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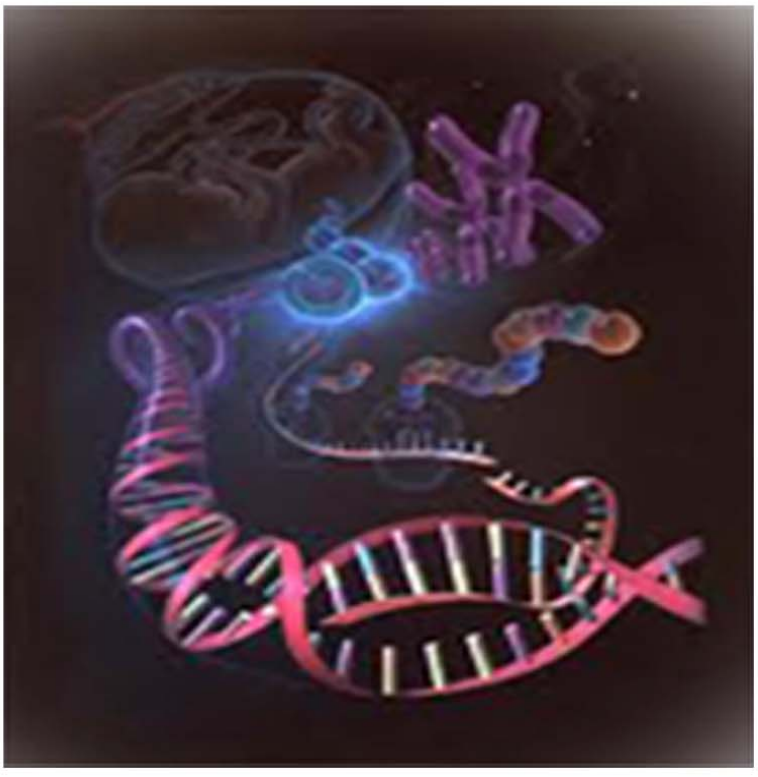

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Research Paper

EVALUATION OF THE ANTI-INFLAMMATORY EFFECT OF *ZINGIBER OFFICINALE* (GINGER) ROOT IN RATS

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Aims and objectives: The purpose of this study was to evaluate and compare the anti-inflammatory activity of extract of *Zingiber officinale* (ginger) in experimental acute inflammatory animal model. Materials and Methods: In this study, the anti-inflammatory activity of *Zingiber officinale* alone and in combination with indomethacin was studied using carrageenan-induced rat paw oedema. Aqueous extract of *Zingiber officinale* (200 mg/kg or 400 mg/kg) was administered alone and in combination with indomethacin (25 mg/kg) to separate group of rats and paw volume was measured by a plethysmometer and compared with the control group. Results: Indomethacin, ginger 200 mg/kg and ginger 400 mg/kg displayed values of 95%, 89.5% and 92.6% inhibition of paw oedema respectively. The combinations of indomethacin with ginger 200 mg/kg and indomethacin with ginger 400 mg/kg displayed values of 95% and 97.5% inhibition of paw oedema respectively. These results indicate a similarity in the anti-inflammatory profile of ginger and indomethacin, and furthermore an enhanced anti-inflammatory profile when both are combined. Conclusion: As ginger root showed significant anti-inflammatory activity in the model studied, it can be investigated further as a promising anti-inflammatory agent.

Keywords: *Zingiber officinale,* Anti-inflammatory, Carrageenan, Indomethacin, Ginger

INTRODUCTION

Inflammation, despite having undergone years of intense study, continues to evoke great interest in the field of research, mainly due to the need of more potent anti-inflammatory agents with fewer side effects. The drugs used most as anti-inflammatory agents, Nonsteroidal Anti-inflammatory Drugs (NSAIDs), are also amongst the most commonly prescribed drugs world over. They account for a massive market share in the pharmaceutical industry. They are prescribed for a variety of acute, subacute and chronic inflammatory conditions and diseases. The duration of use of NSAIDs ranges from days to years depending on the condition and is frequently limited by a spectrum of gastro-intestinal side effects ranging from dyspepsia to life threatening bleeding from ulceration (Bhupinder Singh *et al.,*

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2009 and Perez *et al.,* 1997). In spite of the awareness of these unpleasant side effects they are still the contents of a bracket of popularly prescribed drugs. Their popularity is largely due to the symptomatic relief and decreased morbidity that patients experience when suffering from various inflammatory disorders. They are also among the most commonly self medicated and abused drugs ((Bhupinder Singh *et al.,* 2009).

Zingiber officinale (ginger) which belongs to the family Zingiberaceae, is a slender perennial plant that reaches the height of two feet and has greenish yellow flowers resembling orchids. The dried rhizome of ginger contains approximately 1-4% of volatile oils which are the medicinally active constituents and are also responsible for the characteristic odor and taste (Khushtar *et al.,* 2009). Phytochemical studies showed that the plant is rich in a large number of substances, including a-zingiberene, b-bisabolene, gingerols and shogaols (Khushtar *et al.,* 2009). These compounds have been reported to display anti-inflammatory (Zahra Fatehi-Hassanabad *et al.,* 2005) and anti-ulcerogenic (Chioma A Anosike *et al.,* 2009) activity. Other pharmacological actions of ginger and compounds isolated from it include antioxidant (Ojewole, 2006), hypoglycemic (Ojewole, 2006), analgesic (Ojewole, 2006), antiplatelet (Nurtijahja *et al.,* 2003), antiemetic (Sharma *et al.,* 1997), antithrombotic (Sharma *et al.,* 1997), anti-tumorigenic (Shukla and Singh, 2007), radioprotective (Jagetia, 2004), and antimicrobial (Ficker *et al.,* 2003b) actions.

Considering the vast variety of actions and the fact that ginger, like NSAIDs, reduces inflammation but has the advantage of being gastro protective; this study has been designed to evaluate the anti-inflammatory potential of *Zingiber officinale* powder in albino rats.

MATERIALS AND METHODS

Preparation of Extract

Ginger root extract in the form of a powder, was obtained from Vidya Herbs, Bangalore. It was weighed accordingly and administered in aqueous solution.

Chemicals

Indomethacin (Sun Pharmaceuticals) and Carrageenan (HiMedia) were of analytical grade.

Animals

Albino rats weighing 150-250 g of either sex were used for the study. The animals were housed in an air conditioned environment with natural light and dark cycles for a week following selection to enable acclimatization. They were provided a diet consisting of normal rat pellet food and water *ad libitum*. The experimental protocol was approved by the Institutional Animal Ethics Committee, Navodaya Medical College, Raichur.

Animals were randomly divided into 6 groups of 6 rats each;

Group I: Control rats – receive vehicle (distilled water) only

Group II: Standard rats – receive Indomethacin 25 mg/kg

Group III: Test rats – receive *Z. officinale* 200 mg/kg

Group IV: Test rats – receive *Z. officinale* 400 mg/kg

Group V: Test rats – receives Indomethacin 25 mg/kg + *Z. officinale* 200 mg/kg

Group VI: Test rats – receives Indomethacin 25 mg/kg + *Z. officinale* 400 mg/kg

All the drugs were administered an hour prior to experimentation. Following model was used to screen the anti-inflammatory activity of ginger.

Carrageenan-Induced Oedema in Rat Hind Paw (Winter *et al.*, 1962)

This method is based on the plethysmometeric measurement of oedema produced by sub plantar injection of carrageenan into the hind paw of albino rats. Acute inflammation was produced by sub plantar injection of 0.1 ml of freshly prepared 1% suspension of carrageenan in normal saline in the right hind paw of the rats and paw volume was measured plethysmometrically hourly till the fourth hour after carrageenan injection. Percentage inhibition (protection) against oedema formation was taken as an index of acute anti-inflammatory activity.

It was calculated as follows

Percentage Inhibition = $(V_c - V_t / V_c) \times 100$

where, V_c = Volume of paw oedema in control animals. V_t = Volume of paw oedema in treated animals.

STATISTICAL ANALYSIS

Results were expressed as mean ± standard deviation (SD). Statistical analysis was performed using one-way analysis of variance (ANOVA) followed by Dunnett's t-test for post-hoc analysis. $P < 0.05$ was considered statistically significant and $P < 0.001$ as highly significant. All the statistical methods were carried out through the SPSS software (version 16).

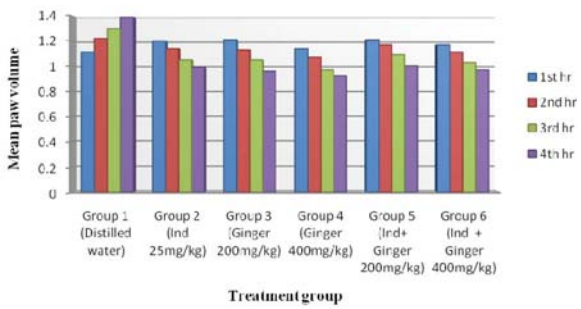
RESULTS

Carrageenan-induced Rat Paw Oedema

In the results obtained, it is clear that none of either the standard or test groups showed any significant decrease in mean paw volume at 1 h of the treatment.

However at the 2nd hour of treatment, group 4 (ginger 400 mg/kg) and group 6 (indomethacin and ginger 400 mg/kg) showed significant decrease in mean paw volume. Amongst these two, the group treated with ginger alone was found to be better than that treated with the combination of indomethacin and ginger. At the 3rd hour, all the five groups showed highly significant decrease in mean paw volume and finally, at the 4th hour of treatment, the decrease in mean paw volume in all five groups was highly significant. The inhibition of inflammation was best in group treated with combination of indomethacin and ginger 400 mg/kg (Figure 1).

Figure 1: Effect of *Zingiber officinale* (ginger) and Indomethacin Alone and in Combination at Various Time Intervals of Carrageenan-induced Paw Oedema in Rats

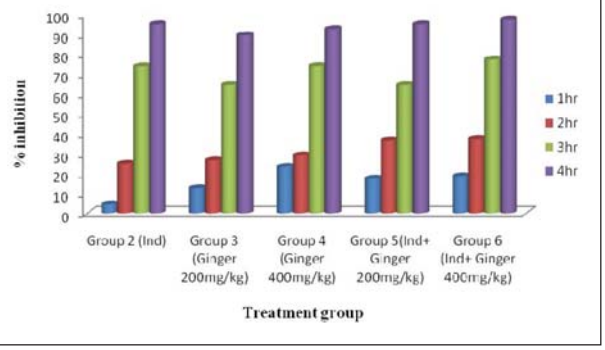


Indomethacin, ginger 200 mg/kg and ginger 400 mg/kg displayed values of 95%, 89.5% and 92.6% inhibition of paw oedema at the 4th h, respectively. The combinations of indomethacin with ginger 200 mg/kg and indomethacin with ginger 400 mg/kg displayed values of 95% and 97.5% inhibition of paw oedema at the 4th h, respectively (Table 1 and Figure 2).

Table 1: Percentage Inhibition of Oedema Produced by Zingiber Officinale (Ginger) and Indomethacin Alone and in Combination at Various Time Intervals of Carrageenan-induced Rat Paw Oedema

Treatment Groups (Dose in body weight)	% inhibition of paw oedema			
	1 h	2 h	3 h	4 h
Group 2(Indomethacin 25mg/kg)	4.5	25	74	95
Group 3(Ginger 200mg/kg)	12.7	26.66	64.5	89.5
Group 4(Ginger 400mg/kg)	23.4	29.1	74.1	92.6
Group 5(Indomethacin 25mg/kg + Ginger 200mg/kg)	17.39	36.66	64.5	95
Group 6(Indomethacin 25mg/kg + Ginger 400mg/kg)	8.6	37.4	77.4	97.5

Figure 2: Percentage Inhibition of Oedema Produced by *Zingiber officinale* (Ginger) and Indomethacin Alone and in Combination at Various Time Intervals of Carrageenan-induced Rat Paw Oedema



DISCUSSION

In the study, the results showed that the ginger root extract possessed significant anti-inflammatory activity when administered alone but when administered in combination with indomethacin it only marginally enhanced the efficacy for reducing paw oedema induced by carrageenan.

Inhibition of carrageenan-induced inflammation in rats has gained popularity as a test procedure to screen anti-inflammatory agents. The development of carrageenan-induced oedema is bi-phasic (Winter *et al.,* 1962 and Gupta, 2009), the first phase (1-3 h after administration) is attributed to the release of histamine, serotonin and kinins, while, the second phase (3-5 h after administration) is related to the release of prostaglandins (Winter *et al.,* 1962, Larsen and Henson, 1963, Brooks and Day, 1991). Ginger root extract, in the present study, was found to be able to inhibit carrageenan-induced rat paw oedema in both phases. These results suggest that ginger extract could inhibit rat paw oedema through the inhibition of prostaglandin production and also by acting either as an inhibitor of mast cell degranulation or as a serotonin antagonist.

Current evidence suggests that a subfraction containing the structurally related compounds like gingerols, shogaols, and paradols accounts for a major portion of ginger's anti-inflammatory properties. These compounds share an aromatic ketone moiety but differ in the length of their alkyl side chain and the substitution pattern on the side chain. Structure-activity relationship analysis suggests that the presence of the phenolic hydroxy group adjacent to the methoxy group is critical for the inhibition of PG synthesis (Tjendraputra *et al.,* 2001; Kiuchi *et al.,*1992).

A study showed that gingerols are somewhat

more potent inhibitors of COX-1 than COX-2, thus identifying them as non-selective COX inhibitors. This was a surprising finding since non-selective NSAIDs are known for their gastrointestinal and renal side effects (Sertie, 1992). In fact, ginger extracts have anti-ulcer activity and are recommended for the treatment of gastrointestinal problems (Sertie, 1992; Yoshikawa *et al.,* 1994; Yamahara *et al.,* 1988). The lack of ginger's gastrointestinal side effects suggested the presence of a yet unidentified pharmacological activity responsible for the protective effects against the toxicity associated with COX-1 inhibition. An important advance in the characterization of the anti-inflammatory properties of ginger was the discovery that some of its constituents not only inhibit PG synthesis but also leukotriene (LT) synthesis (dual inhibitors of COX and 5-LOX). LTs are derived from arachidonic acid through the action of the enzyme 5-LOX. LTs are potent mediators of the inflammatory process and are suspected of playing a key role in the development of gastrointestinal ulcers associated with long-term use of NSAIDs (Hudson *et al.,* 1993; Asako *etal.,* 1992). Moreover it has been shown that ginger inhibits the induction of several genes involved in the inflammatory response that include genes encoding cytokines, chemokines and the inducible enzyme nitric oxide synthase (iNOS) and COX-II (Grzanna *et al.,* 2005; Pan *et al.,* 2005). A possible mechanism involving the antagonism of serotonin receptors has been suggested (Penna *etal.,* 2003).

CONCLUSION

From the present study it is concluded that *Zingiber officinale* possesses significant anti-inflammatory and activity comparable to that of the standard drug indomethacin in the model of carrageenan-induced rat paw oedema, and on co-administration marginally improved the anti-inflammatory profile of indomethacin.

The anti-inflammatory action of *Zingiber officinale* could be speculated to be due to a combination of inhibitory effects on inflammatory mediators such as serotonin, kinins, eicosanoids and other cytokines involved in the process of inflammation.

A significant anti-inflammatory effect of ginger root extract along with gastro-protective effects could warrant the co-administration of it along with NSAIDs. This combined with the various other health benefits offered, could limit the use of NSAIDs and offer exciting new avenues to explore in the treatment of various chronic inflammatory disorders.

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