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(RESEARCH ARTICLE)

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Evaluation of antiarthritic activity of ethanolic extract of Boswellia serrata on CFA induced method in albino rats

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Abstract

Rheumatoid arthritis (RA) is an autoimmune, inflammatory condition mainly characterized by inflammation of the synovial membranes. It predominantly affects women ages 30 to 50, with a prevalence rate of 1in 150.The present study was to evaluate the anti-arthritic activity of ethanolic extract of Boswellia Serrata Bark in complete Freund's adjuvant (CFA)-induced arthritic rats.Arthritis was induced by sub-cutaneous injection of 0.1 ml of CFA in rats. Arthritic arts were divided into different groups and ethanolic extract of Boswellia Serrata Bark (EEBSB) was administered at doses of 100 and 200 mg/kg, p.o for 15 days. The control group received Normal saline. Diclofenac (10 mg/kg, i.p) was used as a standard drug. Paw volumes were recorded on 0, 5and 15 day using a plethysmometer. Blood samples were collected at the end of the experiment from all the groups to analyze the serological rheumatic factors: C-reactive protein (CRP), serum rheumatic factor (SRF) and hematological parameters. EEBSB was also tested for protein denaturation and membrane stabilization activities The collected data were analyzed using paired t-tests and analysis of variance (ANOVA) with SPSS. The data were analyzed and presented as mean differences. A P-value of < 0.05 was considered statistically significant." The EEBSB (100 and 200 mg/kg, p.o) showed significant ($P < 0.01$, $P < 0.05$) reduction in paw volume, change in body weight in CFA rats at 15 day when compared with arthritic control rats. The results obtained from the present study revealed the potential anti-arthritic activity of ethanolic extract from the Barkof B. Serrat.

Keywords: Anti-arthritic activity; Boswelia Serrata Bark; Complete Freund's adjuvant; Diclofenac

1. Introduction

The degradation of joint surfaces, which causes pain, stiffness, and swelling in the joints, is a hallmark of arthritis. Usually, degenerative changes brought on by overuse or injury, like in osteoarthritis (OA), or inflammatory mechanisms, like those found in rheumatoid arthritis (RA), are to blame. RA shares several characteristics with other, less common forms of arthritis, such as psoriatic arthritis, scleroderma, and systemic lupus erythematosus.

350 million individuals worldwide suffer from arthritis, making it one of the most deceptive illnesses. A recent study found that one in four American people suffers from arthritis, which is characterised by excruciating joint pain.[1]Arthritis causes the deterioration of cartilage that typically shields the joints. It triggers an inflammatory response along with an increase in the growth of synovial cells. As a result, excessive accumulation of synovial fluid in the joints forms layers in the synovial cells, leading to inflammation at the joint sites. The condition's histology frequently demonstrates that it also damages the auricular cartilage, leading to joint alkalosis[2]. It is not a single illness, but rather a collection of linked conditions that are all referred to as "Arthritis." About 300,000 children and 47 million adults are impacted in the US alone[3].

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If proper treatment is not received in a timely manner, the problem may result in permanent disability. Due to lost income and the cost of prescription drugs, it causes severe financial hardship on a global scale[4].

1.1. Rheumatoid arthritis (RA):

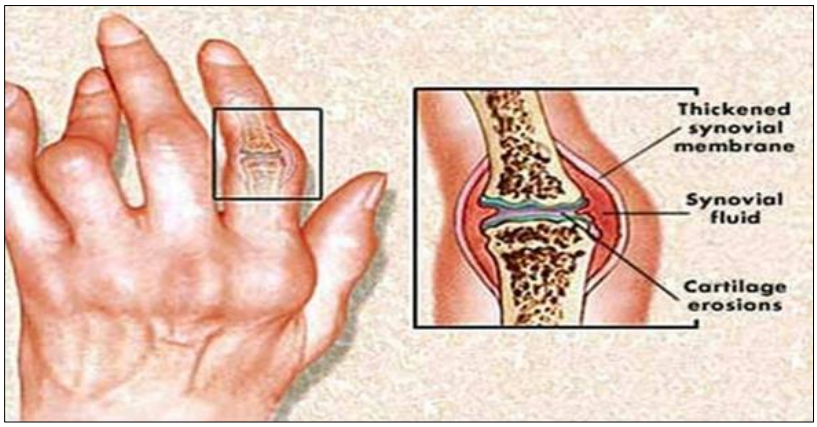

Figure 1 Rheumatoid arthritis

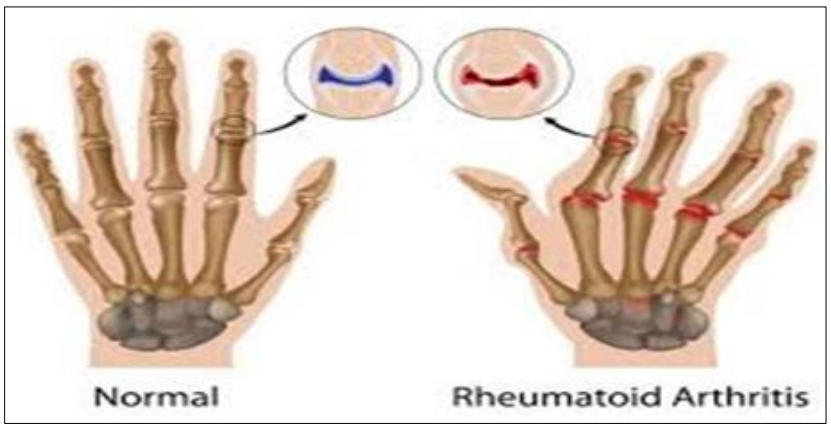

Figure 2 Difference between normal and Rheumatoid arthritis

Rheumatoid arthritis (RA) is an autoimmune, inflammatory condition mainly characterized by inflammation of the synovial membranes. It predominantly affects women ages 30 to 50 years,with a prevalence rate of 1 in 150.

Boswellia serrata (also known as Salai or SalaiGuggal) is a relatively large, branching tree that grows in the hilly regions of India, Northern Africa, and the Middle East. In India, states including Andhra Pradesh, Gujarat, Madhya Pradesh, Jharkhand, and Chhattisgarh are important commercial producers of Boswellia serrata. In different places, this tree is known by different names. Known as Indian olibanum, SalaiGuggal, loban, or kundur, it is one of the most valued plants in Ayurveda.

Its resin has been utilized in religious rituals and cultural celebrations for ages. In Ayurvedic medicine, frankincense (SalaiGuggal) is highly valued for its analgesic, anti-inflammatory, anti-arthritic, and anti-proliferative qualities. Additionally, it is frequently used to treat skin disorders like dermatitis and eczema. Furthermore, Boswelliacarterii frankincense is widely used in Traditional Chinese Medicine (TCM) to encourage vasodilation and alleviate pain in diseases like cancer, gonorrhoea, and leprosy.

2. Materials and Methods

2.1. Drugs and Chemicals

Complete Freund's adjuvant (CFA) was procured from Sigma Aldrich chemicals Pvt. Ltd, Hyderabad, India, Diclofenac was obtained from SD fine chemicals Pvt. Ltd, Chennai, India and all other chemicals used in this study were obtained commercially and were of analytical grade.

2.2. Animals

Male Wistar rats (150-200 g) were obtained from Mahaveer Enterprises, Hyderabad, India. The rats were housed at a temperature of 25 ± 1°C and relative humidity of 45-55% under 12:12 light–dark cycle. The animals had free access to food pellets and water ad labitum. The experimental protocol was approved (IAEC NO:RIPH/2023-24/CPCSEA) by the Institutional Animal Ethics Committee (IAEC), Ratnam Institute ofPharmacy, Nellore and performed in accordance with the guidelines of Committee for Control and Supervision of Experimentation on Animals (CPCSEA), Government of India on animal experimentation.

2.3. Plant Material

Figure 3 *Boswelliaserrata*

2.4. Taxonomical Classification

- Kingdom: Plantae
- Order: Sapindales
- Family: Burseraceae
- Genius: Boswellia
- Species: *B. serrata*
- *Family:: Burseraceae*

2.5. *Collection*

The Fresh Bark of *B. Serrata* were collected from the Tirumala hills, chittor district, A.P, India, and authenticated by Dr. MadhavaChetty from Sri Venkateswara University, Department of Botany, Tirupati, Andhra Pradesh, India.

2.6. Preparation of Ethanolic Extract

Freshly collected plant material was dried under shade and then milled to obtain a coarse powder. The coarsely powdered material (1 kg) was extracted with petroleum ether to remove the fatty material and further, plant material was packed in Soxhlet apparatus and subjected to continuous extraction with ethanol. The liquid extract was collected and concentrated under reduced pressure until a waxy mass was obtained. The mass obtained was weighed in each case.

2.7. Acute Toxicity Studies:

The acute toxicity study was carried out as per the procedure given in Organisation for Economic Co-operation and Development (OECD) Guideline No. 420. The male Wistar albino rats (200-250 g) were used in the study. After the sighting study (allow selection of the appropriate starting concentration for the main study), B. Serrata at the dose of 2 g/kg body weight was given to five animals. The animals were continuously observed for 14 days for mortality and general behavior.

2.8. Pharmacological activity

2.8.1. Adjuvant-Induced Arthritis

Induction of arthritis: Arthritis was induced in rats by the intraplantar injection of 0.1 ml of CFA in the left hind paw. The adjuvant contained heat killed Mycobacterium tuberculosis in sterile paraffin oil (10 mg/ml). The paw volume of all the animal groups was

2.8.2. Experimental design

The arthritic animals were divided into five groups each containing six animals, and one group of normal non-arthritic animals. Ethanolic extract of B. Serrata was given at doses of 100 and 200 mg/kg, for 15 days, as a suspension in CMCat a dose of 0.2 ml/kg to different groups of animals.

- Group I: Normal control (Saline)
- Group II:Positive control (0.1 ml of CFA (CMC))
- Group III: Arthritic animals received Diclofenac a dose of 10 mg/kg
- Group IV: Arthritic animals received EEBSB at a dose of 100 mg/kg Group
- V: Arthritic animals received EEBSB at a dose of 200 mg/kg

"For the induction of arthritis, 0.1 ml CFA was administered subcutaneous injection into the foot pad of the left hind paw of rats, excluding the control group.All rats were monitored for an acute inflammatory response indicative of arthritis. The treatment regimen was carried out fromday5 to day15. Throughout the study, standard protocols were adhered to. Baseline measurements for parameters such as body weight, paw thickness, ankle circumference, and paw volume were recorded onday0. Subsequently, the aforementioned parameters, along with an arthritic score, were assessed on days 5 and 15. Onday15, all rats were euthanized using a high dose of pentobarbital (50 mg/kg i.p.). The inflamed limbs were excised above the ankle joints and analyzed for histopathological evidence of rheumatoid arthritis."

Diclofenac 10 mg/kg was administered in distilled water for oral administration to each rat.The body mass (g) of all rats was recorded on days 0, 5, and 15 during the experiment. The percentage variation in body mass was determined using the formula:

$$\text{Percentage variation}=(Wc - Wt)\times 100/Wc,$$

Where Wc is the average change in body mass of the arthritic control group and Wt is the average change in body mass of the treated group.

Ankle circumference was measured on days 0, 5, and 15 to evaluate inflammation as an acute lesion on the injected limb. The percentage reduction in ankle circumference was calculated using the formula:

$$\text{Percentage reduction}= (Dc - Dt)\times 100/Dc$$

Where Dc is the average change in ankle circumference of the arthritic control group and Dt is the average change in ankle circumference of the treated group."

"Paw volume of the injected limb was measured on days 0, 5, and 15 by immersing it vertically to the level of the lateral malleolus in the plethysmometer. The average change in paw volume was calculated, and the percentage reduction in paw swelling was determined using the formula:

$$\text{Percentage reduction}= (Vc - Vt)\times 100/Vc$$

Where Vc is the average change in paw volume of the arthritic control group and Vt is the average change in paw volume of the treated group.

Rats were monitored and periodically evaluated for arthritis on days 0, 5, and 15.Theseverityof arthritis was assessed using a grading scale:

- Normal Paw =0
- Mild swelling and redness of digits=1
- Swelling and redness of digits = 2
- Severe swelling and redness = 3
- Visible deformity and inability to move the limb=4.

The arthritic score for each rat was calculated by summing the four scores for individual paws.If the adjuvant-injected limb (left hind) showed inflammation, the experimental animal was considered to have developed acute arthritis."

"For histopathological assessments, rats were euthanized on day 15 using a high dose of pentobarbital (50 mg/kg i.p.), and the inflamed limbs were removed above the ankle joints and examined for histopathological signs of rheumatoid arthritis. The excised left hind limb tissue from both control and treated rats was fixed in a 10% buffered formalin solution and sent to a pathologist for evaluation, who was unaware of the group assignments.

2.9. Statistical analysis

The collected data were analyzed using paired t-tests and analysis of variance (ANOVA) with SPSS. The data were analyzed and presented as mean differences. A P-value of < 0.05 was considered statistically significant."

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3. Results and Discussion

3.1. "Impact of *Boswellia serrata* extract on body mass compared to DICLOFENAC

On day 0, body mass was recorded for each rat in all groups and taken as baseline values. Throughout the study, the average %increase in mass in the control group was 2.21 (P = 0.07) from day 0 to day 5, and the average % increase in mass was 0.43 (P = 0.78) from day 5 to day 15. On day 5, a reduction in body mass was observed in all CFA-induced arthritic groups (Groups 2–6). By day 15, body mass had increased in both diclofenac and BSE-treated groups compared to day 5. A significant gain in body mass was observed in the diclofenac group (P < 0.05), while the change was not significant in any of the BSE-treated groups [Table 1a]. Upon intergroup comparison, body mass was significantly higher in the diclofenac-treated group (P < 0.01) and the BSE 180 mg/kg-treated group (P < 0.05) compared to the arthritic control group [Table 1b]."

Table 1a Variation in bodymass (measured in grams) of different animal groups on days 0, 5,and 15 (all values presented as mean ± standard deviation; values on days 0 and 5 represent pre-treatment values, while values on day 15 represent post-treatment values; n=6/group; all treatments administered orally)

GROUPS	Days of study (mean±SD)			% change	
	DAY 0	DAY 5	DAY 15	DAY 0-5	DAY 5-15
I	188.5±5.677	192.67±4.73	193.5±5.42	−2.31	−0.53
II	186.83±6.213	176.83±10.74	169.83±10.404	5.45	3.99
III	185.83±8.185	176.33±9.788	189.5±6.84	5.21#	−7.57#
IV	185±8.538	177.17±9.12	180±8.977	4.33	−1.70
V	184.17±7.648	177.67±9.60	183.33±7.105	3.63	−3.29

Table 1 b Change in bodyweight of treated groups ascompared with arthritic control group

GROUPS	MEAN DIFFERENCE		
	DAY 0	DAY 5	DAY 15
II VERSUS			
III	1.03	0.52	-19.69*
IV	1.85	-0.34	-10.19
V	2.69	-0.85	-13.60

3.2. Impact of*Boswellia serrata* extract on ankle circumference compared to diclofenac

Prior to CFA injection, ankle circumference of both hind limbs of each rat in every group was measured on day 0 and used as baseline values. Throughout the study, ankle circumference remained nearly constant in the normal control group. In CFA-induced arthritic groups (2–6), ankle circumference significantly increased on day 5 compared to day 0 ($P < 0.01$). In Group 2 (arthritic control), ankle circumference increased significantly on day 15 compared to day 5. After drug treatment, ankle circumference values on day 15 were observed to decrease from the day 5 values, with significant reductions in Groups 3, 5, and 6 [Table 2a]. Upon intergroup comparison, ankle circumference was significantly reduced in theindomethacin 3 mg/kg-treated group ($P < 0.05$) and the BSE 180 mg/kg-treated group ($P < 0.05$) compared tothearthriticcontrolgroup[Table2b].

Table 2 a 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	
				Day 0-5	Day 5-15
I	0.33±0.04	0.33±0.07	0.34±0.02	0.02	−1.09
II	0.34±0.03	0.61±0.04	0.65±0.05	−87.25*	−6.91#
III	0.33±0.03	0.63±0.05	0.41±0.04	−94.42*	36.82*
IV	0.32±0.23	0.57±0.56	0.59±0.04	−82.44*	−4.87
V	0.31±0.14	0.67±0.07	0.56±0.5	−117.82*	17.05#

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

variables	groups	Mean difference		
		Day 0	Day 5	Day 15
Ankle diameter	II VERSUS			
	III	-0.006	-0.024	0.343#
	IV	0.0118	0.046	0.160
	V	0.002	-0.054	0.236#

3.3. "Impact of Boswellia serrata extract on paw swelling compared to diclofenac:

Before CFA injection, paw swelling of both hind limbs of each rat in every group was measured on day 0 and used as baseline values. A slight increase in paw swelling was observed in the normal control group on day 15 compared to day 0. Paw swelling values were significantly ($P < 0.01$) higher in all CFA-induced arthritic groups (2–6) on day 5 compared to day 0. After drug treatment, paw swelling values on day 15 showed a decrease from the day 5 values, but this

reduction was significant only in the diclofenac treated group table 3a Intergroup comparison revealed a reduction in paw swelling on day 15 in all groups when compared to the arthritic control group, but the decrease was significant in Groups 3 and 6 [Table 3b]."

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 0-5
I	0.74±0.01	0.75±0.013	0.78±0.01	0.01	−0.26
II	0.73±0.02	0.99±0.29	1.31±0.14	−53.1#	−22.73
III	0.74±0.01	1.22±0.25	0.80±0.03	−74.27*	38.39#
IV	0.76±0.02	1.33±0.41	0.99±0.08	−85.99#	28.16
V	0.74±0.02	0.99±0.20	0.96±0.08	−55.95*	13.44

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	−0.020	−0.136	0.610#
	IV	−0.040	−0.246	0.415
	V	−0.010	0.008	0.365

3.4. Effects of *Boswellia serrata* extract on arthritis index as compared to diclofenac:

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 diclofenac-treated group [Table4a]. Arthritis index kept on increasing from day 5 to 15 in all the groups, whether control or treated with diclofenac/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]

Table 4a Arthritis index of different groups of animals on day 0, 5 and 15 (all values represented hereare in mean±standard deviation;valuesonday0and5representthevalue before treatmentand 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)
I	0	0±0	0±0	0.00
II	0	5.76±0.51	19.7±1.22	−250.12*
III	0	5.76±0.51	10.36±0.98	−80.41*
IV	0	5.43±0.51	16.36±2.04	−206.13*
V	0	5.6±0.54	15.8±2.66	−188.82*

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
	II versus		
	III	0.001	9.43*
Arthritic index	IV	0.343	3.53
	V	0.177	4.02#

3.5. Histopathological studies

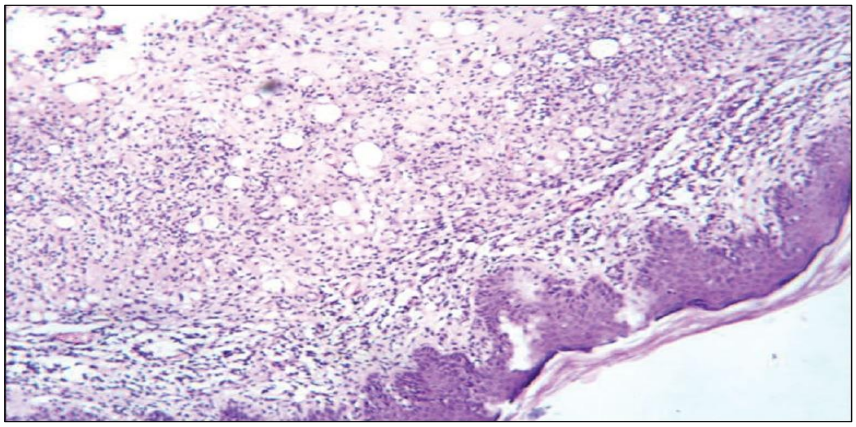

Figure 4 Histopathology of ankle joint cartilage in arthritis control group showing keratinized epidermis with underlying loose subepidermal zone infiltrated by chronic inflammatory cells entrapping fat cells

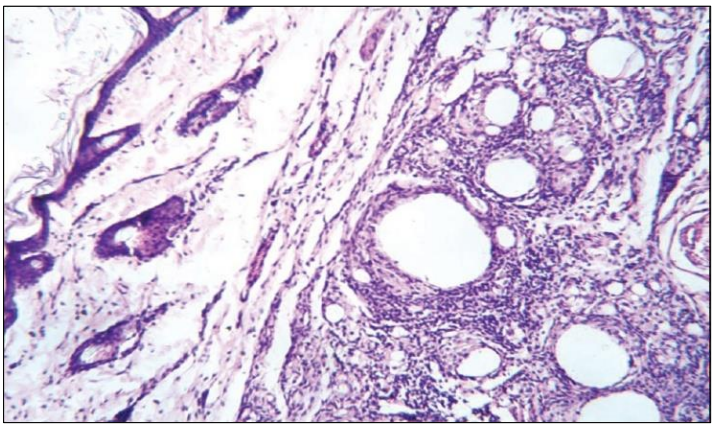

Figure 5 Histopathology of ankle joint bone in arthritis control group showing dense inflammation and pannus

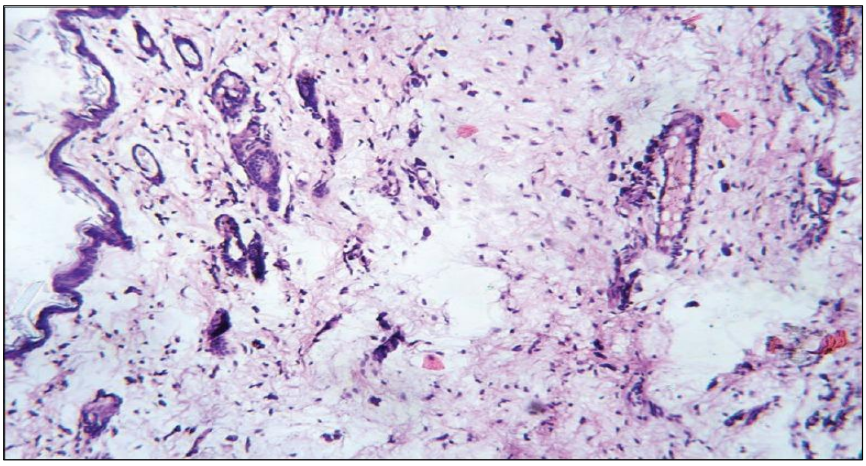

Figure 6 Histopathology of ankle joint in diclofenac treated group. Response to drug seen in the form of normal thin epidermis and skin appendages

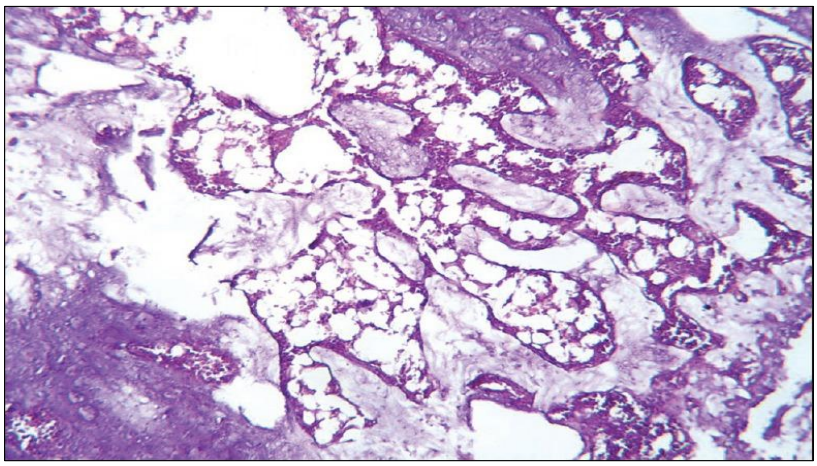

Figure 7 Histopathology of ankle joint bone in diclofenac treated group showing bony spicules with regenerating marrow tissue

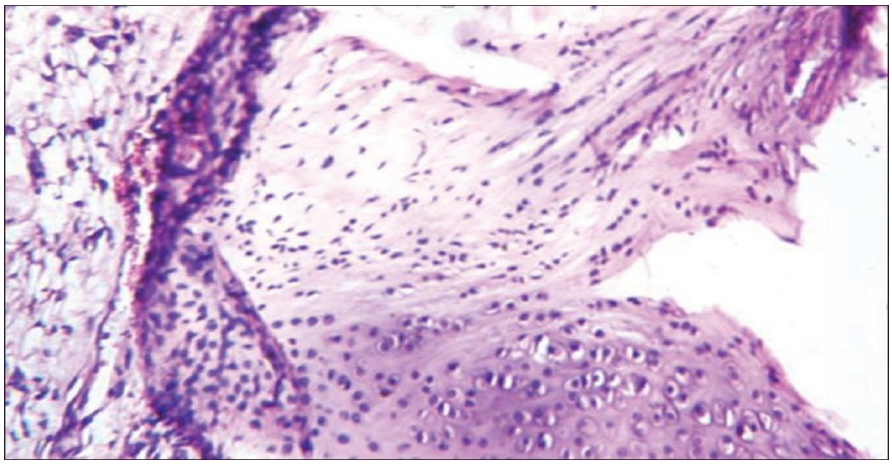

Figure 8 Histopathology of ankle joint cartilage in *Boswelliaserrata* extract treated group

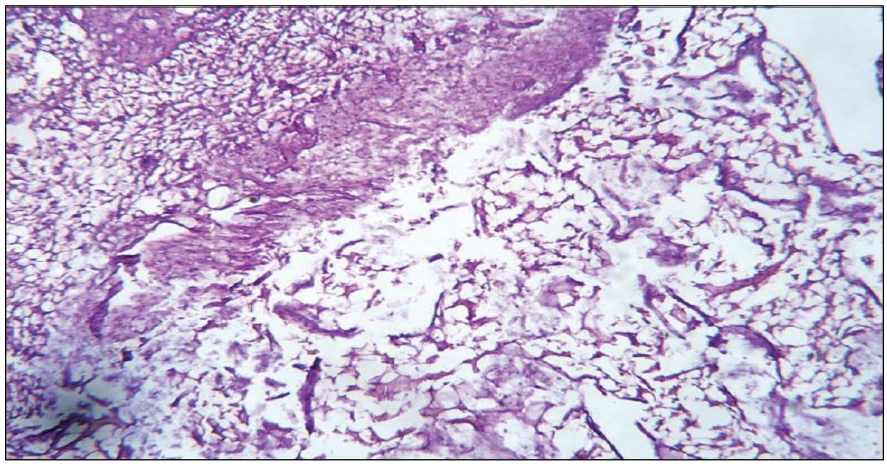

Figure 9 Histopathology of ankle joint bone in *Boswelliaserrata* extract treated group. Partial effect of drug appears as bone, marrow, and connective tissue are seen regenerating

4. Conclusion

The CFA induced method was commonly employed experimental model for evaluating the anti-inflammatory activity of natural compounds. The results treatment of *Boswellia Serrata* inhibited the edema and decreases the inflammatory mediators..The current animal investigation has demonstrated that *Boswellia Serrata* possesses anti-inflammatory properties and could serve as a potential treatment for arthritis. At a dosage of 200 mg/kg, *Boswellia Serrata* proves to be more effective than lower doses (100 mg/kg), though still less potent than the reference drug (diclofenac 10 mg/kg) in terms ofarthritis . The findings from this study are promising and underscore the significance of *BoswelliaSerrata*as a prospective anti-arthritic compound. Given this evidence, its effectiveness should be assessed in human trials, and the combination of *Boswellia Serrata* may hold considerable promise as an adjunct to conventional treatments in the ongoing management of arthritis and potentially other inflammatory disorders.

The anti-arthritic activities of the ethanolic extract may be attributed to the presence of compounds such as terpenoids, flavonoids, and triterpenoids, including taraxerol, taraxerone, rutin, quercetin, delphinidin, kaempferol, and malvidin. Nonetheless, additional research is necessary to isolate and characterize the specific phytochemicals in *Boswellia Serrata* responsible for these effects, which could pave the way for the future use of isolated compounds from *Boswellia Serrata* in the treatment of inflammation-related disorders.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

All experimental procedures involving animals were conducted in strict accordance with the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India. The study protocol was reviewed and approved by the Institutional Animal Ethics Committee (IAEC) of Ratnam Institute of Pharmacy, Nellore (CPCSEA Registration No.:1558/PO/Re/S/11/CPCSEA___, Approval No.: __IAEC/RIPH/2023-24/03. All efforts were made to minimize animal suffering and to reduce the number of animals used in the study.

References

[1] Laev, S.S.; Salakhutdinov, N.F. Anti-arthritic agents: Progress and potential. Bioorg. Med Chem. 2015, 23, 3059-3080. (Google scholar)

[2] Katz, J.N.; Arant, K.R.; Loeser, R.F. Diagnosis and treatment of hip and knee osteoarthritis: A review. JAMA 2021, 325, 568-578 (PubMed).

[3] Arthritis Foundation; www.arthritis.org

[4] Maetzel A, Li LC, Pencharz J, Tomlinson F, Bombardier C. The economic burden associated with osteoarthritis, rheumatic arthritis and hypertension: a comparative study. Ann. Rheum. Dis. 2004; p395 – 401 Vol. 63 (4).

[5] Drake R, Vogl AW, Mitchell AWM in "Grey's Anatomy" 2nd Ed. 2009; Skeletal muscle system. p21 – 52.

[6] Geriatric Education and Research Institute "GERI"; www.foxgen.org.

[7] Lawrence RC, Felson DI, Helmick CG. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum. 2008; p26 – 35 Vol. 58 (1).

[8] Lawrence RC, Felson DI, Helmick CG. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum. 2008; p26 – 35 Vol. 58 (1).

[9] Loeser RF, et al. Osteoarthritis: a disease of the joint as an organ. Arthritis Rheum. 2012;64(6):1697–707.

[10] Pardhy RS, Bhattacharyya SC. β-Boswellic acid, acetyl- β-boswellic acid, acetyl-11-keto-β-boswellic acid and 11-keto-β-boswellic acid, four pentacyclictriterpenic acids from the resin of BoswelliaserrataRoxb. Indian J Chem. 1978;16B:176–8. [Google Scholar]

[11] Mahajan B, Taneja SC, Sethi VK, Dhar KL. Two triterpenoids from Boswelliaserrata gum resin. Phytochemistry. 1995;39:453–5. [Google Scholar]

[12] Handa SS. Herbal raw material and traditional remedies. Eastern Pharmacist. 1995;3:24. [Google Scholar]

[13] Choudhary AC, Dikshit SK. Ayurvedic Pharmacopoeia. Eastern Pharmacist. 1999;10:52. [Google Scholar]

[14] Sane RT. Standardization, quality control, and GMP for herbal drug. Indian Drugs. 2002;39:184–90. [Google Scholar]

[15] Sharma S, Thawani V, Hingorani L. Pharmacokinetic study of 11-keto-beta-boswellic acid. Phytomedicine. 2004;11:255–60. doi: 10.1078/0944-7113-00290. [DOI] [PubMed] [Google Scholar]

[16] Dhiman AK. Delhi: Daya Publishing House; 2006. Ayurvedic Drug Plants; pp. 326–7. [Google Scholar]

[17] Hostanska K, Daum G, Saller R. Cytostatic and apoptosis-inducing activity of boswellic acids toward malignant cell lines in vitro. Anticancer Res. 2002;22:2853–62. [PubMed] [Google Scholar]

[18] Lemenih M, Teketay D. Frankincense and myrrh resources of Ethiopia: II.Medicinal and industrial uses. Ethiop J Sci. 2003;26:161–72. [Google Scholar]

[19] Mathe C, Culioli G, Archier P. Characterization of archeological frankincense by gas chromatography mass spectrometry. J Chromatogr. 2004;1023:277–85. doi: 10.1016/j.chroma.2003.10.016. [DOI] [PubMed] [Google Scholar]

[20] Radiopedia RA Availablefrom: https://radiopaedia.org/articles/rheumatoid-arthritis(accessed 7.6.2021) Rheumatoid Arthritis: Causes, Symptoms, Treatments and More

[21] Arthritis Foundationhttps://www.arthritis.org › diseases › rheumatoid-arthritis

[22] Dalbeth N., Merriman T.R., Stamp L.K. Gout Lancet. 2016;388(10055):2039–2052. doi: 10.1016/S0140-6736(16)00346-9. [DOI] [PubMed] [Google Scholar]

[23] Kuo C.F., Grainge M.J., Zhang W., Doherty M. Global epidemiology of gout: prevalence, incidence and risk factors. Nat Rev Rheumatol. 2015;11(11):649–662. doi: 10.1038/nrrheum.2015.91. [DOI] [PubMed] [Google Scholar]

[24] Mandal A.K., Mount D.B. The molecular physiology of uric acid homeostasis. Annu Rev Physiol. 2015;77:323–345. doi: 10.1146/annurev-physiol-021113-170343. [DOI] [PubMed] [Google Scholar]

[25] Dalbeth N., Merriman T.R., Stamp L.K. Gout Lancet. 2016;388(10055):2039–2052. doi: 10.1016/S0140-6736(16)00346-9. [DOI] [PubMed] [Google Scholar]

[26] Kamei K., Konta T., Hirayama A., Suzuki K., Ichikawa K., Fujimoto S. A slight increase within the normal range of serum uric acid and the decline in renal function: associations in a community-based population. Nephrol, Dialysis, Transplant: official publication of the European Dialysis and Transplant Association – European Renal Association. 2014;29(12):2286–2292. doi: 10.1093/ndt/gfu256. [DOI] [PubMed] [Google Scholar]

[27] Bursill D, Taylor WJ, Terkeltaub R, Abhishek A, So AK, Vargas-Santos AB, Gaffo AL, Hyperuricaemia and Crystal-Associated Disease Network (G-CAN) consensus statement regarding labels and definitions of disease states of gout. Ann Rheum Dis. 2019 Nov;78(11):1592-1600.[PubMed]

[28] Bursill D, Taylor WJ, Terkeltaub R, Kuwabara M, Merriman TR, Grainger R, Pineda C, Louthrenoo W, Edwards NL, Gout, Hyperuricemia, and Crystal-Associated Disease Network Consensus Statement Regarding Labels and Definitions for Disease Elements in Gout. Arthritis Care Res (Hoboken). 2019 Mar;71(3):427-434. [PMC free article] [PubMed]

[29] Dalbeth N, Gosling AL, Gaffo A, Abhishek A. Gout. Lancet. 2021 May 15;397(10287):1843-1855. [PubMed]

[30] Desai J, Steiger S, Anders HJ. Molecular Pathophysiology of Gout.TrendsMol Med. 2017 Aug;23(8):756-768. [PubMed]

[31] Singh JA, Yu S. The burden of septic arthritis on the U.S. inpatient care: A national study.PLoS One.2017;12(8):e0182577.[PMC free article] [PubMed]

[32] Wu CJ, Huang CC, Weng SF, Chen PJ, Hsu CC, Wang JJ, Guo HR, Lin HJ. Septic arthritis significantly increased the long-term mortality in geriatric patients.BMCGeriatr. 2017 Aug 09;17(1):178.PMC free article] [PubMed]

[33] Hassan AS, Rao A, Manadan AM, Block JA. Peripheral Bacterial Septic Arthritis: Review of Diagnosis and Management.JClin Rheumatol.2017 Dec;23(8):435-442.[PubMed]

[34] Margaretten ME, Kohlwes J, Moore D, Bent S. Does this adult patient have septic arthritis? JAMA. 2007 Apr 04;297(13):1478-88.[PubMed]

[35] Horowitz DL, Katzap E, Horowitz S, Barilla-LaBarca ML. Approach to septic arthritis.AmFam Physician.2011 Sep 15;84(6):653-60. [PubMed]

[36] Smith IDM, Milto KM, Doherty CJ, Amyes SGB, Simpson AHRW, Hall AC. A potential key role for alpha-haemolysin of Staphylococcus aureusin mediating chondrocyte death in septic arthritis.Bone Joint Res.2018 Jul;7(7):457-467.[PMC free article] [PubMed]

[37] Wells AU, Denton CP. Interstitial lung disease in connective tissue disease – mechanisms and management. Nat Rev Rheumatol 2014; 10: 728–739.

[38] Gabriel SE, Michaud K. Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases. Arthritis Res Ther 2009; 11: 229.

[39] Radner H, Yoshida K, Smolen JS, et al. Multimorbidity and rheumatic conditions – enhancing the concept of comorbidity. Nat Rev Rheumatol 2014; 10: 252–256. Lakomek HJ, Brabant T, Lakomek M, et al. Multimorbidity in elderly rheumatic patients part 1. Z Rheumatol 2013; 72: 530–538.

[40] Robinson DJr, Hackett M, Wong J, et al. Co-occurrence and comorbidities in patients with immune-mediated inflammatory disorders: an exploration using US healthcare claims data, 2001–2002. Curr Med Res Opin 2006; 22: 989–1000.

[41] Valančienė G, Jasaitienė D, Valiukevičienė S (2010). "Pathogenesis and treatment modalities of localized scleroderma" (PDF). Medicina. 46 (10): 64956. doi:10.3390/medicina46100092. PMID 21393982. Archived (P DF) from the original on 2014-03-06.