

***Zingiber zerumbet* (LEMPOYANG): A POTENTIAL ANTI-INFLAMMATORY AGENT**

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ABSTRACT

Zingiber zerumbet (L) Sm. or locally known as lempoyang or wild ginger, belongs to Zingiberaceae family which is a widely cultivated plant in village gardens throughout the tropics for its medicinal properties. It's normally used in local traditional medicine to cure swelling and loss of appetite. The juice of the boiled rhizomes has also been used as a medicine for worm and ascaris in children. The volatile oils of rhizomes have been shown to contain zerumbone, humulene and camphene. Zingiberaceae has a rich source of compounds of photometrical interest. They have been reported to have anti-inflammatory, anti-ulceration, antioxidant and anti-microbial effects. Preliminary study of *Zingiber zerumbet* had shown to inhibit carrageen an induce oedema, a commonly used acute inflammatory reaction for screening anti-inflammatory drugs. Thus, a study was designed to evaluate the anti-inflammatory activity of *Zingiber zerumbet* water and ethanol extracts in rats. The rhizomes of *Zingiber zerumbet* were processed and extracted using water and ethanol. The extracts (25, 50 and 100 mg/kg concentration) were screened for anti-inflammatory activity in male Sprague Dawley rats using acute Prostaglandin E₂ paw oedema model. All treatment was injected using intra peritoneal route (i.p). 30 min after the dose, prostaglandin E₂ (PGE₂) at 100 ng/ml concentration was injected in the left hind paw oedema. The paw volume was measured initially and every 1 hour for 4 hours. The percentage anti-inflammatory effect was calculated for comparison. It was observed that only the water extract of *Zingiber zerumbet* showed dose-dependent anti-inflammatory activity. However, at 25 mg/kg concentration, no anti-inflammatory activity was observed in the PGE₂-induced paw oedema in rats. At 50 and 100 mg/kg marked anti-inflammatory activity was 22.6% and 46.8% anti-inflammatory effects respectively, which were significantly different than the controls (p<0.05). This activity was similar to that of nonsteroidal anti-inflammatory drug, mefenamic acid. However, piroxicam, another NSAIDs was shown to exhibit the most potent anti-inflammatory activity in which even at 20 mg/kg concentration the potency is still showing significantly. It can be concluded that the extract of *Zingiber zerumbet* rhizomes able to exert a dose-dependent anti-inflammatory activity in rats. Whereas, the ethanol extract of *Zingiber zerumbet* was devoid of any anti-inflammatory effects at 25 to 100 mg/kg concentrations.

INTRODUCTION

Zingiber zerumbet (L) Sm. or locally known as lempoyang or wild ginger, belongs to Zingiberaceae family which is a widely cultivated plant in village gardens throughout the tropics for its medicinal properties. Although in some areas it can be found growing in secondary forests or at the village edges. Normally used in local traditional medicine as a cure for swelling sores and loss of appetite. The juice of the boiled rhizomes has also been used as a medicine for worm or ascaris in children. The volatile oils of the rhizomes

have been shown to contain zerumbone, humulene and camprene. Zingiberaceae has a rich source of compounds of photometrical interest. Plants from this family have been reported to have anti-inflammatory, anti-ulceration, antioxidant and anti-microbial effects. Preliminary study of *Z. zerumbet* had shown to inhibit carrageen an induce oedema, a commonly used acute inflammatory reaction for screening anti-inflammatory drugs. Thus, the objective of this present study was to evaluate the anti-inflammatory activity of *Z. zerumbet* water and ethanol extracts in rats.

MATERIALS AND METHODS

Preparation of extracts

Z. zerumbet and rhizomes were collected from the University Campus, and were identified by the Department of Botany, Faculty of Agriculture, Universiti Putra Malaysia. 1 kg of rhizomes of *Z. zerumbet* was used for the extraction. The rhizomes were washed with distilled water, chopped into small pieces dried in oven (50°C) for about 1 to 2 days and then powdered. Water and ethanol extracts from the rhizomes of *Z. zerumbet* were prepared with distilled water and 98% ethyl alcohol in Soxhlet apparatus. The extracts were then freeze-dried and stored at -20°C prior to use.

Experimental animals

Male Sprague Dawley rats (180 to 200g) were obtained from Institute of Medical Research, Kuala Lumpur, Malaysia. They were kept in polypropylene cages with wood shavings as bedding at $27 \pm 2.0^\circ\text{C}$ in 12 h light dark cycle. The animals were adapted to laboratory condition for 7 days prior to the experiments. They were given tap water *ad libitum*. The extracts of *Z. zerumbet* were devoid of any mortality or behavioral changes when the rats were given up to 500 mg/kg i.p in rats.

Anti-inflammatory test

Rats were divided into treatment groups of 6 animals. The animals received 25, 50 and 100 mg/kg ethanol or water extracts of *Z. zerumbet*. the control rats received equivalent volume of distilled water. Two groups of rats received 20 mg/kg commercial nonsteroidal anti-inflammatory drugs piroxicam and mefenamic acid from Sigma Chemicals, United Kingdom. All treatment was injected using intra peritoneal route (i.p). 30 min after the dose, prostaglandin E₂ (PGE₂), at 100 ng/ml concentration was injected in the left hind paw to induce oedema. The paw volume was measured initially and every 1 hour for 4 hours. The percentage anti-inflammatory effect was calculated for comparison.

RESULTS

The water extract of *Z. zerumbet* elicited moderate to marked anti-inflammatory activities, which was also dose-dependent (Table 1). At 25 mg/kg concentration of the water extract, no anti-inflammatory property was observed in the PGE₂-induced paw edema in rats. At 50 and 100 mg/kg, marked anti-inflammatory activity was 22.6% and

46.8% anti-inflammatory effects respectively, which were significantly different than the control ($p < 0.05$). The anti-inflammatory activity of piroxicam and mefenamic acid, which are the standard reference drugs, was found to statistically reduce the acute inflammation induced by PGE₂ (Table 1). Generally, for all concentration of water extracts and NSAIDs, the peak effects against PGE₂ were at 0.5 to 1.0 h (Table 1). The ethanol extract of *Z. zerumbet* was devoid of any anti-inflammatory effects at 25 to 100 mg/kg concentrations. There was no significant difference at all time points when compared to controls (Table 2).

Table 1: Effect of *Zingiber zerumbet* water extracts on PGE₂-induced paw edema in rats

Time (h)	Treatment (mg/kg, ip-0.5 h)					
	Normal Extract (0.1 mL)	25 mg/kg Extract	50 mg/kg Extract	100 mg/kg Piroxicam	20 mg/kg Mefenamic	20 mg/kg Acid
0.5	0.60±0.03 ^a	0.61±0.02 ^a (-)	0.56±0.03 ^{ax} (-)	0.32±0.01 ^{bx} (46.7)	0.17±0.03 ^{cx} (71.7)	0.29±0.02 ^{bx} (51.7)
1	0.62±0.03 ^a	0.61±0.03 ^{ab} (-)	0.57±0.02 ^{bx} (8.1)	0.33±0.02 ^{cx} (46.8)	0.19±0.03 ^{dx} (69.4)	0.31±0.03 ^{cx} (50.0)
1.5	0.64±0.05 ^a	0.62±0.03 ^{ab} (-)	0.57±0.03 ^{bx} (10.9)	0.45±0.01 ^{cy} (29.7)	0.20±0.04 ^{dxy} (68.9)	0.33±0.03 ^{exy} (48.4)
2	0.64±0.04 ^a	0.63±0.03 ^a (-)	0.57±0.02 ^{bx} (10.9)	0.40±0.02 ^{cz} (37.5)	0.21±0.03 ^{dxy} (67.2)	0.33±0.04 ^{exy} (48.4)
2.5	0.62±0.03 ^a	0.63±0.02 ^a (-)	0.48±0.04 ^{by} (22.6)	0.41±0.03 ^{cyz} (33.9)	0.21±0.04 ^{dxy} (66.1)	0.35±0.02 ^{ey} (43.5)
3	0.62±0.02 ^a	0.62±0.04 ^a (-)	0.50±0.03 ^{by} (19.4)	0.43±0.02 ^{cyz} (30.6)	0.25±0.03 ^{dzy} (59.7)	0.41±0.03 ^{cz} (33.9)
3.5	0.61±0.04 ^a	0.62±0.03 ^a (-)	0.53±0.02 ^{bx} (13.0)	0.45±0.03 ^{cy} (26.2)	0.29±0.02 ^{dz} (52.5)	0.40±0.02 ^{cz} (34.4)
4	0.60±0.03 ^a	0.61±0.03 ^a (-)	0.51±0.02 ^{bx} (15.0)	0.42±0.03 ^{cyz} (30.0)	0.28±0.03 ^{dz} (53.3)	0.42±0.03 ^{cz} (30.0)

Values are mean ± SD of 6 animals. Figures in parentheses indicate % anti-inflammatory effect. ^{a-e}Means with different superscript differ significantly ($p < 0.05$) in the same row. ^{x-z}Means with different superscript differ significantly ($p < 0.05$) in the same column.

DISCUSSION

Anti-inflammatory effects were observed against an acute (PGE₂-induced paw edema) model of inflammation when rats were pre-treated with 50 and 100 mg/kg water extracts of *Z. zerumbet*. The extracts were devoid of any toxicity up to 500 mg/kg in rats. The anti-inflammatory effect of water extract of *Z. zerumbet* was similar to the reference NSAID mefenamic acid where the percentage anti-inflammatory effects were 46.8% and 51.7% respectively. Another NSAIDs, piroxicam showed the highest anti-inflammatory effect of 72.6%. The anti-inflammatory activity of extracts appears to be significant in early phases of the inflammatory process (Table 1), similar to the reference NSAIDs. The rhizomes of *Zingiber officinale* (ginger) have been shown to contain potent inhibitors

against prostaglandin biosynthesizing enzyme (PG synthetase) and arachidonate 5-lipoxygenase, an enzyme of leukotriene (LT) biosynthesis. Gingerols and diarylheptanoids were identified as the active compounds. The anti-inflammatory effect of the methanol extract obtained from the rhizomes of *Zingiber cacuminal Roxb.* had also been published previously. Not surprisingly, in this current investigation, the rhizomes of *Zingiber zerumbet* also contain potent inhibitor of acute inflammation.

Table 2: Effect of *Zingiber zerumbet* ethanol extracts on PGE₂-induced paw edema in rats

Time (h)	Treatment (mg/kg, ip-0.5 h)					
	Normal Extract (0.1 mL)	25 mg/kg Extract	50 mg/kg Extract	100 mg/kg Piroxicam ¹	20 mg/kg Mefenamic	20 mg/kg Acid ¹
0.5	0.62±0.07 ^a	0.63±0.02 ^a (-)	0.66±0.02 ^a (-)	0.63±0.03 ^a (-)	0.17±0.03 ^{bx} (72.6)	0.29±0.02 ^{cx} (53.2)
1	0.64±0.04 ^a	0.64±0.06 ^a (-)	0.67±0.06 ^a (-)	0.63±0.07 ^a (-)	0.19±0.03 ^{bx} (70.3)	0.31±0.03 ^{cxy} (50.6)
1.5	0.65±0.03 ^a	0.63±0.04 ^a (-)	0.66±0.07 ^a (-)	0.65±0.05 ^a (-)	0.20±0.04 ^{bxy} (69.2)	0.33±0.03 ^{cxy} (49.2)
2	0.67±0.04 ^a	0.64±0.02 ^a (-)	0.67±0.03 ^a (-)	0.64±0.03 ^a (-)	0.21±0.03 ^{bxy} (68.6)	0.33±0.04 ^{cxy} (50.7)
2.5	0.66±0.09 ^a	0.63±0.04 ^a (-)	0.65±0.04 ^a (-)	0.64±0.03 ^a (-)	0.21±0.04 ^{bxy} (68.2)	0.35±0.02 ^{cy} (47.0)
3	0.63±0.05 ^a	0.61±0.05 ^a (-)	0.65±0.03 ^a (-)	0.64±0.02 ^a (-)	0.25±0.03 ^{byz} (60.3)	0.41±0.03 ^{sz} (34.9)
3.5	0.64±0.04 ^a	0.62±0.02 ^a (-)	0.63±0.02 ^a (-)	0.63±0.03 ^a (-)	0.29±0.02 ^{bz} (54.7)	0.40±0.02 ^{sz} (37.5)
4	0.63±0.06 ^a	0.63±0.04 ^a (-)	0.61±0.02 ^a (-)	0.62±0.03 ^a (-)	0.28±0.03 ^{bz} (55.6)	0.42±0.03 ^{sz} (33.3)

Values are mean ± SD of 6 animals. Figures in parentheses indicate % anti-inflammatory effect. ^{a-c}Means with different superscript differ significantly (p<0.05) in the same row. ^{x-z}Means with different superscript differ significantly (p<0.05) in the same column.

¹Data for the NSAIDs are from Table 1

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