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ANTI- INFLAMMATORY AND ANTI-ARTHRITIC ACTIVITY OF *JASMINUM AURICULATUM VAHL* FLOWER EXTRACT

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ABSTRACT

Aim: Aqueous extract of flower *Jasminum auriculatum vahl* (Oleaceae) was evaluated for anti-inflammatory and anti-arthritic activity using Carrageenan induced paw edema and Complete Freund's adjuvant induced arthritis model in rats respectively. **Materials and Methods:** The flowers of the plant *Jasminum auriculatum* was collected, shade dried and extracted by maceration method using Chloroform water I.P. Aqueous extract was subjected for phytochemical screening, pharmacognostic evaluation and acute oral toxicity as per OECD guidelines (423). Anti-inflammatory activity was tested by measuring change in rat paw edema induced by Carrageenan subcutaneously in rats. Antiarthritic activity was also evaluated by measuring paw volume, arthritic index, and body weight induced by Complete Freund's adjuvant in rats. The determination of hematological parameters and markers in serum levels of enzymes like SGPT, SGOT, serum RF and histopathological studies also conducted. **Results:** phytochemical screening revealed the presence of alkaloids, flavonoids, terpenoids, phenolsand tannins as active constituents. In acute oral toxicity study, the AEJA has produced no lethality with a maximum dose of 2000 mg/kg body weight hence 1/5th, 1/10th and 1/20th mg/kg body weight were taken as lower, moderate and higher dose respectively. AEJA at concentration of 100, 200 and 400 mg/kg was able to reduce the inflammation induced bycarrageenan in rats. However, 200mg/kg, 400 mg/kg has shown significant inhibition of arthritis in rats when challenge with CFA (0.1 ml) in rats. The AEJA of dose of 200 mg/kg, 400 mg/kg has maintained normal architecture of Bone, normal (areolar) Synovium and normal histology as compared to arthritis control. **Conclusion:** Our study concludes that the AEJA possess anti-oxidant, anti-inflammatory and anti-arthritic activity in a dose dependent manner. The activity of extract may be due to the presence of phytochemicals i.e., flavonoids, terpenoids and phenols as active constituents.

KEYWORDS: Inflammation, RA-Rheumatoid arthritis, Complete Freund's adjuvant, Carrageenan, AEJA-Aqueous extract of *Jasminum auriculatum.*

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory illness that causes severe disability and early mortality. It is characterised by joint swelling, joint discomfort, and destruction of synovial joints. With a prevalence of just under 1%, RA is a relatively prevalent disease.[1] The joint inflammation in RA is immunologically mediated, and genetics, environmental triggers, and chance interact complexly, but the initiating agents are yet unknown.[2]

Traditional non-selective NSAIDs, disease-modifying anti-rheumatic medications (DMARDs), glucocorticoids, and biologics are the therapeutic options utilised to treat RA. These therapies have a limited clinical benefit and are accompanied with high levels of toxicity.[3],[4] Patients with RA frequently look for alternate means for symptomatic relief and are among the greatest consumers of such approaches due to the side-effects and expensive cost of these immunomodulatory medications.[1],[5]

Jasminum auriculatum vahl belonging to family Oleaceae, it is an evergreen shrub; native to Deccan Peninsula, Circars and Carnatic extending south wards to Travancore. It is commercially cultivated for its fragrant flowers mainly in Ghazipur, Jaunpur, Farrukhabad and Kanauj districtsof U.P, Bihar and Bengal. It is also found in Nepal, Srilanka, E.Asia, Thailand. In India it is also cultivated in Karnataka, Tamilnadu, Andhra Pradesh.[6]

Jasminum auriculatum Vahl (Oleaceae) commonly known as Juhi, Needle flower jasmine, Yutika, grows almost throughout South India, on the dry slopes of the Western Ghats. J. auriculatum has been claimed in traditional literature to be valuable against a wide variety

of diseases. Indian Materia Medica describes the use of flowers of J. auriculatum in the treatment of a number of ailments, including burning sensation, diuretic, hyperdesia ulcers, odontalgia, stomatopathy, ophthalmopathy, cardiopathy, urolithiasis, nephrolithiasis, strangury and dermatopathy.[7]

Phytomedicine is the practise of treating human sickness with plant parts or extracts.[8] The use of herbal remedies is a strategy that may be traced back to the prehistoric traditional medical system. Theimmune-mediated disease development that resembles rheumatoid arthritis doesn't start in the complete Freund's adjuvant (CFA) model until 13 days have passed.[9] The main cause of sustained arachidonic acid generated arthacoid-induced articular and periarticular inflammation in arthritis is an immunological hyper-reactive state caused predominantly by tumour necrosis factor (TNF)-a, interleukin (IL)-6, and IL-1b in synovium. Because of this, NSAIDs only effectively reduce inflammation; they have a minimal to no impact on the progression of disease.[10][11]

Therefore, the present study was carried out to evaluate the anti-inflammatory and anti- arthritic efficacy of Aqueous extract of *Jasminum auriculatum* flower in two different experimental models with emphasis on pro-inflammatory cytokines associated with arthritis.

MATERIALS AND METHODS

Plant material and preparation of extract

The plant *Jasminum auriculatum* belonging to the family Oleaceae, it is widespread across South India. For the present study, the flowers of the plant were collected from Ethno Medicinal Graden, FRLHT in Jarakabande Kaval, Post Attur, Bangalore. The dried plant flowers were identified, confirmed and authenticated by Dr. N. M. Ganesh Babu, Associate Professor, Heading Centre for Herbal Garden, Bangalore- 560064. The flowers of the plant were dried in shade. The dried material was then reduced to coarse powder using a mechanical grinder. The resulting powder was then used for extraction by maceration method.

Animals

Healthy female mice weighing (25-30g) were used for acute toxicity studies.

Healthy wistar rats of approximately same age (12 to 13weeks), weighing between 200- 250g were taken for evaluating anti- inflammatory and anti-arthritic study. All the animals were procured from drug testing laboratory, Bangalore.

The animals were acclimatized by keeping them in animal house facility of Government College of pharmacy, Bangalore. They were housed in polypropylene cages containing beddingmaterial as husk and maintained under standard husbandry conditions and 12hrs light and 12hrs dark cycle. They were fed with commercial pelleted rat chow with water ad. libitum. The animals were maintained in accordance with the CPCSEA guidelines. The acute toxicity and anti-inflammatory activity studies were conducted after obtaining the approval from Institutional Animal Ethical committee (IAEC) with a reference no. GCP/IAEC/DOP/2021-2022/53 dated 01/01/2022.

Toxicity studies of the extracts

Acute toxicity study (OECD 423 guidelines) was carried out using female mice (25- 30g) those maintained under standard husbandry conditions. The maximum upper limit dose 2000mg/kg of aqueous extract of *Jasminum auriculatum* flower were administered orally to three female mice. Animals were observed for 48hrs to study the general behaviour of animals, signs of discomfort and nervous manifestation. All the animals were observed for behavioral changes and mortality till 14 days after administration of the dose.

Carrageenan-induced paw edema

Five groups of Wistar albino rats (n=6) were used in this study. Animals were fasted overnightwith free access to water before the experiment. On the day of experiment, baseline paw volumes were recorded by using a plethysmometer (Ugo Basile 7140, Italy). Thereafter groupI received normal saline served as the control, group II received Diclofenac sodium (10 mg/kg)[12] and groups III, IV and V received AEJA in doses of 100, 200 and 400 mg/kg, respectively, by gavage. 1 hr after administration of the vehicle/drug, edema was induced by the subcutaneous administration of 0.1 ml of 1% carrageenan, constituted in normal saline into the sub-plantar surface of the left hind paw of the rat.[13][14] Thereafter the increase in paw volume was measured at 0.5,1, 2, 3, 4 and 5 h post-carrageenan administration.

Adjuvant-induced arthritis

Six groups of Wistar albino rats (n = 6) were used in the study. On the day of the experiment, baseline recording of paw volumes were recorded by using a plethysmometer (Ugo Basile 7140, Italy). 1 hr after administration of the vehicle/drug, except group I are treated with singlesub plantar injection of 0.1 ml of CFA (Each ml of CFA contains 1 mg of heat killed and dried Mycobacterium Tuberculosis,0.855 ml of paraffin oil and 0.15 ml of mannide monooleate) inducing rheumatoid arthritis. For Group III Diclofenac sodium (10 mg/kg) and for Group IV, Group V, Group IV low, intermediate and high doses of *Jasminum auriculatum* extract respectively treated from 1st day to till 28th day once daily by oral route.

On 28th day, all the animals are anaesthetized and the blood samples are collected by retro orbital puncture method for hematological analysis and separated serum is subjected to analysis of RF, SGPT and SGOT. The animals are sacrificed and limbs are isolated, cleaned off and preserved in 10% formalin. The isolated limbs are subjected to histopathological studies. Briefly, serum RF

was measured by using a commercial serum RF latex kit and SGPT and SGOT was estimated by using diagnostic test kits. Hematological parameters were analyzed by hematology analyser.

Statistical method

Statistical analysis was done using one-way analysis of variance followed by Dunnette's Multiple Comparison (Graphpad prism; Version 9.2.0 (332)). $P < 0.05$ was considered to be significant.

RESULTS

Toxicity profile of the test plant

Toxicity studies were done as per OECD guidelines (423). The Aqueous extract of *Jasminum auriculatum* was found devoid of mortality of animals at the dose of 2000 mg/kg body weight. Hence this dose was treated as maximum tried dose and 1/20th (100 mg/kg, p.o.),1/10th (200 mg/kg, p.o.), 1/5th (400 mg/kg, p.o.) of the 2000mg/kg was selected as therapeutic dose (TD) for the screening of anti-inflammatory activity on Carrageenan induced paw edema and CFA induced arthritis.

Effect of AEJA on Carrageenan-induced paw edema

Anti-inflammatory activity of AEJA was evaluated using the carrageenan-induced paw edema model. In this model, the maximum phlogistic response of carrageenan was observed at 3–5 h in control animals. The AEJA group produced a dose-dependent reduction in paw volume throughout the observation period as compared to the control group. AEJA at doses of 200 and 400 mg/kg showed a significant decrease in edema as compared to control animals (Fig. 1).

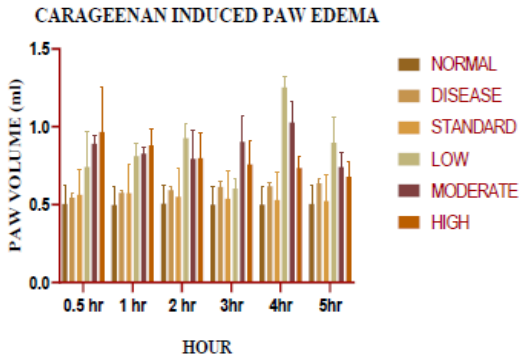

Fig 1: Effect of AEJA on carrageenan induced paw edema.

Effect of EECH on CFA-induced arthritis in rats

Immunization with CFA produce arthritis and an increase in the paw volume of all animals. The standard drug Diclofenac sodium produced a significant decrease in paw volume and wassuperior to the AEJA group at all doses. On day 7, there is maximum swelling of joints after which there was a gradual reduction in all groups except in the control group at day 28. AEJA produced a dose-dependent reduction of joint swelling throughout the study. Except AEJA (100mg/kg), all showed the significant anti-arthritic activity as compared to control at all observation periods (Fig. 2)

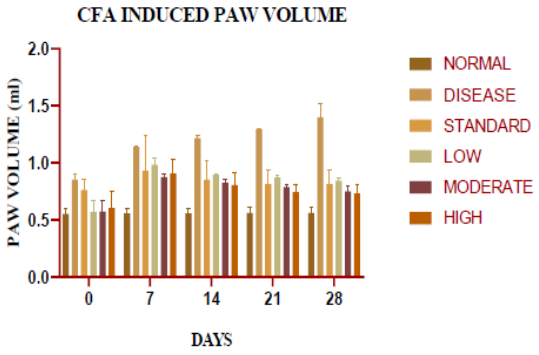

Fig 2: Effect of AEJA on CFA induced arthritis model.

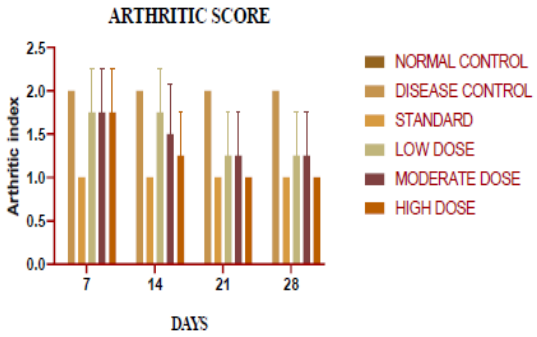

Fig 3: Effect of AEJA on Arthritis score.

Effect of AEJA treatment on serum RF, SGPT and SGPT levels in CFA induced arthritis

The serum collected on day 28 in the CFA study was used for the estimation of levels RF, SGPT and SGOT. The result of serum RF, SGPT and SGOT are presented in figure 4,5 and 6respectively.

AEJA treatment produces a dose-dependent reduction in serum RF, SGPT and SGOT as compared to control group animals. There was reduction in serum RF, SGPT and SGOT expression in the AEJA treated group as compared to control and was found to be statistically significant.

RHEUMATOID FACTOR

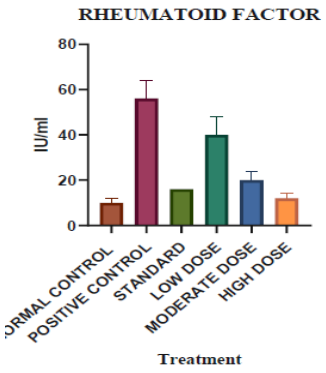

Fig 4: Effect of AEJA on Serum RF

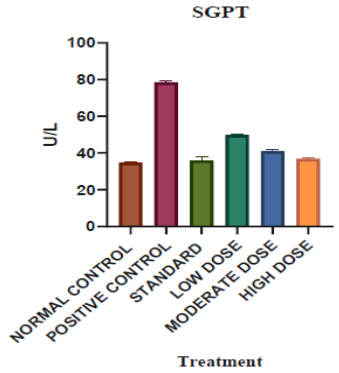

Fig 5: Effect of AEJA on SGPT

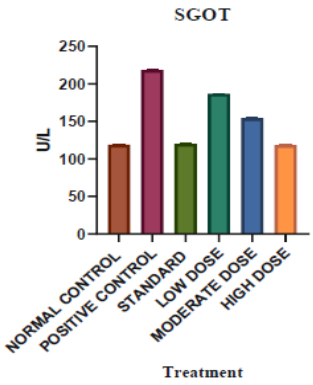

Fig 6: Effect of AEJA on SGOT

Effect of AEJA treatment on hematological parameters in CFA induced arthritis

The blood collected on day 28 in the CFA study was used for the estimation of levels RBC, WBC, HB and ESR. The result of hematological parameters are presented in figure 7,8,9 and 10 respectively.

AEJA treatment produces a dose-dependent reduction in serum RF, SGPT and SGOT as compared to control group animals. There was reduction in serum RF, SGPT and SGOT expression in the AEJA treated group as compared to control and was found to be statistically significant.

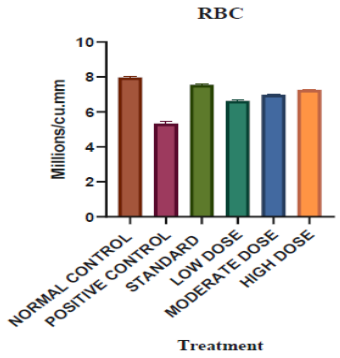

Fig 7: Effect of AEJA on RBC.

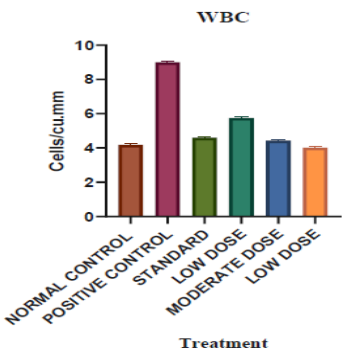

Fig 8: Effect of AEJA on WBC.

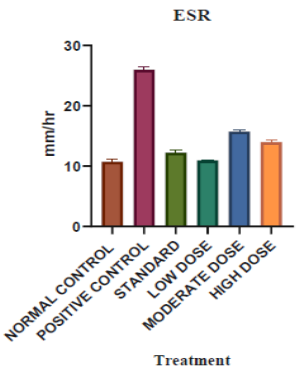

Fig 9: Effect of AEJA on ESR.

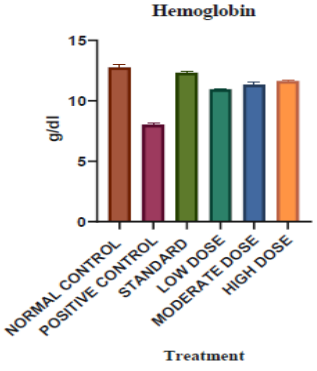

Fig 10: Effect of AEJA on Hb.

Effect of AEJA treatment on histopathology in CFA induced arthritis

The normal control animals show normal architecture of Bone and normal(areolar) Synovium normal histology was observed in slide no.1 and 2. The disease control animals injected with CFA (0.1 ml) shows lymphoid follicular fibrosis, extensive inflammation and arterial fibrosis was observed in slide no 3 and 4. The standard group animals shows normal architecture of Bone and normal (areolar) synovial cells with follicles was Observed in slide no.5 and 6. The lower group animals shows moderate edema with mixed inflammation and congested vascular spaces was observed in slide no.7 and 8. The moderate group animals shows intact articular hyaline cartilage and few congested vascular spaces was observed in slide no. 9 and 10. The higher group animals shows intact articular hyaline cartilage occasional macrophages with abundant fibrocollagenous stroma and intact vascular spaces were observed in slide no.11 and 12. because of due reduction in the release of chemical mediators of the inflammatory process.

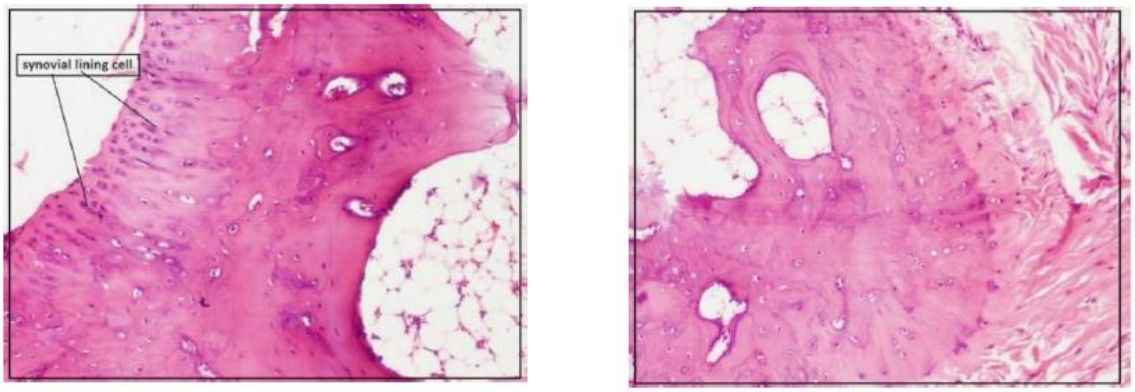

Fig 11 & 12: Normal architecture of Bone; The normal (areolar) synovial lining cells normal histology is observed.

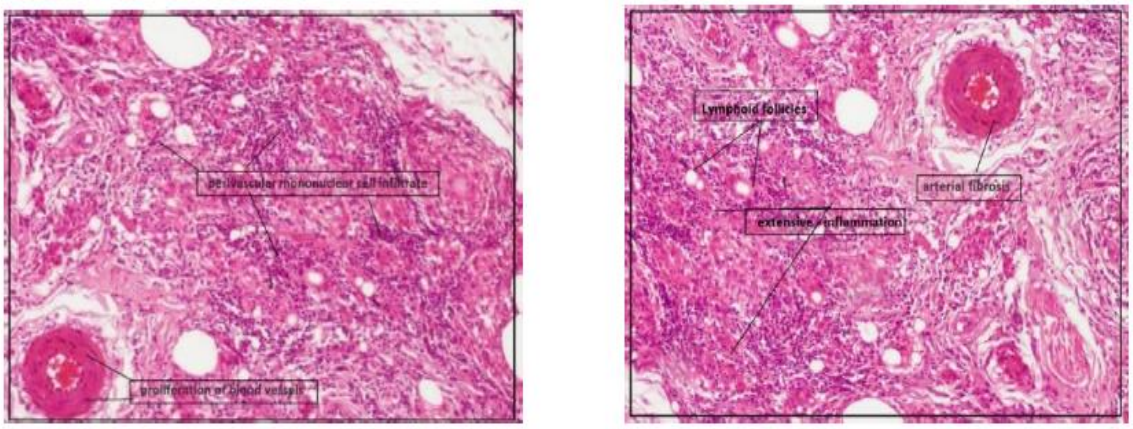

Fig 13 &14: Lymphoid follicles in rheumatoid arthritis, extensive inflammation and arterial fibrosis.

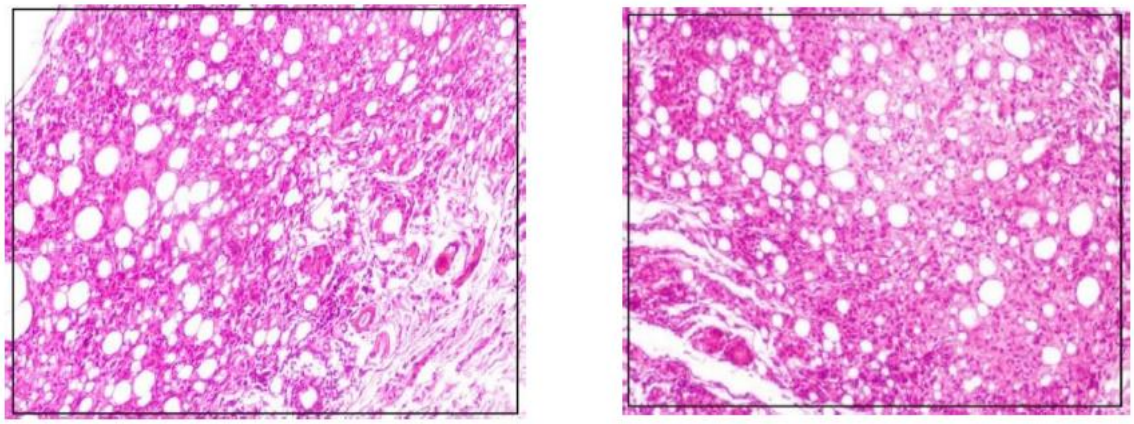

Fig 15 &16: Normal architecture of Bone The normal (areolar synovial cells with follicles normal histology is observed.

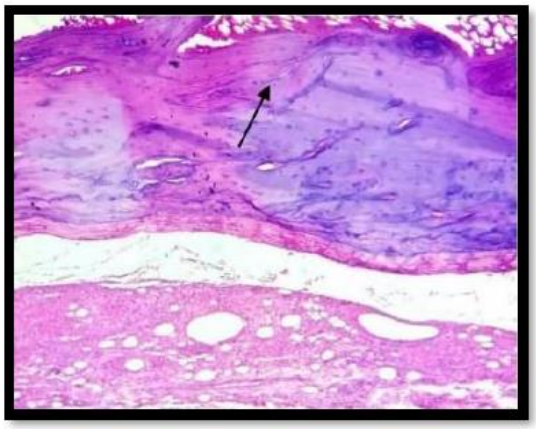
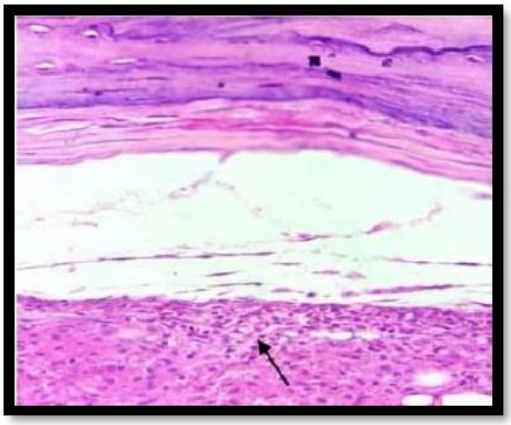

Fig 17 & 18: The synovial layer shows mild hyperplasia of the synovial lining cells. The synovial subepithelium shows moderate edema with mixed inflammation. consisting of lymphocytes, neutrophils and macrophages with fibro collagenous stroma and congested vascular spaces.

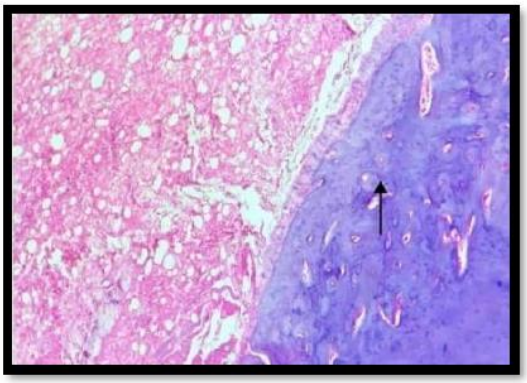
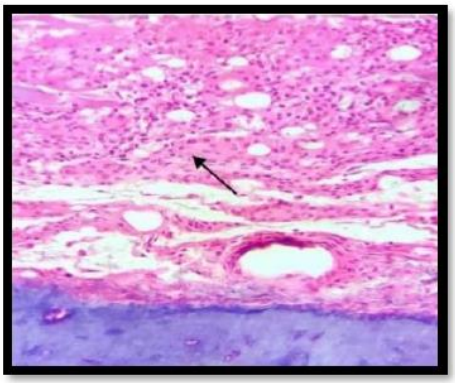

Fig 19 & 20: Synovial joint shows intact articular hyaline cartilage. subchondrial bone layer and adjacent synovial layer. The synovial subepithelium shows mixed inflammation [moderate] consisting of lymphocytes, neutrophils and macrophages with fibrocollagenous stroma and few congested vascular spaces.

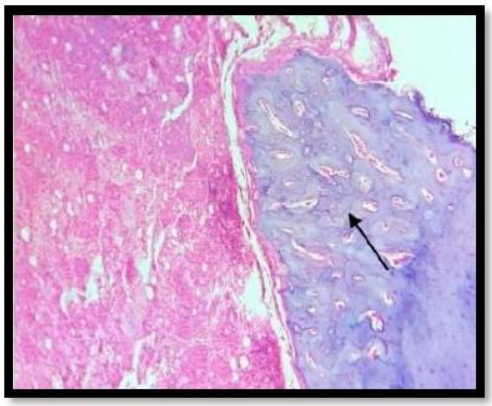
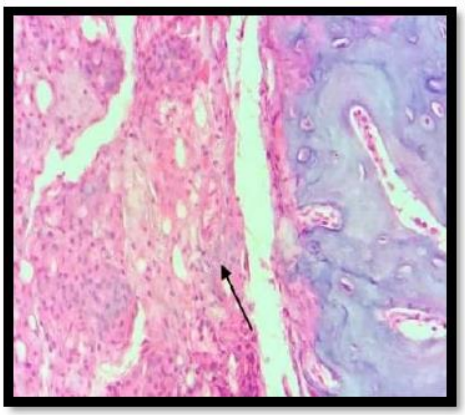

Fig 21 & 22: Section studied from the synovial joint shows intact articular hyaline cartilage. subchondrial bone layer and adjacent synovial layer. The synovial layer shows intact synovial lining cells. The synovial subepithelium shows mixed inflammation [mild] consisting of lymphocytes and occasional macrophages with abundant fibrocollagenous stroma and intact vascular spaces.

DISCUSSION AND CONCLUSION

In the present study, carrageenan-induced paw edema and CFA-induced arthritis models demonstrated that Aqueous extract of *Jasminum auriculatum* had anti-inflammatory and anti-arthritic potential.

For the evaluation of anti-inflammatory agents, carrageenan-induced paw edema is the most commonly used model, as the development of paw edema in rats by carrageenan is highly correlated with the early exudative stages of inflammation. After sub plantar injection, there is a sudden elevation of paw volume which can be

observed and correlated with vascular permeability induced by the action of histamine and serotonin. During 4–6 hr of induction period, paw edema gradually elevates to a peak which is the second phase due to the production of prostaglandins. [15]

In our study, we observed a similar pattern in the control group. Diclofenac sodium produced inhibition of inflammation only at 3 and 6 h post-carrageenan administration, which shows the effect of Diclofenac sodium on prostaglandins are produced during the second phase in carrageenan-induced paw edema. The dose-dependent inhibition of inflammation was observed in the AEJA group during all observation periods, thus clearly depicting inhibitory activity of AEJA against multiple autacoid mediators.

To confirm the anti-arthritic activity of the test drug, the efficacy of AEJA in reducing joint inflammation in the CFA-induced arthritis model was evaluated, as this model shares many common features with human disease.[9],[16]

In this study along with the measurement of joint swelling, we also measured the serum levelof RF, SGPT and SGOT in arthritis animals and play an important role in progression of the disease.

AEJA produced a dose-dependent reduction in joint swelling throughout the observation period. Even though the reduction in joint swelling was not significant at the lowest dose (100 mg/kg), treatment with moderate dose (200 mg/kg) and higher doses (400 mg/kg) produced a significant reduction on all observation days as compared to the control.

Consistent with these findings, AEJA treatment produced a significant reduction in serum levels of RF, SGPT and SGOT as compared to control animals. Serum RF, SGPT and SGOT levels was found to be elevated in all the CFA immunized animals. AEJA produced a dose- dependent reduction in elevated RF, SGPT and SGOT levels and this decrease was significant at the higher doses (400 mg/kg) as compared to the control.

AEJA produced a significant decrease in the WBC and ESR and a significant increase in thelevels of RBC and Hb as compared with control animals.

In present study histopathological examination revealed that the extract of doses of 200 mg/kg and 400 mg/kg have markedly inhibited the severe soft tissue swelling and narrowingof the joint spaces after the CFA challenge in arthritis control animals.

The aqueous extract of *Jasminum auriculatum* flower may possibly act by preventing production of ROS and nitric oxide from nitric oxide synthase or by preventing neutrophilic infiltration thereby decreasing the generation/ release of chemotactic factors and inflammatory mediators such as IL, TNF-α, Leukotrienes in acute inflammation. Whereas, in arthritis it may possibly act by decreasing synthesis/ release of T cell mediators such as IL, TNF-α as it was evident that, decreased cartilage and bone destruction were observed from the histopathological studies.

The main phytoconstituents present in AEJA are flavanoids, tannins, triterpenoids, etc., which are principle phytoconstituents responsible for antioxidant properties. A lot of these secondary plant metabolites identified so far exhibit anti-arthritic properties. Hence this seed extract AEJA can be a therapeutic approach in reduction of free radicals and can be used as anti-inflammatory and anti-arthritis drug.

REFERENCES

1. Astin JA, Beckner W, Soeken K, Hochberg MC, Berman B. Psychological interventions for rheumatoid arthritis: a meta-analysis of randomized controlled trials. Arthritis Rheum, 2002; 47: 291–302.
2. Mclnnes IB, Schett G. The Pathogenesis of rheumatoid arthritis. N Eng J Med., 2011; 365: 2205–19.
3. Fionula MB, Iain BM Evidence that cytokine play a role in rheumatoid arthritis. JClin Invest, 2008; 118: 3537–45.
4. Goldbatt F, Isenberg DA New therapies of rheumatoid arthritis. Clin Exp Immunology, 2005; 140: 195–204.
5. Venkatesha SH, Rajaiah R, Berman BM, Moudgil KD Immunomodulation of autoimmune arthritis by herbal CAM. Evid Based Complement Alternat Med., 2011; 986797.
6. Sing R.P More T.A The production and perfume potential of jasminum collections. Indian perfume, 1982; 26: 156-159
7. Yogendr Bahuguna, Mohan Singh Maniyari Rawat1, Vijay Juyal, Vikas Gupta "Antilithiatic effect of flowers of Jasminum Auriculatum Vahl". International Journal ofGreen Pharmacy-155.
8. Shalavadi MH, Mangannavar CV, Iranna S, Muchchandi BH. Qualitative and quantitative phytochemical analysis of seeds Cassia hirsuta. Asian Journal of Pharmacy and Pharmacology, 2019; 5(2): 290-7.
9. Newbold BB Chemotherapy of arthritis induced in rats by mycobacterial adjuvant. Br J Pharmacol, 1963; 21: 127–36.
10. Ulfgren AK, Lindblad S, Klareskog S, Anderson J, Anderson U. Detection of cytokine producing cells in the synovial membrane from patients with rheumatoid arthritis. Ann Rheum Dis., 1995; 54: 654–61.
11. Singh S, Nair V, Gupta YK Linseed Oil: an investigation of its anti-arthritic activity in experimental models. Phytother Res., 2012; 26: 246–52.
12. Nair V, Singh S, Gupta YK Evaluation of disease

modifying activity of Colchicum luteum Baker in experimental arthritis. J Ethanopharmacol, 2011; 133: 303–7.
13. Nair V, Kumar R, Singh S, Gupta YK Investigation into the anti-inflammatory and anti-granuloma activity of Colchicum luteum in experimental models. Inflammation, 2012; 35: 881–8.
14. Winter CA, Risley EA, Nuss GW Carrageenan induced inflammation in hind paw of the rat as an assay for anti-inflammatory drugs. Proc Soc Exp Bio Med., 1962; 111: 544–7.
15. Vinger R, Truax JF, Selph JL, Johnston PR, Venable AL, McKenzie KK Pathway to carrageenan-induced inflammation in the hind limb of the rat. Fed Proc, 1987; 46: 118–26.
16. Kleinau S, Erlandsson H, Klareskog L. Percutaneous exposure of adjuvant oil causes arthritis in DA rats. Clin Exp Immunol, 1994; 96: 281-4.