

## Effect of *Boswellia Serrata* Extract on Acute Inflammatory Parameters and Tumor Necrosis Factor- $\alpha$ in Complete Freund's Adjuvant-Induced Animal Model of Rheumatoid Arthritis

### Abstract

**Context:** The worldwide prevalence of rheumatoid arthritis (RA) is about 1%, whereas in India, it is approximately 0.75%. The current therapy for RA includes nonsteroidal anti-inflammatory drugs corticosteroids, disease-modifying anti-rheumatic drugs and some recently developed biologic agents, but all of these are associated with adverse effects. Some herbal drugs, such as *Boswellia serrata*, have been reported to possess anti-inflammatory activity. **Aims:** The aim of this study is to evaluate the anti-arthritic activity of *Boswellia serrata* extract (BSE) in complete Freund's adjuvant (CFA)-induced arthritis in rats. **Materials and Methods:** Thirty-six Wistar rats were divided into six equal groups. RA was induced by intradermal injection of 0.1 ml CFA in hind paw. Body weight, ankle diameter, paw volume, arthritic index, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and histopathological examination were assessed. The experimental data were statistically assessed by one-way analysis of variance (ANOVA). **Statistical Analysis Used:** The recorded data were analyzed using paired *t*-test and ANOVA test using SPSS. The data were analyzed and represented as mean difference. Value of  $P < 0.05$  was considered statistically significant. **Results:** BSE at dose 180 mg/kg showed statistically significant improvement in body weight and decrease in ankle diameter and arthritic index ( $P < 0.05$ ); however, there was insignificant change in paw volume ( $P = 0.056$ ). This improvement was comparable with Indomethacin. The level of TNF- $\alpha$  did not show any statistically significant change ( $P = 0.076$ ). Histopathological results also exhibited a reduction in inflammatory parameters. **Conclusions:** BSE might have usefulness as an adjunct to conventional therapy of RA.

**Keywords:** *Boswellia serrata* extract, complete Freund's adjuvant, rheumatoid arthritis

### Introduction

Rheumatoid arthritis (RA) is an inflammatory condition of synovial tissue leading to the destruction of joints.<sup>[1]</sup> When this tissue remains constantly inflamed, it leads to deformity by loosening joint ligaments and joint destruction by eroding nearby cartilage and bones.<sup>[2]</sup> The prevalence of RA varies between 0.3% and 1% worldwide and approximately 0.75% in India.<sup>[3]</sup> The current treatment of RA only provides symptomatic relief but not totally prevent joint damage. The commonly used drugs for the treatment of RA such as nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, disease-modifying antirheumatic drugs (DMARDs), and biological response modifiers are associated with many adverse effects.<sup>[4]</sup> The gastrointestinal adverse drug effects of NSAIDs range from minor

uneasiness to life-threatening peptic ulcers. The common adverse effects such as nausea, anorexia, gastritis, epigastric pain, peptic ulcers, flatulence, or diarrhea may occur in 15%–60% of patients.<sup>[5]</sup> Renal and cardiovascular complications such as acute kidney failure, hypertension, and electrolyte abnormalities can also be attributed to NSAIDs. Prolong use of steroids is associated with impaired wound healing, osteoporosis, muscular weakness, cataract, and peptic ulcer.<sup>[6]</sup> Side effects of DMARDs include dysfunction of gastrointestinal organ, liver, kidney coupled with stomatitis, and bone marrow suppression.<sup>[7]</sup> Secondary infections and malignancies such as lymphoma and nonmelanoma skin cancers may develop with the use of biological response modifiers like infliximab.<sup>[8]</sup>

As a result, there is a need for alternative well-tolerated anti-inflammatory remedies.

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Rajendra Kumar,  
Sarvesh Singh,  
Anil Kumar  
Saksena, Rishi Pal,  
Riddhi Jaiswal<sup>1</sup>,  
Rahul Kumar

Departments of Pharmacology  
and <sup>1</sup>Pathology, King George's  
Medical University, Lucknow,  
Uttar Pradesh, India

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### Address for correspondence:

Dr. Rahul Kumar,  
Department of Pharmacology,  
King George's Medical  
University, Lucknow,  
Uttar Pradesh, India.  
E-mail: rahulkgmu@gmail.com

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Gum resin of *Boswellia serrata* extract (BSE) has been found to possess anti-inflammatory potential with better tolerability.<sup>[9]</sup> In India, extract of BSE has been used for centuries as traditional Ayurvedic medicine for treatment of the inflammatory conditions.<sup>[10]</sup> *Boswellia serrata* has also shown the ability to inhibit pro-inflammatory cytokines. It suppresses interleukin-1  $\beta$  (IL-1  $\beta$ ), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interferon- $\gamma$  (IFN- $\gamma$ ), and enhances production IL-10 in collagen-induced arthritis rats. These cytokines have a crucial role in chronic inflammation and tissue damage during the progression of RA.<sup>[11,12]</sup>

Several animal models were developed for RA and complete Freund's adjuvant (CFA)-induced arthritis is commonly used model which shares many features of RA in humans. Hence, we planned this study to evaluate the anti-inflammatory effect of BSE in the acute condition of CFA-induced animal model of RA in Wistar rats.

## Materials and Methods

After being approved by the Institutional Animal Ethics Committee (Project No-72/IAEC/2016 dated 24/09/2016), this study was carried out in 36 healthy adult male Wistar rats having an almost similar physical constitution (in terms of age and body weight), weighing between 150 and 200 g, 6 in each group as-Group 1-Normal Control, Group 2-Arthritic Control, Group 3-Arthritic rats treated with indomethacin (3 mg/kg), Group 4-Arthritic rats treated with *Boswellia serrata* (45 mg/kg), Group 5-Arthritic rats treated with *Boswellia serrata* (90 mg/kg), and Group 6-Arthritic rats treated with *Boswellia serrata* (180 mg/kg). They were kept under standard laboratory conditions of temperature ( $25^{\circ}\text{C} \pm 2^{\circ}\text{C}$ ), humidity ( $55\% \pm 5\%$ ) and 12 h light-dark cycle controlled environment. The animals were provided pellet food diet and water *ad libitum*.

For induction of arthritis, 0.1 ml CFA was injected intradermally in the footpad of left hind paw in rats barring control group.<sup>[13]</sup> All rats studied for an acute inflammatory lesion of arthritis. The treatment was scheduled from day 5 to 15. During the entire course of the study, the standard protocols were followed. Baseline measurement for parameters body weight, paw thickness, ankle diameter, and paw volume was done on day 0. Subsequently, above-mentioned parameters along with an arthritic index and TNF- $\alpha$  was measured on day 5 and 15. On day 15, all rats were sacrificed by using a high dose of pentobarbitone (50 mg/kg i. p).<sup>[14]</sup> The inflamed limbs were excised above the ankle joints and examined for a histopathological finding of rheumatic arthritis.

CFA was purchased from Sigma Aldrich Chemical Co, USA. *Boswellia serrata* tablets (containing *Boswellia serrata* ole-gum resin extract; Oleo-gum-resin is tapped from the incision made on the trunk of the tree) were purchased from Himalaya Healthcare Co., India. Indomethacin 25 mg

tablet was purchased from Jagsonpal Pharmaceuticals. An enzyme-linked immunosorbent assay (ELISA) kit for TNF- $\alpha$  was obtained from Diaclone, France. BSE in the dose of 45 mg/kg, 90 mg/kg, 180 mg/kg, and indomethacin 3 mg/kg was administered in distilled water for oral administration to each rat.<sup>[15,16]</sup>

The body weight (g) of all rats was recorded on day 0, 5, and 15 in the experiment. The percentage change of body weight was calculated using the formula: Percentage change =  $(W_c - W_t) \times 100/W_c$  where  $W_c$  is mean change in body weight of arthritic control group and  $W_t$  is mean change in body weight of the treated group.

Ankle diameter was measured on day 0, 5, and 15 to assess inflammation as acute lesion on an injected limb. The percentage inhibition of ankle diameter was calculated using the formula: Percentage inhibition =  $(D_c - D_t) \times 100/D_c$  where  $D_c$  is mean change in ankle diameter of the arthritic control group and  $D_t$  is mean change in ankle diameter of the treated group.

Paw volume of the injected limb was measured on day 0, day 5, and day 15 by immersed vertically to the level of the lateral malleolus in the plethymometer. Mean change in paw volume was calculated and percentage inhibition of paw edema was calculated using the formula: Percentage inhibition =  $(V_c - V_t) \times 100/V_c$ : where  $V_c$  is mean change in paw volume of the arthritic control group and  $V_t$  is mean change in paw volume of the treated group.

Rats were kept under observation and periodic parametric evaluation for arthritis was done on day 0, 5, and 15. The severity of arthritis was evaluated by grading system: Normal Paw = 0, Mild swelling and erythema of digits = 1, Swelling and erythema of digits = 2, Severe swelling and erythema = 3, Gross deformity and inability to bend the limb = 4. Arthritic index for each rat was calculated by adding the four scores of individual paws.<sup>[17]</sup> If adjuvant injected limb (left hind) was inflamed, the experimental animal was considered to have developed acute arthritis.

The blood sample was withdrawn from the retro-orbital route and serum was separated by centrifugation. Serum level of TNF- $\alpha$  was determined by using commercially available ELISA kits.

For histopathological examinations, rats were sacrificed on day 15 by using a high dose of pentobarbitone (50 mg/kg i. p) and the inflamed limbs were excised above the ankle joints and examined for histopathological findings of rheumatic arthritis. Excised left hind limb tissue fixed in 10% buffer formalin solution from control and treated rats sent to the pathologist for evaluation who was blind to the specimen.

The recorded data were analyzed using paired *t*-test and analysis of variance test using SPSS (IBM SPSS Statistics

Version 24.0. Armonk, NY). The data were analyzed and represented as mean difference. Value of  $P < 0.05$  was considered statistically significant.

## Results

### Effects of *Boswellia serrata* extract on body weight as compared to indomethacin

On day 0, body weight was measured of each rat from every group and taken as baseline values. During the course of the study, the mean % increase in weight in control group was 2.21 ( $P = 0.07$ ), from day 0 to 5 and mean % increase in weight was 0.43 ( $P = 0.78$ ) from day 5 to 15. On day 5, the body weight was found to be decreased in all CFA induced arthritic groups (Groups 2–6). On day 15, weight was increased in indomethacin and BSE treated groups as compared to day 5. Body weight was gained significantly in indomethacin ( $P < 0.05$ ) while insignificant in all BSE treated groups [Table 1a]. On intergroup comparison, body weight was significantly increased in indomethacin-treated group ( $P < 0.01$ ) and BSE 180 mg/kg treated group ( $P < 0.05$ ) as compared to the arthritic control group [Table 1b].

### Effects of *Boswellia serrata* extract on ankle diameter as compared to indomethacin

Before CFA injection ankle diameter of both hind limbs of each rat from every group was measured on day 0 and taken as baseline values. During the course of the study, ankle diameter remained almost unchanged in normal control. In CFA-induced arthritic groups (2–6), ankle diameter values were significantly increased on day 5 as compared to day 0 ( $P < 0.01$ ). In Group 2 (arthritic control), ankle diameter was increased significantly on day 15 as compared to day 5. Following the drug treatment ankle diameter values on day 15 were found to have decreased from day 5 values which were significant in Groups 3, 5, and 6 [Table 2a]. On intergroup comparison, ankle diameter was significantly reduced in indomethacin 3 mg/kg treated group ( $P < 0.05$ ) and BSE 180 mg/kg treated group ( $P < 0.05$ ) as compared to that of arthritic control group [Table 2b].

### Effects of *Boswellia serrata* extract on paw volume as compared to indomethacin

Before CFA injection paw volume of both hind limbs of each rat from every group was measured on day 0 and taken as baseline values. Slight increase in paw volume was observed in the normal control group on day 15 as compared to day 0. Paw volume values were significantly ( $P < 0.01$ ) increased in all CFA-induced arthritic groups (2–6), on day 5 as compared to day 0. Following the drug treatment, paw volume values on day 15 were found to have decreased from day 5 values, but it was significant only in indomethacin-treated group [Table 3a]. Intergroup comparative analysis showed that there was reduction in paw volume on day 15 in all the groups when compared to the arthritic control group, but it was significantly reduced in Group 3 and 6 [Table 3b].

### Effects of *Boswellia serrata* extract on arthritis index as compared to indomethacin

Complete Freund's Adjuvant-induced arthritic rats produced statistically significant ( $P < 0.01$ ) increase in the arthritic index in all arthritic group. Following the drug treatment, arthritic index values on day 15 were found to have decreased from day 5 values, but it was significant only in indomethacin-treated group [Table 4a]. Arthritis index kept on increasing from day 5 to 15 in all the groups, whether control or treated with indomethacin/BSE [Table 4a]. Intergroup comparative analysis showed that there was reduction in the arthritic index on day 15 in all the groups when compared to the arthritic control group, but it was significantly reduced in Group 3, 5, and 6 [Table 4b].

### Effects of *Boswellia serrata* extract on serum tumor necrosis factor- $\alpha$ as compared to indomethacin

In CFA-induced arthritic rats, TNF- $\alpha$  was increased as compared to the normal control group on day 5. TNF- $\alpha$  is an inflammatory marker so its increased level promotes inflammation and joint tissue destruction [Table 5a]. When compared day 15 values from day 5, TNF- $\alpha$  values kept on increasing significantly in the arthritic control group. Only indomethacin-treated group showed a significant decrease in TNF- $\alpha$  levels while treatment with BSE (in any dose) did

**Table 1a: Change in body weight (recorded in grams) of different groups of animals on day 0, 5, and 15 (all values represented here are in mean $\pm$ standard deviation; values on day 0 and 5 represent the value before treatment and values on day 15 are after treatment;  $n=6$ /group; all treatment administered orally)**

Groups	Days of study (mean $\pm$ SD)			% change	
	Day 0	Day 5	Day 15	Days 0-5	Days 5-15
I	188.5 $\pm$ 5.577	192.67 $\pm$ 4.63	193.5 $\pm$ 5.32	-2.21	-0.43
II	186.83 $\pm$ 6.113	176.83 $\pm$ 10.64	169.83 $\pm$ 10.304	5.35	3.96
III	185.83 $\pm$ 8.085	176.33 $\pm$ 9.688	189.5 $\pm$ 6.74	5.11#	-7.47#
IV	185 $\pm$ 8.438	177.17 $\pm$ 9.02	180 $\pm$ 8.877	4.23	-1.60
V	184.17 $\pm$ 7.548	177.67 $\pm$ 9.50	183.33 $\pm$ 7.005	3.53	-3.19
VI	183.17 $\pm$ 6.338	175.83 $\pm$ 6.79	186.33 $\pm$ 7.11	4.01	-5.97

# $P < 0.05$ . SD: Standard deviation

**Table 1b: Change in body weight of treated groups as compared with arthritic control group**

Groups	Mean difference		
	Days 0	Day 5	Day 15
II versus			
III	1.00	0.50	-19.67*
IV	1.83	-0.33	-10.17
V	2.67	-0.83	-13.50
VI	3.67	1.00	-16.50 <sup>#</sup>

\*P<0.01, <sup>#</sup>P<0.05

**Table 2a: Change in ankle diameter (measured in cm) of different groups of animals on day 0, 5, and 15 (all values represented here are in mean±standard deviation; values on day 0 and 5 represent the value before treatment and values on day 15 are after treatment; n=6/group; all treatment administered orally)**

Groups	Day 0	Day 5	Day 15	% change	
				Days 0-5	Days 5-15
I	0.32±0.03	0.32±0.06	0.33±0.01	0.01	-1.03
II	0.33±0.02	0.60±0.03	0.64±0.04	-86.15*	-6.89 <sup>#</sup>
III	0.32±0.02	0.62±0.04	0.40±0.03	-93.32*	35.81*
IV	0.31±0.22	0.56±0.55	0.58±0.03	-81.64*	-4.77
V	0.30±0.13	0.66±0.06	0.55±0.04	-116.82*	16.05 <sup>#</sup>
VI	0.32±0.03	0.65±0.03	0.51±0.03	-105.72*	22.53*

\*P<0.01, <sup>#</sup>P<0.05

**Table 2b: Change in ankle diameter of treated groups as compared with arthritic control group**

Variables	Groups	Mean difference		
		Days 0	Day 5	Day 15
Ankle diameter	II versus			
	III	-0.005	-0.023	0.243 <sup>#</sup>
	IV	0.0116	0.045	0.060
	V	0.0133	-0.060	0.088
	VI	0.001	-0.053	0.136 <sup>#</sup>

<sup>#</sup>P<0.05

**Table 3a: Change in paw volume (measured in ml) of different groups of animals on day 0, 5, and 15 (all values represented here are in mean±standard deviation values on day 0 and 5 represent the value before treatment and values on day 15 are after treatment; n=6/group; all treatment administered orally)**

Groups	Day 0	Day 5	Day 15	% change	
				Days 0-5	Days 5-15
I	0.64±0.01	0.65±0.013	0.68±0.01	0.01	-0.26
II	0.63±0.02	0.99±0.29	1.21±0.14	-52.1 <sup>#</sup>	-21.73
III	0.64±0.01	1.12±0.25	0.70±0.03	-73.27*	37.39 <sup>#</sup>
IV	0.66±0.02	1.23±0.41	0.89±0.08	-84.99 <sup>#</sup>	27.16
V	0.64±0.02	0.99±0.20	0.86±0.08	-54.95*	12.44
VI	0.63±0.02	0.98±0.11	0.80±0.07	-56.08*	17.80 <sup>#</sup>

\*P<0.01, <sup>#</sup>P<0.05

not show any significant change. Intergroup comparative analysis also showed that there was reduction only in

**Table 3b: Effects of Boswellia serrata extract on paw volume in control and treatment group-on day 0, 5, and 15**

Variables	Groups	Mean difference		
		Day 0	Day 5	Day 15
Paw volume	II versus			
	III	-0.018	-0.126	0.510 <sup>#</sup>
	IV	-0.036	-0.236	0.315
	V	-0.010	0.005	0.345
	VI	0.001	0.013	0.405 <sup>#</sup>

<sup>#</sup>P < 0.05

**Table 4a: Arthritis index of different groups of animals on day 0, 5 and 15 (all values represented here are in mean±standard deviation; values on day 0 and 5 represent the value before treatment and values on day 15 are after treatment; n=6/group; all treatment administered orally)**

Groups	Day 0	Day 5	Day 15	% change (days 5-15)	
				Day 0-5	Day 5-15
I	0	0±0	0±0		0.00
II	0	5.66±0.51	19.5±1.22		-244.12*
III	0	5.66±0.51	10.16±0.98		-79.41*
IV	0	5.33±0.51	16.16±2.04		-203.13*
V	0	5.5±0.54	15.5±2.66		-181.82*
VI	0	5.66±0.51	12.66±2.94		-123.53*

\*P<0.01

**Table 4b: Effects of Boswellia serrata extract on Arthritis index in control and treatment group-on day 5 and 15**

Variables	Groups	Mean difference	
		Days 5	Days 15
Arthritic index	II versus		
	III	0.001	9.33*
	IV	0.333	3.33
	V	0.167	4.00 <sup>#</sup>
	VI	0.001	6.83*

\*P<0.01, <sup>#</sup>P<0.05

**Table 5a: Tumor necrosis factor-α of different groups of animals on day 5 and 15 (all values represented here are in mean±standard deviation; values on day 5 represent the value before treatment and values on day 15 are after treatment; n=6/group; all treatment administered orally)**

Groups	Day 5	Day 15	% change (days 5-15)	
			Day 0-5	Day 5-15
I	24.47±0.83	24.35±0.63		0.49
II	24.08±1.04	32.72±1.03		-16.52*
III	27.93±1.25	25.25±0.81		9.60 <sup>#</sup>
IV	28.8±0.17	28.08±2.81		2.50
V	27.43±1.16	26.32±1.75		4.05
VI	28.47±1.01	26.3±1.22		7.62

\*P<0.01, <sup>#</sup>P<0.05

TNF-α on day 15 in indomethacin-treated groups when compared to the arthritic control group [Table 5b].

### Histopathological changes

The histopathological results of inflamed hind limb of arthritic control were compared with that of the normal control group and found that in arthritic control the synovial membrane was thickened, synovial space was reduced and edematous; the articular cartilage found to be damaged with edematous background along with dilated blood vessels; dense inflammatory cells were also present [Figures 1 and 2]. Indomethacin-(3 mg/kg) treated Group-III showed a significant low influx of inflammatory cells and revealed a reduction in pannus formation with reduced neutrophil infiltration and also showing bony spicules along with regenerating marrow tissue [Figures 3 and 4]. BSE treated Group-VI (180 mg/kg) showed reduction in inflammation, cartilage disruption, fibro-osseous proliferation, pannus formation, vascular proliferation, synovial hyperplasia, vasculitis, and fibrinoid necrosis [Figures 5 and 6].

### Discussion

Oleo-gum-resin is prepared from the bark of *Boswellia* tree found in dry deciduous forests of India, Pakistan, and Arabia.<sup>[18]</sup> BSEs consist of Boswellic acids such as 11-keto-beta-boswellic acid (KBA) and acetyl-KBA which affect the cellular defense system by alteration in the levels of different cytokines.<sup>[19]</sup> Anti-inflammatory, antioxidant, antipyretic, antiatherosclerotic, and analgesic activity of *Boswellia serrata* has been described in earlier studies.<sup>[7,9,20]</sup>

The symptoms of RA such as pain, stiffness, swelling, redness, and weight loss are mainly due to inflammation and immunological injury. The present study showed that BSE lessened the inflammation observed by changes in inflammatory parameters of joint-like reduction in ankle diameter, paw volume, and arthritis index. Singh and Atal also showed the anti-inflammatory effects of *Boswellia serrata* in carrageenan-induced rat model of inflammation.<sup>[9]</sup> Anti-inflammatory effects of BSE were further supported by our histopathological findings of the joints. BSE showed a marked reduction in cartilage disruption, fibro-osseous proliferation, pannus formation, vascular proliferation, synovial hyperplasia, vasculitis,

and fibrinoid necrosis which are the hallmark of RA. Our histopathological observations are also supported by a

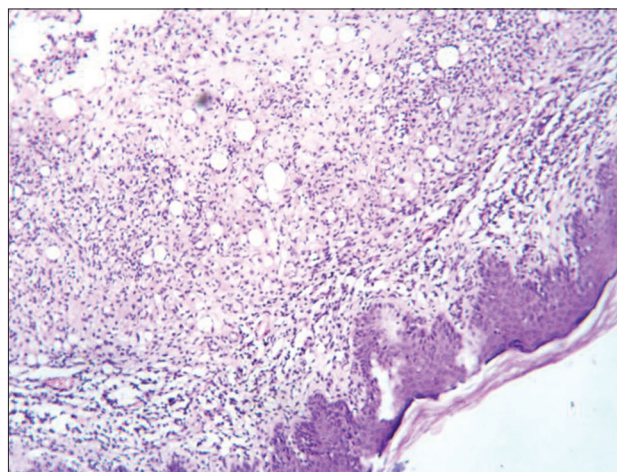


Figure 1: Histopathology of ankle joint cartilage in arthritis control group showing keratinized epidermis with underlying loose subepidermal zone infiltrated by chronic inflammatory cells entrapping fat cells

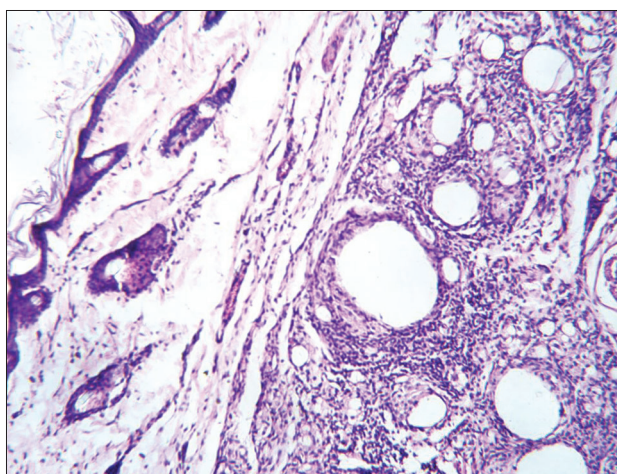


Figure 2: Histopathology of ankle joint bone in arthritis control group showing dense inflammation and pannus

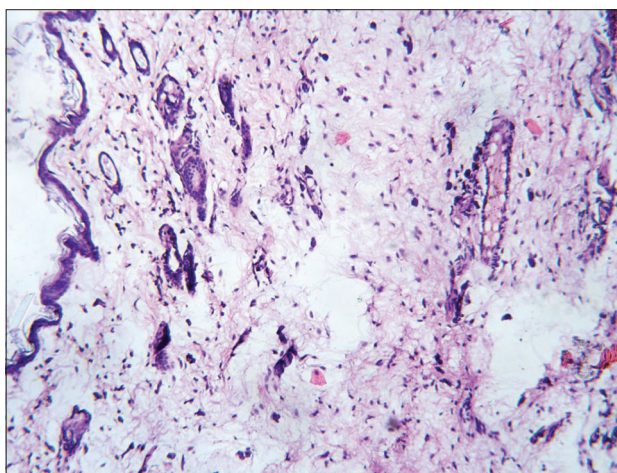
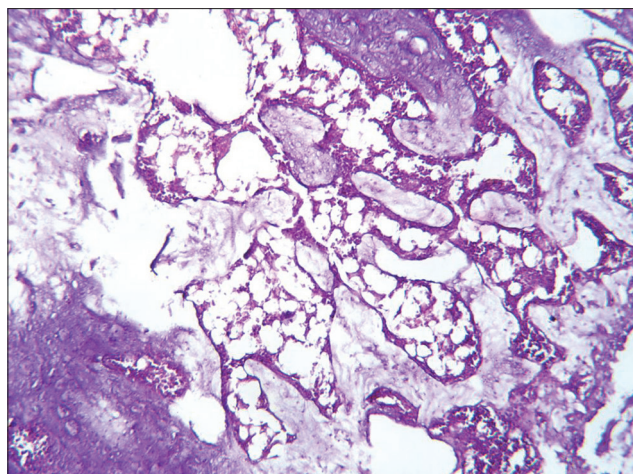


Figure 3: Histopathology of ankle joint in Indomethacin treated group. Response to drug seen in the form of normal thin epidermis and skin appendages

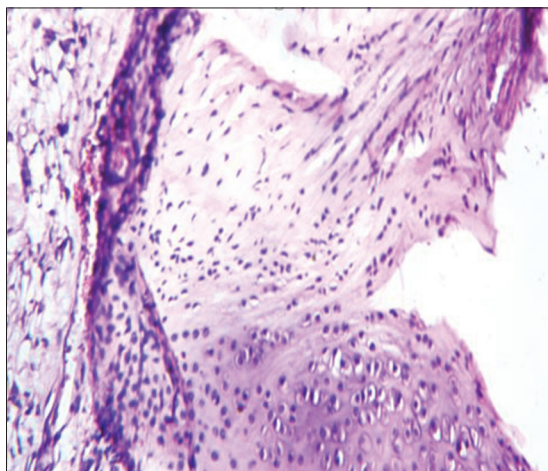
**Table 5b: Effects of *Boswellia serrata* extract on tumor necrosis factor- $\alpha$  in control and treatment group on day 5, and 15**

Variables	Groups	Day 5		Day 15	
		Mean difference	P	Mean difference	P
TNF- $\alpha$	II versus				
	III	0.15	0.94	7.46 <sup>#</sup>	0.01
	IV	-0.71	0.82	3.63	0.08
	V	0.65	0.87	5.40	0.07
	VI	-0.38	0.98	5.41	0.07

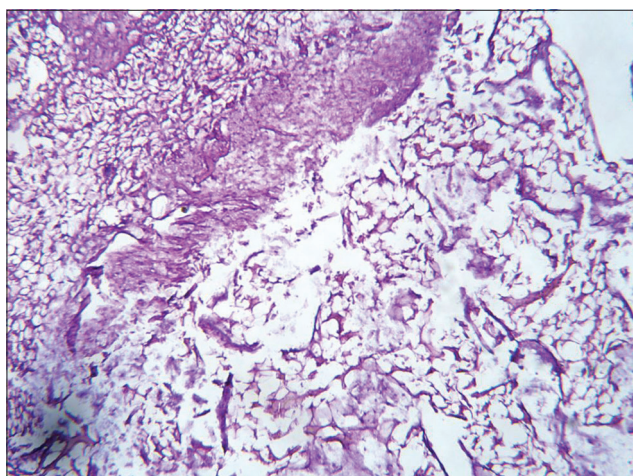
<sup>#</sup>P<0.05. TNF- $\alpha$ : Tumor necrosis factor- $\alpha$



**Figure 4:** Histopathology of ankle joint bone in Indomethacin treated group showing bony spicules with regenerating marrow tissue



**Figure 5:** Histopathology of ankle joint cartilage in *Boswellia serrata* extract treated group



**Figure 6:** Histopathology of ankle joint bone in *Boswellia serrata* extract treated group. Partial effect of drug appears as bone, marrow, and connective tissue are seen regenerating

study in which *Boswellia serrata* reduces cellular infiltrates in carrageenan-induced inflammation model of RA.<sup>[21]</sup>

Along with other symptoms, decrease in weight also has been observed in RA. This condition has been referred to as rheumatoid cachexia (RC). RC is attributed to the increased levels of pro-inflammatory cytokines as IL-1 beta and TNF-alpha.<sup>[22,23]</sup> The present study showed that body weight improves after treatment with different doses of BSE.

However, no significant change was found on serum TNF- $\alpha$  levels by any dose of BSE. Only indomethacin treated group showed a significant decrease in TNF- $\alpha$  levels. While in other studies, BSE treatment showed a significant reduction in levels of several inflammatory mediators including TNF- $\alpha$ .<sup>[24,25]</sup> We were unable to find the reason for this no significant change on serum TNF- $\alpha$  levels by BSE in our study.

Thus, this study suggests that the antiarthritic effect of BSE on joints, bone, and cartilage in CFA-induced arthritic rats was probably mediated by anti-inflammatory action. Therefore, BSE has significant potential as a phytomedicine and might represent an alternative for classical medicine treatments for chronic inflammatory diseases like RA. We believe that our results will contribute to the clinical applications in the treatment of RA. Keeping in view the results obtained in the present study, the following conclusions may be drawn regarding the potential effectiveness of BSE against RA. An effective and dose-dependent anti-arthritis effect of BSE in three doses, i.e., 45, 90, and 180 mg/kg was clearly evident with a more pronounced effect at 180 mg/kg.

A higher dose of BSE was more effective than its lower dose by showing improvement in the body weight, reduction of the paw thickness, reduction of the ankle diameter, reduction of the paw volume, reduction of the arthritic index for acute inflammation in RA. However, it was less effective than the standard drug (Indomethacin) for acute inflammation in RA that shows good anti-inflammatory effect.

### Conclusions

The present animal study has revealed that the BSE has anti-inflammatory potential and can be used as an antiarthritic drug. BSE at the dose of 180 mg/kg is more effective as compared to other BSE doses (45, 90 mg/kg), but less than standard drug (indomethacin 3 mg/kg) in RA parameters. The results of the present study are encouraging and reveal the importance of BSE as a potential anti-arthritis agent. In light of the above evidence, its efficacy should be evaluated in human subjects and the combination of BSE might have potential usefulness as an adjunct to conventional modern therapy in the further management of RA as well as in other inflammatory diseases.

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## Conflicts of interest

There are no conflicts of interest.

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