-hydroxy-3-methoxybenzaldehyde) is one of the primary chemical components extracted from the seedpods of *Vanilla planifolia*, a monocotyledonous orchid and is widely used in foods, cosmetics, beverages, and drugs. It is believed that the high level of vanillin intake from foods and beverages will have beneficial effects on human health.[2] Previous studies have demonstrated oral anti-inflammatory and antinociceptive properties of vanillin using carrageenan-induced rat paw edema and acetic acid-induced visceral pain models,[3,4] along with its anti-invasive and metastatic suppression potential by inhibiting enzymatic activity of matrix metalloproteinase.[3] Objective of this study is to evaluate the claim of vanillin as anti-inflammatory and antinociceptive agent interperitonially.

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Materials and Methods

Drugs and reagents

Drugs and chemicals

The drugs and fine chemicals were purchased from Sigma Aldrich, Ranbaxy, India and MS Pharmaceuticals, India. All other chemicals and solvents were obtained from local firms and were of highest purity and analytical grade.

Animals

Wister rats (150-200 g) of either sex were procured from Haryana Agriculture University (Hisar, India) and housed in Central Animal House, Punjabi University (Patiala,

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India). They were exposed to 12 h light/dark cycle and given standard laboratory feed and water *ad libitum*, both being withdrawn 12 h before experiment. The experimental protocol involving use of animals for the study was approved by the duly constituted Institutional Animal Ethical Committee in accordance with the guidelines of Committee for the Purpose of Control and Supervision of Experimental Animals (CPCSEA), Ministry of Environments and Forests, Government of India (Reg. No. CPCSEA/107/1999).

Anti-inflammatory activity

The anti-inflammatory activity was performed using carrageenan-induced rat paw edema assay using digital plethysmometer (Labco, India).[5] The rats were divided into groups of six each. Control group was given normal saline in dose not exceeding 5 ml/kg body weight, interperitoneally (i.p.). Test groups were administered vanillin in mixture of normal saline and dimethyl sulphoxide (DMSO) (25, 50 and 100 mg/kg, i.p.) and reference drug (diclofenac, 20 mg/kg, i.p.) in normal saline 30 min before carrageenan challenge. The anti-inflammatory effect of vanillin was demonstrated by the reduction in the paw volume.

Antinociceptive activity

Tail flick method was used to study the antinociceptive activity in albino mice. The mice were divided into groups of six each. Control group was given normal saline in dose not exceeding 5 ml/kg body weight, i.p. Test groups were administered vanillin in a mixture of normal saline and DMSO (25, 50, and 100 mg/kg, i.p.) and reference drug in normal saline (pethidine, 12 mg/kg, i.p.); tail flick latencies were converted to maximum possible effect (MPE), according to the following formula:[6]

MPE (%) = 100 × (post-extract latency – pre-extract latency)/ (cutoff time — pre-extract latency).

Statistical analysis

Results are expressed as mean ± standard error mean (SEM). The statistical significance of the observed data was determined by two-way analysis of variance (ANOVA) and results were reported to be statistically significant at $P < 0.0001$.

Results

Vanillin produced lesser anti-inflammatory effect in lower doses (25 and 50 mg/kg, i.p.) as compared with diclofenac, but at the dose of 100 mg/kg, i.p. it showed considerable response although effect was lower than diclofenac, 20 mg/kg i.p. [Figure 1]. It has also been evident that at higher doses analgesic effect of vanillin exceeds effect of pethidine. The analgesic effect of vanillin in dose of 50 mg/kg, orally (with percentage MPE of 20.98 at third hour), was comparable with pethidine (20.92%) but at higher doses of 200 and 300 mg/kg, orally (36.49 and 40.33%, respectively), was more pronounced than the standard drug [Figure 2].

Discussion

In the present study, we have investigated the anti-inflammatory and antinociceptive activity of vanillin. Inflammation induced by carrageenan was observed to have two phases i.e. early phase (upto 1 h) and late phase (1-3 h). The early phase was associated with significantly severe inflammation where as late phase was observed to have slow increase in volume of paw edema. After 3 h, there is automatic regression of inflammation. The early phase has been attributed to the action of mediators such as histamine, serotonin, and bradykinin on vascular permeability.[7] The late phase edema has been shown to be a result of overproduction of prostaglandins.[8] The result of the anti-inflammatory activity demonstrated by vanillin in higher doses was effective in the early phase of inflammation, which can be hypothesized due to the inhibition of release histamine and serotonin primarily, which are responsible for early phase of inflammation. Based on this an assumption can be made that the vanillin may be showing

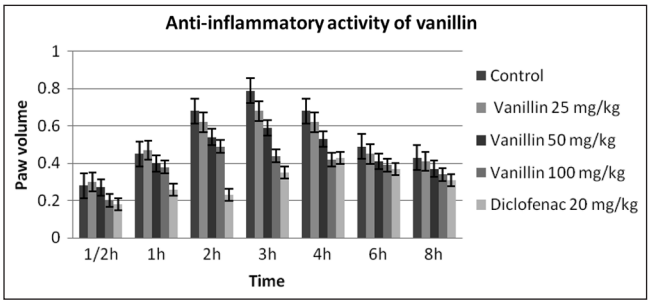

Figure 1: The reduction pedal inflammation in rats by vanillin
Results are expressed as mean ± SEM of six animals in each group. $P < 0.0001$ ($F_1 = 15.98$, $F_2 = 15.63$), $\alpha = 0.05$, and $P \leq 0.0001$ for all treatment versus control (two-way ANOVA). SEM = standard error mean, ANOVA = analysis of variance

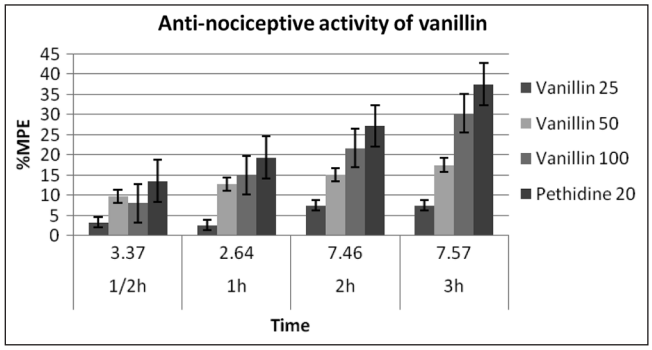

Figure 2: The percentage MPE of the vanillin
Results are expressed as mean ± SEM of six animals in each group. ($F_1 = 16.49$, $P < 0.0001$; $F_2 = 8.960$, $P = 0.0022$). *$P \leq 0.0001$ for all treatment versus control (two-way ANOVA test). SEM = standard error mean, MPE = maximum possible effect, ANOVA = analysis of variance

its effect through inhibition of histamine release. Further the anti-inflammatory activity could also be associated with antioxidant activity of vanillin, as inflammatory activity of carrageenan has been demonstrated to be accompanied by elevation in the free radicals level.[9] Antinociceptive activity confirmed vanillin's central analgesic activity.[7] Recently studies have shown that a large number of vanilloid substances like capsaicin and resiniferatoxin possess analgesic activity as they agonistically desensitize transient receptor potential-vanilloid 1 (TRPV1) channels found in dorsal root and trigeminal ganglia, in dorsal horn of spinal cord and caudal nucleus of spinal trigeminal complex that play a major role in pain.[10-14] It can also be proposed that antinociceptive activity of vanillin is due to its ability to agonistically desensitize TRPV1 channels.

The results thus obtained in the above study strengthen the claim of vanillin as anti-inflammatory and antinociceptive agent.

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