

Evaluation of anti-arthritic potential of the methanolic extract of the aerial parts of *Costus speciosus*

Shruti Srivastava, Pradeep Singh, Keshri K. Jha, Garima Mishra, Sourabh Srivastava, Ratan L. Khosa¹

Department of Pharmacognosy, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh,

¹Department of Pharmacy, Bharat Institute of Technology, Meerut, Uttar Pradesh, India

ABSTRACT

Objective: *Costus speciosus* Koen. (Keu, Crape ginger), an ornamental plant, widely distributed in India is traditionally used as astringent, aphrodisiac, purgative, anthelmintic, depurative, febrifuge and expectorant. The plant is also used in rheumatism, dropsy, urinary diseases and jaundice. The purpose of this study is to evaluate the anti-arthritic activity of the methanolic extract of the aerial parts of *Costus speciosus* (CS) in experimental animal models. **Materials and Methods:** The powdered drug was subjected to successive solvent extraction, with solvents in increasing order of polarity to obtain the methanolic extract of the aerial parts of the plant. CS was evaluated for anti-arthritic action by Freund's adjuvant induced arthritis test in adult Albino rats (150-200 gm). Rats were injected 0.1 ml of complete Freund's adjuvant into the planter region of the left hind paw. Statistical analysis was performed using One way analysis of variance (ANOVA) followed by Bonferonni test. $P < 0.05$ was considered statistically significant. **Results:** The methanolic extract of CS in doses of 400 and 800 mg/kg showed 75.50% and 68.33% protection against increase in paw edema, respectively. CS showed dose-dependent action in all the experimental models. **Conclusion:** The present study indicates that CS has significant anti-arthritic properties.

Key words: Arthritis, *Costus speciosus*, diclofenac sodium, Freund's complete adjuvant, paw volume

INTRODUCTION

Rheumatoid arthritis is a systemic autoimmune disorder characterized by polyarticular symmetrical arthritis. Various inflammatory mediators produce joint inflammation with pain function loss, joint destruction and permanent deformity after certain time if left untreated.^[1] The prevalence of rheumatoid arthritis is consistent worldwide affecting about 0.5-1.0% of the population. It usually

occurs in people between 25 and 55 years of age. Women are affected more often than men at a ratio of 3 to 1. It is characterized by synovial hyperplasia, angiogenesis and mononuclear infiltration. It progresses in 3 stages. The first stage is the swelling of the synovial lining, causing pain, warmth, stiffness, redness and swelling around the joint. Second is the rapid division and the growth of the cells, which causes the synovium to thicken. In the third stage, the inflamed cells release enzymes that may digest bone and cartilage, often causing the involved joint to lose its shape and alignment, leading to excessive pain and loss of movement.^[2]

The drugs commonly in use for the treatment of inflammation and arthritis include glucocorticoids like cortisone and prednisone etc., NSAIDs like Ibuprofen and naproxen etc., disease-modifying anti-inflammatory and anti-rheumatic drugs like Methotrexate (MTX) and leflunomide etc., and newer therapies such as biological response modifiers like tumor necrosis factor, alpha blocking agents, anti-CD 20 therapy (rituximab) and abatacept which are often required to inhibit or halt the underlying immune processes. However, besides high costs, all of these drugs are associated with numerous side effects, severe adverse reactions and toxicity, including some risk of

Address for correspondence:

Mr. Pradeep Singh, Department of Pharmacognosy, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh - 244 001, India.
E-mail: pradeep_2682@yahoo.co.in

Received: 29-Mar-2012

Revised: 29-Apr-2012

Accepted: 04-Jun-2012

Access this article online

Quick Response Code:



Website:

www.jaim.in

DOI:

10.4103/0975-9476.104443

infections in subsets of patients who are being treated with biological response modifiers. In recent days, researchers are directed towards traditional system of medicine for the discovery of drugs that are long acting anti-inflammatory agents displaying minimum side effects.^[3,4]

In India, many Ayurvedic practitioners are using various indigenous plants for the treatment of different types of arthritic conditions. Although the application of these medicaments has a sound tradition and a rational background according to the Indian system of medicine, perhaps it is essential to investigate the rationality of their use in modern scientific terms.^[5]

Costus speciosus Koen. (Keu, Crape ginger), an Indian ornamental plant, has long been medicinally used in traditional systems of medicine. This plant of Costaceae (Zingiberaceae) family is commonly known as *keukand* (Hindi) and variegated Crepe Ginger (English). It is an erect, succulent, perennial herb, up to 2.7 meters in height, arising from a horizontal rhizome, found in tropical region of India and also cultivated for ornament.^[6] The rhizomes and roots are ascribed to be bitter, astringent, acrid, cooling, aphrodisiac, purgative, anthelmintic, depurative, febrifuge, expectorant, tonic which improves digestion, clears toxins and is a stimulant herb. Juice of the rhizome is applied to the head for cooling and relief from headache.^[7-11]

An alkaloid ext. from *Costus speciosus* rhizomes is known to display papaverine-like smooth muscle relaxant and anti-spasmodic activities.^[12] Rhizomes are given in pneumonia, rheumatism, dropsy, urinary diseases, jaundice and leaves are given in mental disorders. Bruised leaves are applied in fever; decoction of stem is used in fever and dysentery.^[6] The plant possesses purgative, anti-inflammatory and anti-arthritic effect, anti-fungal activities and is used in gout rheumatism and bronchial asthma.^[10]

C. speciosus plant extracts were previously tested for anti-inflammatory activity using carrageenan induced paw edema. However, the aerial parts of *C. speciosus* were not tested using arthritis or chronic inflammatory models to prove its efficacy. The scientific studies are essential to work out the actual efficacy and to widen their scope for future use if they come out to be really effective. Hence, the aim of this study is to prove the therapeutic potential of the plant as an anti-arthritic agent against Freund's complete adjuvant (FCA) induced arthritis.

MATERIALS AND METHODS

Plant material

Fresh aerial parts of *Costus speciosus* Koen. (Costaceae),

for the proposed work were collected from the Bahadurpur forests of Kolkata in the month of September 2010 and authenticated in Birbal Sahni Institute of Palaeobotany, Lucknow, India. A voucher specimen (Specimen No: 11723) is preserved in herbarium section of taxonomic department of Birbal Sahni Institute of Palaeobotany, Lucknow, India and crude drug sample was preserved in the department of Pharmacognosy, Teerthanker Mahaveer College of Pharmacy, Moradabad. The whole plant material was dried under shade and mechanically reduced to moderate coarse powder and stored in air tight containers for further use in extraction process.

Preparation of extracts

Exactly 2.5 kg dried and coarsely powdered aerial parts of the plant were used for the extraction procedure. The coarse powder of the plant was successively extracted using soxhlet apparatus with the solvents in increasing order of polarity starting with petroleum ether, chloroform, ethyl acetate and methanol. By using rotary evaporator, the extracts were concentrated under reduced pressure and then dried in open air. The dried methanolic extract was suspended in 0.5% CMC in distilled water (vehicle) and used for anti-arthritic activity.

Experimental animals

All the experiments were carried out using male Albino rats weighing between 150 gm and 200 gm. All the experimental procedures and protocols used in this study were reviewed by the Institutional Ethical Committee and were allotted the No. 1205/C/08/CPCSEA/21.04.08. All animals were housed in polypropylene cages and maintained under standard laboratory conditions. Animals were housed at a temperature of 24±2°C and relative humidity of 60-70%. They were fed with a standard diet and water was given *adlibitum* and they were left for a week for acclimatization to animal house conditions. All experiments were conducted after overnight fasting but there was free access to water. A minimum of six animals were used in each group.

Chemicals and drugs

The chemicals used were Freund's Complete Adjuvant Injection (Sigma Chemicals, USA), Petroleum ether, Chloroform (Rankem, New Delhi), Carboxy methyl cellulose (Loba Chemie, Mumbai), and Diclofenac sodium (Akums Drugs and Pharmaceuticals, India). All the drugs used in this study were of pharmaceutical grade.

Freund's adjuvant induced arthritis

The male albino rats were divided into four groups, i.e. control, standard, drug treated (two groups of methanolic extract low and high dose treated group). Group 1 served as the control group and received 1% CMC (1 ml/1kg body weight), group II was the standard group and received

diclofenac sodium 15 mg/kg suspended in CMC, group III was the first test group receiving methanolic extract at dose of 400 mg/kg orally and the last 4th group was given methanolic extract at dose of 800 mg/kg orally. Rats were injected with 0.1 ml of Freund's complete adjuvant (FCA) into the planter region of the left hind paw. The paw volumes of both the hind paws were measured using a plethysmometer and body weight was recorded on the day of adjuvant injection. The methanolic extract of the aerial parts of the plant (400 and 800 mg/kg) and diclofenac sodium (15 mg/kg) doses were administered orally for 14 days from the day of Freund's adjuvant injection. The changes in the paw volume were measured on various days up to 21 days following Freund's adjuvant injection. The change in the inflammatory reaction was measured by using mercury plethysmometer on 1st, 7th, 14th and 21st day from the day of adjuvant injection. The animals were weighed, using digital weighing balance on 1st, 7th, 14th and 21st day from the day of adjuvant injection. At the end of experiment, on the 21st day all animals were anaesthetized and blood was withdrawn by retro-orbital puncture and collected in plain and EDTA containing tubes, respectively for serum separation. The homogenized samples were subjected to biochemical examination like Serum glutamate pyruvate transaminase (SGPT), Serum glutamate oxaloacetate transaminase (SGOT), Alkaline Phosphatase (ALP) and bilirubin.^[2,13]

Statistical analysis

Statistical analyses were performed by ANOVA followed by the Bonferroni test by using statistical software package, Graph Pad Prism; version 5.03. Values were expressed as mean \pm SEM and the $P < 0.05$ were considered as statistically significant.

RESULTS

FCA induced rat paw edema

There is a significant increase in rat paw volume in FCA injected control rats when compared to the standard and drug treated rats. Methanolic extract treatment at the dose of 400 mg/kg and 800 mg/kg showed significant reduction in rat paw edema volume when compared with the control group. Table 1 shows the effect of extract on Freund's adjuvant model induced arthritis. After 21 days it was found that methanolic extract significantly shows dose dependant inhibition in paw thickness i.e. the chronic inflammation induced by adjuvant shows decrease in paw thickness. Standard diclofenac sodium significantly decreased the paw thickness i.e. 40.0 ± 0.5774 after induction of Freund's adjuvant; where as the extract at high dose significantly decreased the paw thickness. It was found that in case of the high dose of the methanolic extract, the percent protection against increase in paw volume was found to

be $68.33 \pm 1.145\%$ as compared to that of the low dose which was found to be $75.50 \pm 0.9220\%$.

Body weight changes

In the present study, it is clear from the data obtained that there is a close relationship between the extent of joint inflammation and the degree of weight loss. The control group when compared to the standard and both of the test treated groups, it was found that the weight of the rats was highest in case of the standard group 177.2 ± 0.54 gms. Standard drug and the alcoholic extract at high and low doses significantly increased the body weight of the animal as compared to control group which was recorded to be 167.2 ± 0.47 and 169.7 ± 0.91 gms for low and high dose groups respectively, as depicted in Table 2. The extract showed a dose dependant increase in the body weight of the rats.

Biochemical estimation

As a result of inflammation induced by adjuvant, the levels of SGPT, SGOT and ALP were increased in all arthritis rats as compared to control rats. After extract treatment, the levels of these enzymes were significantly decreased in group 3rd and 4th rats as compared to control rats. Diclofenac sodium (15 mg/kg) treatment prevented biochemical changes to a greater extent than the methanolic extract of the plant. The SGOT, SGPT, ALP (Ka) and bilirubin levels of all the groups were evaluated and compared with each other. The SGOT and SGPT levels of the standard group were found to be 63.00 ± 0.57 and 73.50 ± 0.76 IU/L, respectively, which was least as compared to extract treated group for which the level was found to be 85.00 ± 1.52 , 92.50 ± 0.76 and 78.83 ± 1.30 , 89.50 ± 0.76 IU/L for low dose and high dose groups, respectively. However, treated groups were able to reduce the SGOT and SGPT levels better, as compared to control (145.0 ± 0.57 and 129.8 ± 0.60) proving its anti-arthritis efficacy. Similarly, other parameters like ALP (Ka) and bilirubin were also studied and the respective results are shown in Table 3.

DISCUSSION

Rheumatoid arthritis is an autoimmune disorder, the immunologically mediated complete Freund's adjuvant induced arthritic model of chronic inflammation is considered as the best available experimental model of rheumatoid arthritis. Complete Freund's adjuvant-induced arthritis is a model of chronic polyarthritis with features that resemble rheumatoid arthritis.^[14]

The determination of paw swelling is apparently simple, sensitive and quick procedure for evaluating the degree of inflammation and assessing of therapeutic effects of drugs.^[15]

In adjuvant-induced arthritis model rats developed a chronic swelling in multiple joints with influence of inflammatory cells, erosion of joint cartilage and bone destruction and remodeling which have close similarities to human rheumatoid disease. These inflammatory changes ultimately result in the complete destruction of joint integrity and functions in the affected animal. Also, the CFA administered rats showed soft tissue swelling around the ankle joints during the development of arthritis, which was considered as edema of the particular tissues.^[16]

Assessment of the levels of SGOT, SGPT, ALP and bilirubin provides an excellent and simple tool to measure the anti-arthritis activity of the target drug. The activities of these enzymes were significantly increased in arthritic rats. These are good indicators of liver and kidney impairment, which are also considered to be features of adjuvant arthritis.^[17,18]

In our study the methanolic extract of *C. speciosus* exhibited a significant anti-arthritis activity in a dose dependent manner. In the present study, we showed that methanolic extract of *C. speciosus* could significantly inhibit the progression of the rheumatoid arthritis in treated animals. However, standard drug and alcoholic extract significantly suppressed the swelling of the paws in both acute and chronic phase which may be due to the suppression of inflammatory mediator released due to induction of Freund's adjuvant. Though the actual mechanism of suppressing inflammation is not known but it can be correlated with the presence of alkaloids and flavonoids in suppressing the inflammation and anti-oxidant activity.

Numerous studies have suggested a role of oxidative stress in the pathogenesis of rheumatoid arthritis.^[19] Therefore; it was assumed that the reported and well established anti-oxidant properties of *C. speciosus* and its ability to block the COX-2 pathway during the progression of inflammation justify the usage of the plant extract in the treatment of rheumatoid arthritis.

There was a significant reduction in the paw volume in Freund's complete adjuvant induced arthritic rats. The cardinal signs of the chronic inflammatory reactions like redness, swelling, arthralgia and immobility of affected joints were significantly less in the drug treated animal than those of the control. Biochemical parameters also showed a significant improvement from the arthritic condition. The pathogenesis or reasons for development of arthritis following injection of FCA are not fully understood.

CONCLUSIONS

From the present experimental findings of both pharmacological and biochemical parameters observed from the current investigation, it is concluded that at the doses of 400 mg/kg and 800 mg/kg alcoholic extract of *C. speciosus* possesses potentially useful anti-arthritis activity since it gives a positive result in controlling inflammation in adjuvant induced arthritic model in rats. The drug is a promising anti-arthritis agent of plant origin in the treatment of inflammatory disorders.

Table 1: Percentage protection against increase in paw volume

Groups	Day 1	Day 7	Day 14	Day 21
Control	0.50±0.0040	51.17±0.4773	87.83±0.4773	130.3±0.8819
Standard	0.24±0.0006	19.17±0.4773	48.83±0.6009	40.0±0.5774***
Test extract 400 mg/kg	0.26±0.0057	33.17±1.078	77.50±0.8851	75.50±0.9220*
Test extract 800 mg/kg	0.25±0.0085	32.50±0.7638	70.00±0.7303	68.33±1.145**

Table 2: Body weight (grams)

Treatment days	Control	Standard	Test extract 400 mg/kg	Test extract 800 mg/kg
1	151.8±1.07	151.5±1.25	152.0±1.57	151.7±1.62
7	154.0±1.00	160.0±1.23	155.8±0.98	157.8±1.85
14	158.8±0.65	169.7±0.88	164.0±0.59	166.2±1.68
21	163.5±0.99	177.2±0.54***	167.2±0.47*	169.7±0.91**

Table 3: Liver function tests after treatment

Groups	SGPT (IU/L)	SGOT (IU/L)	ALP (Ka)	Bilirubin
Control	145.0±0.57	129.8±0.60	39.67±0.88	4.5±0.42
Standard	63.00±0.57*	73.50±0.76*	22.00±0.57*	1.83±0.30*
Test extract 400 mg/kg	85.00±1.52*	92.50±0.76*	26.17±0.47*	3.50±0.42
Test extract 800 mg/kg	78.83±1.30*	89.50±0.76*	24.67±0.33*	2.00±0.25*

All the results are expressed as Mean±SEM (n=6), for each experimental group. The statistical analysis was carried out using one way ANOVA method. Significant after analysis of variance (ANOVA) followed by Bonferroni's test. *P<0.05, **P<0.01, ***P<0.001 when compared to control group

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How to cite this article: Srivastava S, Singh P, Jha KK, Mishra G, Srivastava S, Khosa RL. Evaluation of anti-arthritis potential of the methanolic extract of the aerial parts of *Costus speciosus*. J Ayurveda Integr Med 2012;3:204-8.

Source of Support: Nil, **Conflict of Interest:** None declared.

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