Original Article

Anti-inflammatory activity of root of *Alpinia galanga* Willd

Abstract

Objective: The objective of the study is to evaluate the acute and chronic anti-inflammatory activities of root extract of *Alpinia galanga* in rodents. **Materials and Methods:** The study was carried out using albino rats of either sex (150-200 g). An extract of the root of *A. galanga* was prepared using absolute alcohol and distillation in a Soxhlet apparatus. The acute anti-inflammatory effects of this extract were evaluated using carrageenan-, bradykinin-, and 5-HT-induced rat paw edema. The chronic anti-inflammatory effects were evaluated using formaldehyde-induced rat paw edema. **Results and Analysis:** Inhibition of inflammation was seen to be 32.22% in carrageenan-induced, 37.70% in 5-HT-induced, and 35.21% in bradykinin-induced anti-inflammatory models. In chronic inflammatory model, a progressive inhibition of 34.73% (3rd day), 37.50% (5th day), 38.83% (7th day), 44.66% (9th day), 49.59% (11th day), and 55.75% (13th day) was observed with study compound. The efficacy was comparable with the standard drugs. **Conclusion:** It can be thus concluded that *A. galanga* has anti-inflammatory properties and probably acts by blocking histaminic and serotonin pathways. It may be an effective alternative to NASAIDs and corticosteroid in inflammatory disorders.

Key words:
A. galanga, anti-inflammatory activities, rodents

Introduction

Inflammation is part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells, or irritants. Inflammation is a protective attempt by the organism to remove the injurious stimuli and to initiate the healing process. Inflammation is not a synonym for infection, even in cases where inflammation is caused by infection. Although infection is caused by a microorganism, inflammation is one of the responses of the organism to the pathogen. Without inflammation, wounds and infections would never heal. Similarly, progressive destruction of the tissue would compromise the survival of the organism. However, chronic inflammation can also lead to a host of diseases, such as hay fever, atherosclerosis, rheumatoid arthritis, and even cancer. It is for that reason that inflammation is normally closely regulated by the body.

Drugs that are currently used for the management of inflammatory conditions are non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids. All these drugs carry potential toxic effects, of which gastrointestinal side effects are the commonest.

Plant and plant products have been thus used as a source of indigenous drug for multiple indications for a long time in order to offset the toxicities of conventional drugs. *Alpinia galanga* Willd (Family - Zingiberaceae) is used in medication, culinary, and cosmetics for centuries.[1,2] It is widely used as a spice in food as well as in traditional system of medicine, such as Ayurveda, Unani, and Chinese and Thai folk medicine.[3] It is commonly known as Rasna in Sanskrit, Kulanjan in Hindi, and Galangal in English. The plant is a perennial herb found commonly throughout the Western Ghats, Mysore, Goa, and Gujarat. It is also found in other countries like Thailand, Indonesia, China, and Malaysia.

It is commonly known as "greater galanga" and reported

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to be used as carminative, antipyretic, anti-inflammatory, and in the treatment of bronchitis, heart diseases, chronic enteritis, diabetes, rheumatism, etc.[4]

Studies have shown the plant to possess anti-inflammatory, analgesic, antioxidant, antifungal, antibiotic, antibacterial, antiulcer, and anticancer properties.[5-7] The anti-inflammatory and analgesic effects of *A. galanga* has been studied in a variety of rheumatologic conditions.[8,9] Study of phytochemical constituents have shown that the rhizome contains 1' S'-1' acetoxychavicol acetate, 1' S-1'-hydroxychavicol acetate, trans-p-hydroxycinnamaldehyde, and trans-p-coumaryl alcohol.[10,11] The active principle 1' S'-1' acetoxychavicol acetate has been reported to possess various activities like anti-inflammatory, antioxidative, antimicrobial, and antioxidative activities.[12] The rhizome also contains flavonoids which are responsible for anti-inflammatory effects of this indigenous plant. The flavonoids which have been isolated from galangal roots are galangin, alpinin, and kaempferide.[13] Galangin (3,5,7-trihydroxyflavone) is a flavonoid with other properties like antimicrobial and anticancer activities.[14]

Materials and Methods

Animals

Albino rats of either sex weighing between 150 and 200 g were procured from animal house of WBUAFS. They were kept in clean polysulfone rat cages and maintained at 12-hour light/dark cycle. The temperature was maintained at 22°C to 26°C, while the relative humidity was 50 to 60%. Rats were fed on standard diet and provided with filtered autoclaved *ad libitum* drinking water.

The rats were divided into four sets (n=24). Sets A, B, and C were used for evaluating anti-inflammatory activity after inducing acute inflammation with carrageenan, bradykinin, and 5-HT, respectively. Set D was used for evaluating anti-inflammatory activity after inducing chronic inflation with formaldehyde.

Each set was again subdivided into four groups (n=6). In all sets, GR 1 served as control and received gum acacia only, GR II received root extract of *A. galanga* at the dose of 50 mg/kg, GR III received phenylbutazone 50 mg/kg, and GR IV received dexamethazone 0.5 mg/kg.

The study protocol was approved by the Institutional Animal Ethics Committee of WBUAFS. The experiment was carried out in the Department of Pharmacology, Medical College Kolkata in collaboration with West Bengal University of Animal Fishery sciences, Mohanpur Campus.

Plant extract

Root of *A. galanga* was obtained from Chemical Research and extraction Supply Unit of central chemical reagent and supply (CCRAS). It was shade dried at room temperature and was subjected to size reduction to get coarse powder. The powdered material was subjected to extraction twice using solvent absolute alcohol. The filtrate was pooled and solvent was recovered by distillation in a Soxhlet apparatus. The resultant extract was then evaporated to dryness using a rotary evaporator and lyophilized. The residual gummy material obtained was suspended in 5% gum acacia and used for oral administration to the experimental animals at a dose of 50 mg/kg of body weight. Before selecting the dose of *A. galanga,* LD_{50} and ED_{50} was determined.

Drugs and chemicals

Carrageenan (Sigma), 5HT (Roche Pharmaceuticals), bradykinin (BRA 640, San Doz), formaldehyde, phenylbutazone (SG Pharmaceutical), dexamethazone (MSD), and gum acacia were used for the experiment.

Procedure

As the indigenous drug is insoluble in water, it was suspended in 5% gum acacia solution. Rats were divided into four groups (n=6). They were kept fasting overnight prior to the experiment. The drugs were given orally with the help of feeding cannula fitted with 2 ml glass syringe keeping volume of the medicine constant (1 ml), 1 hour prior to injection of the phlogistic agent for inducing acute inflammation.

GR I served as control (receiving gum acacia only)
GR II received root extract of *A. galanga* 50 mg/kg
GR III received phenylbutazone 50 mg/ kg
GR IV received dexamethazone 0.5 mg/kg

The average volume of hind paw of all the rats was measured with the help of a Plethysmometer by the method *Buttle et al.*[15] after some modification and considered before inducing acute inflammation with the phlogistic agent.

Paw edema induced to produce acute inflammation

Carrageenan-, 5-HT-, and bradykinin-induced edema was adopted as introduced by *Winter, Risley, and Nuss 1962* with slight modification by Ghosh and Singh.[16] Carrageenan 1% in 0.9 % w/v sodium chloride was taken and 0.1 ml of this solution was injected in subplanter region of hind paw of all the rats of set A, one hour after the administration of the drugs. The paw volume was measured after 1 hour and again after 3 hours using a plethysmometer. Increase in volume of paw edema was recorded by subtracting the initial paw volume from final paw volume measured after 1 hour and 3 hours of carrageenan injection. Percentage of inflammation rate was calculated as

$$\frac{Vc - Vt}{Vc} \times 100$$

Vc - mean increase in volume of paw edema in control group.
Vt - mean increase in paw volume in treated group of animals.

The same procedure was followed after inducing acute inflammation with subplanter injection of 0.1 ml of 1% solution of 5-HT in animals of set B and 0.1 ml of 1 mcg of bradykinin in animals of set C, respectively.

Paw edema induced to produce chronic/ immunologically induced inflammation

The rats of set D were grouped in a similar manner and evaluated for chronic inflammation. 0.1 ml of 2% formaldehyde was injected in the sub planter region of left hind paw of each rat. Rats of Group I, II, III, and IV received the drugs daily in similar dosage as given for evaluation of acute anti-inflammatory effect, for 13 consecutive days. The degree of inflammatory change was assessed from 3rd day onward on alternate days till the 13th day. Percentage inhibition of inflammation was calculated in similar manner.

Results

Effects *A. galanga*, phenylbutazone, and dexamethazone on carrageenan-induced acute inflammation are shown in Table 1. There was inflammatory inhibition of 32.22% with extract of *A. galanga*, which is significant ($P<0.05$).

Effects of the same substances on 5-HT-induced acute inflammation are shown in Table 2. Inhibition of inflammation with extract of *A. galanga* was 37.70% which is also significant ($P<0.01$).

Effects on bradykinin-induced acute inflammation are shown in Table 3. Inhibition of inflammation with extract of *A. galanga* was 34.21% which is also significant ($P<0.01$).

Table 4 shows the comparative effects in formaldehyde-induced chronic inflammatory model. A progressive inhibition of 34.73% (3rd day), 37.5% (5th day), 38.83% (7th day), 44.66% (9th day), 49.59% (11th day), and 55.75% (13th day) was observed with *A. galanga*. The results are significant at all study points ($P<0.05$).

Discussion

Inflammation is a protective response intended to eliminate the initial cause of cell injury as well as the necrotic cells and tissues resulting from the original insult.[17] Without inflammation, infections would go unchecked, wounds would never heal, and injured organs might remain permanent festering sores. Inflammation and repair may be potentially harmful, however. Inflammatory reactions underlie common chronic diseases, such as rheumatoid arthritis, lung fibrosis, and atherosclerosis.

Repair by fibrosis may cause disfiguring scars. For this reason, there are various anti-inflammatory drugs to control such harmful sequelae.

Medicinal plants are nature's hidden unexplored treasure of the world and have been the source of effective medicines from ancient age. They are less toxic, cheap, and suitable for use over a prolonged period. The potential resource has hardly been commercially been tapped. India has endowed with about 8000 species of medicinal plants. According to recent estimate of planning commission, Government of India, the potential of plant-based crude drugs is about Rs. 400 billion. Globally, the demand of medicinal plants and their derivatives is growing at a rate of 7 to 15%. Moreover, the active principles responsible for alleged disease-curing activity need to be identified and isolated to elucidate their exact mode of action.

Long back in 1958, Chopra pioneered the usefulness of indigenous drugs in various diseases including arthritic conditions. Anti-inflammatory and analgesic effects of *A. galanga* in variety of rheumatologic conditions

Table 1: Effects of *A. galanga*, phenylbutazone, and dexamethazone in carrageenan-induced edema of rat hind paw

Group	Increase in paw volume in ml (Mean±SE)	% inhibition	*P* value
Control	0.9±0.10	–	–
A. galangal	0.61±0.03	32.22	$P<0.05$
Phenylbutazone	0.23±0.02	74.44	$P<0.05$
Dexamethazone	0.3±0.03	66.66	$P<0.05$

Data were analyzed by unpaired student's *t* test; $n=6$

Table 2: Effects of *A. galanga*, phenylbutazone, and dexamethazone on 5-HT-induced paw edema of rat hind paw ($n=6$)

Group	Increase in paw volume in ml (Mean±SE)	% inhibition	*P* value
Control	0.61±0.04	–	–
A. galanga	0.38±0.03	37.70	$P<0.01$
Phenylbutazone	0.18±0.03	70.49	$P<0.001$
Dexamethazone	0.3±0.03	50.81	$P<0.001$

Data were analyzed by unpaired student's *t* test; $n=6$

Table 3: Effect of *A. galanga*, phenylbutazone, and dexamethazone on bradykinin-induced paw edema of rat hind paw

Group	Increase in paw volume in ml (Mean±SE)	% inhibition	*P* value
Control	0.71±0.03	–	–
A. galanga	0.46±0.o4	34.21	$P<0.01$
Phenylbutazone	0.22±0.04	69.01	$P<0.001$
Dexamethazone	0.32±0.03	54.92	$P<0.001$

Data were analyzed by unpaired student's *t* test; $n=6$

Table 4: Effects of *A. galanga*, phenylbutazone, and dexamethazone on formaldehyde-induced paw edema in rats

Group	Mean increase in Paw Volume in ml (Mean±SE) (% inhibition of inflammation)					
	3rd Day	5th Day	7th Day	9th Day	11th Day	13th Day
Control	0.95±0.02	0.96±0.02	1.03±0.05	1.16±0.12	1.23±0.13	1.13±0.09
A. galangal	0.62±0.04* (34.73%)	0.6±0.03* (37.5%)	0.63±0.04* (38.83%)	0.59±0.03* (44.66%)	0.62±0.02* (49.59%)	0.5±0.05* (55.75%)
Phenylbutazone	0.7±0.03* (26.32%)	0.65±0.04* (32.29%)	0.62±0.04* (39.80%)	0.58±0.03* (50%)	0.5±0.04* (59.34%)	0.4±0.04* (64.8%)
Dexamethazone	0.71±0.03* (25.26%)	0.66±0.04* (31.25%)	0.58±0.03* (43.68%)	0.6±0.03* (48.27%)	0.55±0.03* (55.28%)	0.48±0.03* (57.52%)

Data were analyzed by unpaired student's *t* test; All values are significant *$P<0.05$; $n=6$

have been studied by several authors. Yu *et al.* isolated *p*-coumaryl alcochol-γ-0- ether having phenylpropanoid structure, which selectively and substantially suppress IFN_γ production in CD4 T lymphocyte (T helper) cells.[18] Isolated chavicol analogues, viz, acetoxychavicol acetate (ACA) and hydroxychavicol acetate (HCA), have been comparably examined, where ACA exhibited potent antioxidant activity, increased cell apoptosis, and decreased cytokine production by T helper cells, whereas HCA suppressed T-bet expression and might act as a beneficial therapeutics for treating inflammatory immune disorders caused by extravagant activation.[19] Joint Care B, a herbal formulation containing *A. galanga* has shown dose-dependent inhibition of carrageenan-induced paw inflammation and granuloma weight in *croton oil-induced* granuloma pouch model in rats.[20] Evaluation of anti-inflammatory activity has been done on alcoholic extract of *Kaempferia Galanga* in rats, which is a plant belonging to the same species.[21] Topical preparation containing methanol extract of rhizome has significant analgesic activity in formalin test.[22] In a randomized, doubled-blind, placebo-controlled, multicenter trial, conducted in 261 patients with osteoarthritis (OA) of the knee joint with moderate to severe pain, highly concentrated extract has been found statistically significant on reducing symptoms of OA of the knee.[23]

The essential oil of rhizome is responsible for its antimicrobial activity.[24] In study performed by using broth dilution method, ethanol extract of *A. galanga* showed the strongest inhibitory effect against *S. aureus*.[25] This activity is due to presence of 1, 8- Cineole, 4-allyphenyl acetate and α-bisabolene.[26]

The present study also co-relates with earlier observations. Though NSAIDs are most commonly used in treatment of acute and chronic inflammation, prolonged use has limited its efficacy as approximately 25% of NSAID users develop GI symptoms.[27] The advent of this herbal medicine with antibacterial, antioxidative, and anti-inflammatory action together therefore would be unique and highly beneficial to patient of acute inflammation and also in chronic inflammatory disorders. Further studies in this regard in higher animals are necessary for anticipated beneficial outcome.

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