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EVALUATION OF ANTIINFLAMMATORY AND ANALGESIC ACTIVITIES OF ALCOHOLIC EXTRACT OF *KAEMPFERIA GALANGA* IN RATS

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Abstract : Alcoholic extract of *Kaempferia galanga* was tested for analgesic and antiinflammatory activities in animal models. Three doses, 300 mg/kg, 600 mg/kg and 1200 mg/kg of the plant extract prepared as a suspension in 2 ml of 2% gum acacia were used. Acute and sub acute inflammatory activities were studied in rats by carrageenan induced paw edema and cotton pellet induced granuloma models respectively. In both models, the standard drug used was aspirin 100 mg/kg. Two doses 600 mg/kg and 1200 mg/kg of plant extract exhibited significant ($P<0.001$) antiinflammatory activity in carrageenan model and cotton pellet granuloma model in comparison to control. Analgesic activity was studied in rats using hot plate and tail-flick models. Codeine 5 mg/kg and vehicle served as standard and control respectively. The two doses of plant extract exhibited significant analgesic activity in tail flick model ($P<0.001$) and hot plate model ($P<0.001$) in comparison to control. In conclusion *K. galanga* possesses antiinflammatory and analgesic activities.

Key words : antiinflammatory activity analgesic activity *Kaempferia galanga* carrageenan hot plate reaction time tail flick latency

INTRODUCTION

Inflammation is a pathophysiological response of living tissue to injury that leads to local accumulation of plasmatic fluid and blood cells. Although it is a defense mechanism that helps body to protect itself against infection, burns, toxic chemicals, allergens or other noxious stimuli, the complex events and mediators involved in the inflammatory reaction can induce, maintain or aggravate many diseases (1).

Pain has been defined by International Association for the Study of Pain (IASP) as an unpleasant sensory and emotional experience associated with actual or potential tissue damage (2). Failure to relieve pain is morally and ethically unacceptable.

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Drugs that are currently used for the management of pain are opioids or non-opioids and that for inflammatory conditions are non-steroidal antiinflammatory drugs (NSAIDs) and corticosteroids. All these drugs carry potential toxic effects. One study suggests that risk of gastrointestinal bleeding was significantly associated with acute use of non-steroidal anti-inflammatory drugs (NSAIDs) like regular-dose aspirin, diclofenac, ketorolac, naproxen or nimesulide. Piroxicam increased the risk of bleeding in both acute and chronic therapy (3). Opioids are the commonly used drugs for the management of acute postoperative pain (4).

It is not surprising that from conception to market most compounds face an uphill battle to become an approved drug. For approximately every 5,000 to 10,000 compounds that enter preclinical testing, only one is approved for marketing (5). Drug research and development (R & D) is comprehensive, expensive, time-consuming and full of risk. It is estimated that a drug from concept to market would take approximately 12 years and capitalizing out-of-pocket costs to the point of marketing approval at a real discount rate of 11% yields a total pre-approval cost estimate of US$ 802 million (6).

On the contrary many medicines of plant origin had been used since ages without any adverse effects. It is therefore essential that efforts should be made to introduce new medicinal plants to develop more effective and cheaper drugs. Plants represent a large natural source of useful compounds that might serve as lead for the development of novel drugs.

In the present study, *Kaempferia galanga* was selected because it is one of the medicinal plants commonly used in the ayurvedic system of medicine. *Kaempferia galanga*, commonly known as kencur, aromatic ginger, sand ginger or resurrection lily, is a monocotyledonous plant in the ginger (Zingiberaceae) family. The rhizome finds an important place in indigenous medicine as stimulant, expectorant, diuretic and carminative (7). It was used as an ingredient for the treatment of various skin disorders. It was widely used in the treatment of diabetes mellitus, various inflammatory and lipid disorders (8, 9). It also possesses larvicidal activity (10), anti-oxidant (11), anti-ulcer (12), antiinflammatory (13) and anti-hypertensive (14) properties.

Kaempferia galanga has been widely used in remedies to treat abdominal pain, toothache, and as an embrocation or sudorific to treat muscular swelling and rheumatism in the traditional medicine (15). It is known that the major chemical constituents of the volatile oil from dried rhizome were ethyl-*p*-methoxycinnamate (31.77%), methylcinnamate (23.23%), carvone (11.13%), eucalyptol (9.59%) and pentadecane (6.41%), respectively. Other constituents of the rhizome include cineol, borneol, 3-carene, camphene, kaempferal, cinnamaldehyde, *p*-methoxycinnamic acid and ethyl cinnamate. A methanolic extract of the rhizome contains ethyl *p*-methoxy-*trans*-cinnamate, which is highly cytotoxic to HeLa cells (16).

Up to date no pharmacological study has been systematically conducted to evaluate the antiinflammatory and antinociceptive action of ethanolic extract of *Kaempferia galanga*, supporting traditional uses of this

plant in folklore medicine. Hence present study was undertaken to evaluate the antiinflammatory and antinociceptive activity of *Kaempferia galanga* in Wistar albino rats using ethanol extract. The ethanolic extract was used in this investigation because ethanol being nonpolar, the major active chemical constituents of *Kaempferia galanga* including volatile oils, would be expected to be more soluble in ethanol fraction of the extract.

MATERIALS AND METHODS

Description of plant material:

The fresh rhizomes of *K. galanga* plants were procured locally in the month of December 2005. The plants were identified and authenticated by Professor of Botany, Mahatma Gandhi Memorial College (MGMC), located in Udupi (Karnataka). After authentification, the plants were cleaned and shade dried and milled into coarse powder by a mechanical grinder.

Preparation of alcoholic extract of *K. galanga*:

The dried powder (total 2 kg) was loaded into Soxhlet extractor with glass thimble (cat no.3485) in 8 batches of 250 g each and was subjected to extraction for about 30-40 h with 95% ethanol. After extraction the solvent was distilled off and the extract was concentrated under reduced pressure on a water bath at a temperature below 50°C to give a semi-solid syrupy consistency residue of 60.8 g (yield 3%, w/w) which was stored in a closed bottle and kept in a refrigerator at temperature below 4°C until tested. The ethanolic extract of *K. galanga* at doses of 300, 600 and 1200 mg/kg were prepared by suspending this residue in the cosolvent (2% gum acacia).

Selection of animals, caring and handling:

This was done as per the guidelines set by the Indian National Science Academy New Delhi, India. A total of 120 healthy Wistar rats (150–200 g), aged twelve weeks of either sex, bred locally in the animal house of Kasturba Medical College, Manipal were selected for the study. They were housed under controlled conditions of temperature of 23±2^{0}C, relative humidity of 30–70% and 12 h light–12 h dark cycle. The animals were housed individually in polypropylene cages containing sterile paddy husk (procured locally) as bedding throughout the experiment. All animals were fed with sterile commercial pelleted rat chow supplied by Hindustan Lever Ltd. (Mumbai, India) and had free access to water *ad libitum*. Animals were kept under fasting for overnight and weighed before the experiment. The study was undertaken after obtaining approval of Institutional Animal Ethics Committee (IAEC approval letter No. IAEC/KMC/04/2002-2003 Dated Dec.14.2005).

Study design:

The rats were randomly allocated into five groups of six rats each for the four different experimental animal models. We used two animal models each for testing antiinflammatory and analgesic activities.

Group I (control) received 2 ml of 2% gum acacia (E. Merck India Ltd.), po through intragastric tube.

Group II received *K. galanga*, 300 mg/kg, po

Group III received *K. galanga*, 600 mg/kg, po

Group IV received *K. galanga*, 1200 mg/kg, po

Group V received standard drug, aspirin 100 mg/kg, po (for antiinflammatory study) and codeine 5 mg/kg, po (for analgesic study).

MATERIALS

Drugs : aspirin (Sigma chemical Co. St Louis, USA), Alcoholic extract of *K.galanga*, 2% Gum acacia (E. Merck India Ltd.), codeine (Sigma chemical Co. St Louis, USA), Ether (Sigma chemical Co. St Louis, USA), **Inflammatory agents used :** inj. carrageenan (0.1 ml of 1% w/v suspension) (Sigma chemical Co. St Louis, USA), cotton pellets, **Instruments :** Eddy's hot plate or Techno heated plate analgesiometer mark-3 (model no. HPA), Analgesiometer-(Techno electronics, Lucknow, India), Digital plethysmometer (Ugo Basile Company Cat. No. 7140 VA, Italy).

Determination of the drug dosage and dosing schedule : Doses were selected and determined according to the previous acute toxicity studies of ethanolic extract of *K.galanga* (17). Three different doses were selected 300 mg/kg, 600 mg/kg and 1200 mg/kg for antiinflammatory and analgesic activities. The suspension of the alcoholic extract of *K. galanga* and aspirin were made in 2% gum acacia.

METHODS

Acute inflammatory model

Carrageenan induced paw edema in rats

In the present study, antiinflammatory activity was determined in albino rats of either sex according to the method of Winter (18). All drugs were given orally to the respective groups as a suspension in gum acacia one hour before carrageenan injection. The procedure followed was, acute inflammation produced by injection of carrageenan (0.1 ml of 1% w/v suspension) (19), in the right hind paw of the rats under the plantar aponeurosis. It was injected +1h after the oral administration of the drug. The inflammation was quantitated in terms of ml i.e. displacement of water by edema using a digital plethysmometer immediately before and after carrageenan injection at +1, +2, +3, +4, +5 and +6 h. The percentage inhibition of edema was calculated for each group with respect to its vehicle-treated control group (20, 21, 22).

Percentage inhibition of paw edema = $(1–Vt/Vc) \times 100$

Where Vc represent average increase in paw volume (average inflammation) of the control group of rats at a given time; and Vt was the average inflammation of the drug treated (i.e. plant extracts or test drug aspirin) rats at the same time.

The difference in the initial 0h and volume at +1h indicate paw edema at 1h following carrageenan administration. Accordingly paw edema at +2, +3, +4, +5 and +6h was calculated. Then percentage inhibition of paw edema was calculated.

Sub acute inflammatory model

Cotton pellet induced granuloma model

Sub acute inflammation was produced by cotton pellet induced granuloma model in

rats (23, 24). On day 1, with aseptic precautions sterile cotton pellets (50±1 mg) were implanted subcutaneously, along the flanks of axillae and groins bilaterally under ether anaesthesia. All drugs were given orally to the respective group of rats as a suspension in gum acacia daily for six consecutive days from day 1. The animals were sacrificed on the 7th day. The granulation tissue with cotton pellet was dried at 60^{o}C overnight and then the dry weight was taken. Weight of the cotton pellet before implantation was subtracted from weight of the dissected dried pellets. Only dry weight of the granuloma formed was used for statistical analysis.

Analgesic study

Hot plate method

The analgesic activity of the extract, was measured by hot-plate method (25). All drugs were given orally to the respective group rats as a suspension in gum acacia. The rats were placed on a hot plate maintained at 55±0.5^{o}C. The reaction time was taken as the interval from the instant animal reached the hot plate until the moment animal licked its feet or jumped out. A cut off time of +10 s was followed to avoid any thermal injury to the paws. The reaction time was recorded before and after +30, +60, +90, +120 and +180 min following administration of test or standard drug.

Evaluation

The mean reaction time for each treated group was determined and compared with that obtained for each group before treatment. Percentage increase in reaction time (I %), was derived, using the formula I% = {(It – Io)/Io} × 100, Where It = reaction time at time, t, and Io = reaction time at time zero (0 h) (26). The animals were subjected to the same test procedure at +30, +60, +120, and +180 min after the administration of test/standard/control drug.

Radiant heat tail-flick method

The central analgesic activity was determined by radiant heat tail-flick model in rats (27). The analgesic activity of the plant extract was studied by measuring drug-induced changes in the sensitivity of the pre-screened rats (the intensity of the light beam has been experimentally defined such that naive animals will withdraw their tails within 2 to 4 s) to heat stress applied to their tails by using analgesiometer. Tail-flick latency was assessed by the analgesiometer. All drugs were given orally to the respective group rats as a suspension in gum acacia. The strength of the current passing through the naked nichrome wire was kept constant at 5 ampere. The distance between heat source and the tail was 1.5 cm and the application site of the heat on the tail was maintained within 2 cm, measured from the root of the tail. Cut-off reaction time was +10 s to avoid any tissue injury during the process. Tail-flick latency was measured from +30 min after the drug administration.

Evaluation

The time taken by rats to withdraw (flick) the tail was taken as the reaction time. The animals were subjected to the same test procedure at +30, +60, +120, and +180 min after the administration of test/standard/ control drug.

Statistical analysis

The results were analysed for statistical significance using One way ANOVA, followed by Scheffe's test. A P-value <0.05 was considered significant. Computer statistical package SPSS (version 16) was used for analysis.

RESULTS

Antiinflammatory activity in rats

Effect on carrageenan induced paw edema (Table I, Fig. 1)

Pretreatment with *K.galanga* resulted in dose-dependent reduction in carrageenan evoked hind paw edema and differed significantly (P<0.001) among the different groups of rats (Table I). In carrageenan induced rat paw edema test, the two doses of plant extract showed statistically significant (P<0.001) inhibitory effect on "mean increase in paw volume" at all the time intervals (+1 h, +2 h,+ 3 h, +4 h, +5 h, and +6 h) as shown in (Table I). After +1 h and +3 h of carrageenan administration, *K. galanga* exhibited maximum % inhibition of paw volume (P<0.01) by 36.95%, 33.55% and 42.31%, 44.19%, at the higher two doses of plant extract 600 mg/kg and 1200 mg/kg body weight respectively, however % inhibition of paw volume was less than that of standard drug aspirin 54.96%, 69.59% (P<0.001) at the dose of 100 mg/kg body weight (Table I, Fig. 1).

Antigranulation effect in rats (Table II)

The dry weight of cotton pellet granuloma in control, three different doses of *K. galanga* and aspirin treated groups is shown in the table 2. It can be noted from table 2, that the two doses of *K. galanga* 600 mg/kg and 1200 mg/kg, and aspirin showed significant (P<0.001) activity in inhibiting dry weight of granuloma. The extract administered at 1200 mg/kg, p.o. had a greater anti-granulation (36.70%) effect but less than aspirin (42.17%).

Analgesic activity in rats

Hot plate method (Table III)

In the hot-plate method, both the extract and codeine caused significant increase

TABLE I: Antiinflammatory effect of alcoholic extract of *K. galanga* on carrageenan-induced rat paw edema.

Drugs	*Dose/ route*	*Increase in paw volume (Mean±SEM) (ml) (% Inhibition of paw edema)*						
		Before	*+1h*	*+2h*	*+3h*	*+4h*	*+5h*	*+6h*
gum acacia	2 ml po	0.633±0.023	0.408±0.025	0.868± 0.033	1.196±0.031	1.316±0.028	1.433±0.027	1.266±0.031
K. galanga	300 mg/ kg po	0.672±0.006	0.348±0.010 (13.42)	0.776± 0.009 (10 .02)	1.12±0.017 (5.670)	1.22±0.025 (7.26)	1.310±0.014 (8.41)	1.241±0.024 (1.456)
	600 mg/ kg po	0.735±0.015	0.246±0.019[a] (36.95)	0.631± 0.018[ab] (26.41)	0.79±0.022[ab] (33.55)	0.985±0.031[ab] (24.83)	1.025±0.016[ab] (28.31)	0.978±0.028[ab] (22.32)
	1200 mg/ kg po	0.780±0.006	0.228±0.008[a] (42.314)	0.520± 0.008[ab] (39.71)	0.665±0.016[ab] (44.195)	0.952±0.021[ab] (27.489)	0.990±0.011[ab] (30.81)	1.08±0.010[ab] (14.25)
aspirin	100 mg/ kg po	0.551±0.006	0.185±0.045[a] (54.96)	0.271± 0.01[a] (68.46)	0.363±0.009[a] (69.59)	0.415±0.011[a] (68.45)	0.480±0.008[a] (66.48)	0.481±0.008[a] (61.85)

[a]P<0.001 vs Control, [b]P<0.001 vs aspirin, (n=6/group), One-way ANOVA; SEM = Standard error of mean.

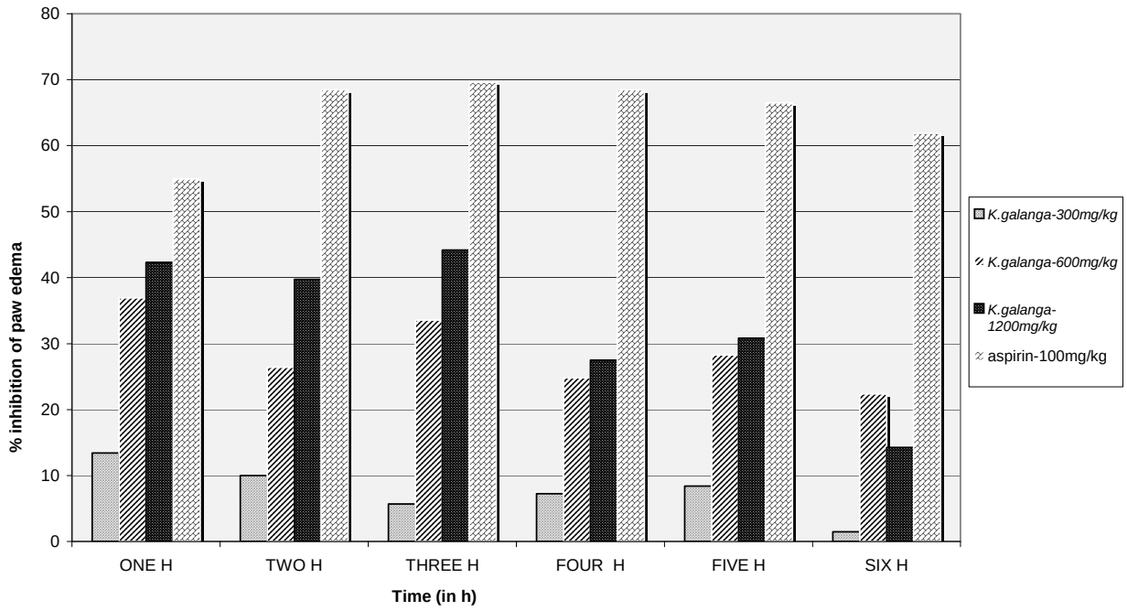

Fig. 1: Antiinflammatory effect of *K. galanga* on carageenan induced rat paw edema.

TABLE II: Antiinflammatory effect of alcoholic extract of *K. galanga* on cotton pellet induced granuloma formation in rats.

Drugs	*Dose/ route*	*Weight of dry cotton pellet granuloma (mg) (Mean±SEM)*	*% inhibition of granuloma formation*
gum acacia	2 ml of 2% po	81.712±0.433	–
K. galanga	300 mg/ kg/day po	82.5±0.868	–0.964
	600 mg/ kg/day po	59.4±0.909[ab]	27.305
	1200 mg/ kg/day po	51.72±2.007[ab]	36.70
aspirin	100 mg/ kg/day po	47.25±1.878[a]	42.17

[a]P<0.001 vs Control, [b]P<0.001 vs aspirin, (n=6/ group), One-way ANOVA; SEM = Standard error of mean.

(P<0.001) in the reaction time. The increase in latency period at different time points significantly differed (P<0.01) compared to baseline values within the same drug treated groups. The percentage increase in the reaction time was dose-dependent and differed significantly among the groups of rats (P<0.001) receiving different dose levels of the extract and codeine (Table III).

The percentage increase in the reaction time caused by the extract and codeine was detectable and peaked, at +1 h and +30 min respectively but thereafter declined relatively at +3h after the administration of the extract or codeine.

At +3 h after administration, codeine retained a significantly greater activity (P<0.001) than the extract. At all the specified time intervals, the percentage increase in reaction time differed significantly (P<0.001) between the extract and codeine, being greater for codeine.

At the peak of activity, 600 mg/kg and 1200 mg/kg extract caused 52.04% and 56.56% increase in the reaction time respectively whilst codeine gave 82.16% increment. Time to peak activity was different for the extract (+1 h) and codeine (+30 min).

Tail flick method (Table IV)

In the tail flick method, the increase in latency period at different time points significantly differed (P<0.01) compared to baseline values within the same drug treated groups. The extract and codeine caused significant increase (P<0.01) in the percentage reaction time whilst the control and lower dose of extract (300 mg/kg) caused no change. The percentage increase in reaction time was dose dependent. At all the specified time intervals, the percentage of tail flick elongation time differed significantly

TABLE III: Analgesic effect of alcoholic extract of *K. galanga* by hot plate method in rats.

Drugs	*Dose/ route*	*Reaction time in s (mean±SEM)*				
		Basal	*30 min (% elongation)*	*60 min (% elongation)*	*120 min (% elongation)*	*180min (% elongation)*
gum acacia	2 ml po	4.56±0.03	5.183±0.03* (13.66)	5.42±0.031* (18.84)	6.067±0.012* (33.03)	6.23±0.014* (36.60)
K. galanga	300 mg/ kg po	4.780±0.016	5.360±0.01* (12.14)	5.60±0.014* (17.16)	6.083±0.008* (27.27)	6.313±0.009* (32.08)
	600 mg/ kg po	5.052±0.016	7.29±0.04*[ab] (44.28)	7.68±0.033*[ab] (52.04)	6.96±0.017*[a] (37.78)	7.04±0.01*[ab] (39.43)
	1200 mg/ kg po	4.917±0.024	7.022±0.02*[ab] (42.83)	7.69±0.04*[ab] (56.56)	7.29±0.02*[ab] (48.31)	7.15±0.008*[ab] (45.37)
codeine	5 mg/ kg po	4.334±0.030	7.890±0.05*[a] (82.16)	7.25±0.04*[a] (67.40)	7.02±0.015*[a] (61.80)	6.81±0.011*[a] (57.20)

*P<0.01 vs Baseline value of the respective drug group, [a]P<0.001 vs Control, [b]P<0.001 vs codeine, (n=6/ group), One-way ANOVA; SEM = Standard error of mean.

TABLE IV: Analgesic effect of alcoholic extract of *K.galanga* on radiant heat tail-flick response in rats.

Drugs	*Dose/ route*	*Reaction time in s (mean±SEM)*				
		Basal	*30 min (% elongation)*	*60 min (% elongation)*	*120 min (% elongation)*	*180min (% elongation)*
gum acacia	2 ml po	4.25±0.015	4.37±0.015 (2.95)	4.61±0.021* (8.39)	4.79±0.006* (12.78)	4.65±0.033* (9.49)
K.galanga	300 mg /kg po	4.39+0.006	4.44±0.020 (1.10)	4.71±0.048* (7.20)	4.86±0.009* (10.77)	4.72±0.009* (7.58)
	600 mg/ kg po	4.81±0.008	6.91±0.016*[ab] (43.66)	6.34±0.015*[ab] (31.86)	5.89±0.033*[ab] (22.36)	5.46±0.007*[ab] (13.43)
	1200 mg/ kg po	4.78±0.006	7.02±0.012*[ab] (46.76)	6.66±0.020*[ab] (39.23)	5.85±0.01*[ab] (22.43)	5.55±0.013*[ab] (16.09)
codeine	5mg/ kg po	4.93±0.008	8.87±0.033*[a] (80.08)	7.88±0.035*[a] (59.90)	6.64±0.077*[a] (34.75)	6.11±0.008*[a] (23.93)

*P<0.01 vs Baseline value of the respective drug group, [a]P<0.001 vs Control, [b]P<0.001 vs codeine, (n=6/ group), One-way ANOVA; SEM = Standard error of mean.

(P<0.001) between the extract and codeine at both the doses of plant extract, being greater for codeine. At the peak of activity, 600mg/kg and 1200mg/kg extract showed 43.66% (P<0.001) and 46.76% (P<0.001) percentage of tail flick elongation time respectively, whilst codeine gave 80.08% (P< 0.001) elongation of tail flicking time **(**Table 4). Time to reach peak activity was same (+30 min) for the extract and codeine.

DISCUSSION

The carrageenan-induced paw edema model in rats is known to be sensitive to cyclooxygenase inhibitors and has been used to evaluate the effect of non-steroidal antiinflammatory agents, which primarily inhibit the cyclooxygenase involved in prostaglandin synthesis (28).

Carrageenan-induced hind paw edema is the standard experimental model of acute-inflammation. The time course of edema development in carrageenan-induced paw edema model in rats is generally represented by a biphasic curve (29). The first phase of inflammation occurs within an hour of carrageenan injection and is partly attributed to trauma of injection and also to histamine, and serotonin components (30). The second phase is associated with the production of bradykinin, protease, prostaglandin, and lysosome (30). Prostaglandins (PGs) play a major role in the development of the second phase of inflammatory reaction which is measured at +3 h (31).

The doses 600 mg/kg and 1200 mg/kg of alcoholic extract of *K. galanga* produced a significant inhibition of carrageenan induced paw edema at +3h and +6h. Therefore, it can be inferred that the inhibitory effect of alcoholic extracts of *K. galanga* on carrageenan induced inflammation could be due to inhibition of the enzyme cyclooxygenase and subsequent inhibition of prostaglandin synthesis. Significant inhibition of paw edema in the early hours of study by *K. galanga* could be attributed to the inhibition of histamine (32) and/or serotonin. The decrease in paw edema inhibition at +6h may be attributed to the termination of test drug action.

Cotton pellet granuloma model was used to evaluate the antiinflammatory activity of *K.galanga* in sub acute inflammation. Three phases of the inflammatory response to a subcutaneously implanted cotton pellet in the rats have been described: (A) a transudative phase, that occurs during the first 3 h; (B) an exudative phase, occurring between 3 and 72h after implanting the pellet; (C) a proliferative phase, measured as the increase in dry weight of the granuloma that occurs between 3 and 6 days after implantation (33). The suppression of proliferative phase of sub acute inflammation could result in decrease in the weight of granuloma formation (34). The dry weight of cotton pellet granuloma was significantly reduced (P<0.001) by 600mg/kg and 1200 mg/kg doses of *K. galanga*, however the antiproliferative effect of *K.galanga* was lesser than that of the standard drug. To evaluate for a possible central antinociceptive effect of the *K. galanga* , the hot plate and tail-flick tests are used for evaluation of the central pain at the supraspinal and spinal levels (35), respectively, possibly acting on a descending inhibitory pain pathway (36). The tail-flick response is believed to be a spinally mediated reflex and the paw-licking hot plate response is more complex supraspinally organized

behaviour (37). The effectiveness of analgesic agents in the tail-flick pain model is highly correlated with relief of human pain perception (38).

In the two models used, though the data showed that the extract of *Kaempferia galanga* dose-dependently increased the pain threshold, the increase in the pain threshold/ tail flick latency profiles of the extract were less than that of the standard drug, codeine (Table III). The μ receptor stimulation is generally associated with pain relief and has been shown to be potent in regulating thermal pain (39). Nonanalgesic effects through the μ receptors include respiratory depression and most importantly for therapeutic considerations is its induction of physical dependence. Activation of μ_2 opioid subtype leads to spinal analgesia and commonly causes constipation as adverse effect (40). Therefore, taking all these data together we believe that the antinociceptive activity of ethanolic plant extract is most likely to be mediated by central action (spinally and supraspinally) (35) and indicates a codeine like mechanism by binding with opioid receptors. Although opioids possess dependence and abuse liabilities, new drugs producing less euphoria at onset and withdrawal symptoms as the medication wear off would be more beneficial. *K. galanga* could be a better substitute for the opioid drugs like methadone is an excellent choice over morphine for the management of chronic severe pain like in cancer. Methadone is an orally active, slow-onset opioid with a long duration of action (41).

In the tail-flick and hot plate methods, both the doses (600 & 1200 mg/kg body wt.) of plant extract increased the stress tolerance capacity of the animals and hence indicate the possible involvement of a higher centre (42). The time attained to reach the peak analgesic activity was same for codeine (+30min) but the plant extract showed at (+60min) and (+30 min) in hot plate and tail flick model respectively, which had no explanation and attributed as a limitation of our study.

On the basis of these findings, it may be inferred that alcoholic extract of *K. galanga* has analgesic and antiinflammatory activities. These activities were related to the dose and these results corroborate the potential traditional use of the plant in folk medicine. At present, there are no reports on investigation to identify the active components present in ethanolic extract of *K.galanga*. Further investigations are anticipated to identify the active components and lead to their further clinical use.

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