Antiinflammatory and antinociceptive activities of *Zingiber officinale* Roscoe essential oil in experimental animal models

Ginger, *Zingiber officinale* Roscoe (Zingiberaceae), in folk medicine has been used against pain, inflammation, arthritis, urinary infections, and gastrointestinal disorders.[1] The oil of ginger is a mixture of constituents, consisting of monoterpenes (phellandrene, camphene, cineole, citral, and borneol) and sesquiterpenes (zingiberene, zingiberol, zingiberenol, ß-bisabolene, sesquiphellandrene, and others). Aldehydes and alcohols are also present.[1,2]

Gingerol and its analogs found in rhizome extracts are responsible for many pharmacological activities.[1] Few works have reported the properties of ginger essential oil (GEO). However, several types of terpene compounds are known to present antiinflammatory and antinociceptive activities.[1,2]

The aim of the present study was to evaluate the antiinflammatory and analgesic effects of GEO administered orally in rodents. Groups of 10 male Swiss mice (25–30 g) and male Wistar rats (190–230 g) were used for evaluation of the antinociceptive and antiinflammatory effects, respectively. All animals were housed in groups of five and maintained in standardized conditions (12/12 h light/dark cycle, 25°C) with free access to water and food. The protocol for these experiments was approved and was in accordance with the guidelines of the Brazilian Committee of Animal Experimentation.

Fresh rhizomes of *Z. officinale* were collected from the herbarium of the State University of Maringá, identified, and authenticated. GEO was obtained from 250 g of rhizomes by conventional steam distillation using Clevenger apparatus during 3 h. The oil obtained was kept refrigerated and protected form direct light.

Pleurisy was induced in anesthetized mice by intraperitoneal (i.p.) injection of carrageenan (200 μg/cavity). Four hours later, the rats were sacrificed and the exudate was collected to determine the total volume and leukocyte number. Exudates smears were prepared, air-dried, and fixed with Rosenfeld stain for leukocyte differential count. The parameters studied were leukocyte migration and fluid leakage. GEO (100, 200, and 500 mg/kg, p.o.) and indomethacin (5 mg/kg, p.o.) were administered 30 min before the test.

The antinociceptive activity of the GEO was assessed using the writhing test. Acetic acid solution (10 ml/kg, 0.6%) was i.p. injected and abdominal muscles constriction together with stretching of the hind limbs was counted over a period of 20 min, starting immediately after acetic acid injection. GEO (50, 100, and 200 mg/kg, p.o.) and indomethacin (5 mg/kg, p.o.) were administered 30 min before the acid injection. Antinociceptive activity was expressed as the percentage of inhibition of writhings compared with control animals.

The hot-plate test was performed to measure response latencies. The hot plate was maintained at 55.0 ± 1°C. The time taken (s) to cause a discomfort reaction (licking paws or jumping) was recorded as the response latency 0, 15, 30, 60, and 90 min after administration of GEO (100 and 200 mg/kg, p.o.), meperidine (50 mg/kg, i.p.) or saline solution 0.9% (control group). A latency period of 25 s was defined as complete analgesia and the experiment was stopped if it exceeded the latency period in order to avoid injury.

Data are reported as mean ± SEM. Statistical differences in all groups were determined using one-way ANOVA. P values <0.05 were considered significant.

In the pleurisy test, indomethacin and GEO 200 and 500 mg/kg reduced significantly the exudate volume ($P<0.05$ and $P<0.001$) without promoting alteration of total leukocyte migration. [Table 1] Data suggest that GEO does not have influence on cells' recruitment, different to that observed for others essential oils.[3] The antiinflammatory activities of compounds obtained from GEO have been reported by other investigations using ginger extract.[1] These antiinflammatory actions could be owing to the inhibition of prostaglandin release, and hence ginger may act in a way similar to other nonsteroidal antiinflammatory drugs which interfere with prostaglandin biosynthesis. Gingerol has been reported to have antiinflammatory actions, which include suppression

Table 1

Exudate volume and leukocyte number count 4 h after carrageenan injection (200 mg into the pleural cavity) in treated (GEO or indomethacin) and nontreated rats

Groups	*Exudate volume (ml)*	*Leukocyte count (cells/mm³) x 10³*	*Cells x 10⁶*	
			MN	*PMN*
Control	1.05±0.07	68250±3056	15±2	49±5
Indomethacin (5 mg/kg)	0.52±0.02*	63180±4207	14±1	49±4
GEO (100 mg/kg)	0.88±0.05	56100±2905	15±1	41±2
GEO (200 mg/kg)	0.80±0.06**	60380±3884	15±2	45±4
GEO (500 mg/kg)	0.69±0.06*	62080±3469	13±2	49±4

Values are mean ± SEM. *n* = number of animals in each group (10). MN, mononuclear leukocytes; PMN, polymorphonuclear leukocyte. * $P<0.001$ compared with control values. ** $P<0.05$ compared with control values.

Table 2

Effects of GEO (*Z. officinale*) on acetic acid-induced writhing

Group	*No. of writhings*	*Percentage inhibition (%)*
Control	70.4±3.2	–
Indomethacin (5 mg/kg)	44.4±1.2**	36.9
GEO (50 mg/kg)	54.1±2.9*	23.2
GEO (100 mg/kg)	54.9±3.6*	22.0
GEO (200 mg/kg)	35.5±5.4**	49.6

Values are mean ± SEM. *n* = number of animals in each group (10). **P* <0.05 compared with control values.***P*<0.001 compared with control values.

of both cyclooxygenase and lipooxygenase metabolites of arachidonic acid.[4] Furthermore, constituents of essential oils obtained from many other plants have been proposed to have antiinflammatory activity.[1]

Essential oils' constituents such as (-)-linalool antagonize different pain responses elicited by exposure to a chemical stimulus such as acetic-induced, by a thermal stimulus or by a tissue injury produced by formalin injection.[5] Suekawa *et al*.[2] showed analgesic and antipyretic properties from ginger extracts in a range of laboratory animals. In the present experiments, GEO (50, 100, and 200 mg/kg, p.o.) and indomethacin significantly suppressed the acetic acid-induced writhing response in a dose-dependent manner (Table 2). Maximum inhibition of GEO was observed at the dose of 200 mg/kg.

In the hot-plate test, the time course of the antinociceptive reaction produced by saline or GEO (100 and 200 mg/kg) administration did not result in significant prolongation of the response latency as observed for meperidine group animals (data not shown).

GEO was found to contain monoterpenes and sesquiterpenes as principal compounds,[1,2], suggesting that the antiinflammatory and analgesic effects could be correlated to these essential oil constituents. Further studies are needed to reveal the mechanisms of action for these activities of GEO.

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