

Modulation of inflammatory pathways by *Caryota mitis* in rheumatoid arthritis: *In-vitro* and *in-vivo* insights

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ARTICLE HISTORY

Received on: 26/09/2025
Accepted on: 18/02/2026
Available Online: 15/04/2026

Key words:

Inflammation, oxidative stress, rheumatoid arthritis, pro-inflammatory cytokines, adjuvant-induced arthritis model.

ABSTRACT

Rheumatoid arthritis (RA) is a chronic immune-mediated illness characterised by joint damage, oxidative stress, and inflammation. *Caryota mitis* Lour. (*C. mitis*) generally termed as Fish tail plants, belong to the family Arecaceae. *Caryota mitis* stands out as a significant ethnopharmacological relevance, traditionally used in various disease elements such as inflammatory disorders, hyperglycemia, diarrhoea, asthma, and for snake bite poisoning. Diverse scientific validation of this plant has been proven, such as anti-tumour, anti-diabetic, anti-inflammatory, anti-asthmatic, and anti-microbial. However, the exact anti-arthritis potential of this plant has not been validated till today. Thus, this study examines the anti-inflammatory and anti-arthritis potential of the methanol extract of *C. mitis* (MECM) fruit through *in-vitro* and *in-vivo* models. The *in-vitro* models include membrane stabilisation and protein denaturation, which confirmed that MECM effectively inhibited protein denaturation and stabilized membranes and protein denaturation, suggesting anti-inflammatory activity. In *in-vivo* Complete Freund's adjuvant-induced arthritis rat models were employed to determine the therapeutic efficacy of MECM. MECM treatment to rat led to decreased paw swelling, enhanced body weight, and lowered arthritic scores. Further, biochemical investigation revealed decreased levels of "Tumor necrosis factor alpha, Interleukin-6," oxidative stress markers, and restoration of antioxidant enzymes and anti-inflammatory cytokines. Histopathological investigation of bone joint determinations established protection against joint damage. Overall, the results indicate that *C. mitis* reduces rats' inflammation and joint degeneration, likely through modulation of cytokines and oxidative stress, supporting its potential.

1. INTRODUCTION

Rheumatoid arthritis (RA) is a chronic immune-mediated illness. It is characterised by swelling, pain in the joint, stiffness, disability of the patient's bone, and cartilage damage [1,2]. While arthritis is not limited to a certain demographic, it is more frequent in individuals aged 40–50 [3]. Globally, RA affects around (0.5% to 1%) of the population, thereby being among the most prominent autoimmune illnesses, in which females have 2–3 times greater incidence of RA than males

[4,5]. The estimated prevalence of RA is around 0.7% among the Indian population [6]. On a worldwide basis, forecasts suggest that by 2040, nearly 78.4 million individuals aged 18 years and older will be affected by arthritis, underlining the growing burden of the disease [2].

As it is a multifactorial disease, multiple etiological factors are responsible for disease progression, including genetic, physiological, and environmental factors [1]. RA stimulates macrophages, polymorphonuclear cells, and synoviocytes, leading to the overproduction of T lymphocytes that drive inflammation [7]. In the course of the inflammatory progression, pro-inflammatory cytokines ("IL-1 β " and "Tumor necrosis factor alpha (TNF- α)") are produced, which activate the production of proteolytic enzymes. These enzymes contribute to joint deformation by causing chronic cell proliferation, the destruction of cartilage tissue, and bone percentage of membrane

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stabilization [8,9]. Conversely, IL-10 anti-inflammatory cytokines serve to counteract these effects by limiting the level of pro-inflammatory cytokines [10]. Furthermore, RA states that the rise in reactive oxygen species. This alteration between the antioxidant defence system and ROS further exacerbates joint inflammation and tissue damage [11].

To underscore therapeutic strategies for treating RA, it is essential to understand the molecular mechanisms driving disease progression. Current treatment options for inflammatory diseases such as RA are not curative. “Disease-Modifying Antirheumatic Drugs” (DMARDs) and symptomatic treatment are recommended by the “American College of Rheumatology” as the cornerstone of RA treatment [12]. DMARDs, including sulfasalazine, leflunomide, and methotrexate (MTX), help to slow disease progression by targeting the underlying mechanisms of inflammation, with side effects such as weakening the immune system and hepatic problems [13]. Symptomatic medications, which involve corticosteroids and “nonsteroidal anti-inflammatory drugs”, are often used to lessen pain and reduce inflammation by targeting cyclooxygenase 1 (COX-1) and COX-2 in the short term [14]. These medications provide relief from the symptoms of RA but do not alter the long-term progression of the disease. While specific suppression of COX-2 has been linked to an increased risk of stroke and myocardial infarction, COX-1 inhibitors cause renal, gastrointestinal, hepatic, and brain problems [13].

With this, all the side effects have necessitated the need to find safe and cost-effective alternatives. Herbal remedies stand out as promising alternatives due to their natural origin, lower side effects, and cost-effectiveness [15]. Traditionally, numerous plants have been used to alleviate symptoms of RA, and countless herbal plants are currently being studied to develop new medications with proven potential anti-arthritis activity, both pre-clinical and clinical [16,17]. *Caryota mitis* Lour (*C. mitis*), which is commonly known as the Fishtail plant, belongs to the Arecaceae family, which has a native range across Asia and North Africa [18]. This plant is widely recognised as an ornamental plant around the globe. This plant has been utilised as a folk remedy to treat various disease elements such as diabetes, asthma, and so on [18]. Of note is that the fruits of the plant have been used to treat laxatives, hemorrhoids, loss of virility, and RA in Bangladesh [19]. Previous study stated that plants possess multiple pharmacological properties: analgesic, anti-inflammatory, antipyretic, anti-allergic, anti-asthmatic, and anti-tumour activity [18]. As far as we are aware, the anti-inflammatory and anti-arthritis potential of *C. mitis* fruits has not been systematically studied scientifically. Thus, the anti-inflammatory and anti-arthritis potential of *C. mitis* was assessed using an *in-vitro* membrane stabilization and protein denaturation, followed by a Complete Freund’s adjuvant (CFA)-induced arthritic rat model and the potential effects of the methanol extract *C. mitis* (MECM) on the antioxidant defence system. The present study was designed as a preliminary pharmacological investigation to evaluate its anti-inflammatory and anti-arthritis efficacy through *in-vitro* and *in-vivo*.

2. MATERIALS AND METHODS

2.1. Plant sampling and extraction

2.1.1. Plant substantial

The fruits of *C. mitis*, locally called “Salapa”, were obtained from Bhubaneswar, (“Regional Plant Resource Centre”), in 2024 April. Taxonomist Professor “Dr. Pratap Chandra Panda” of our same institute performed the botanical authentication. Additionally, a voucher specimen number (2535/CBT) has been archived in “School of Pharmaceutical Sciences (SPS), SOA University, Bhubaneswar, Odisha” herbarium.

2.1.2. Extract preparation

The fruits were rinsed with tap water and sliced into little pieces. They were dried in the shade at room temperature for 15–20 days. Then the sample was defatted using n-hexane, after which methanol extraction was conducted out with methanol for 72 hours under controlled conditions (30°C–40°C) employing a Soxhlet apparatus. Furthermore, the resulted methanol extract was concentrated by employing a rotary evaporator and preserved in a desiccator until further investigation.

2.2. In-vitro study

2.2.1. Protein denaturation assay

The protein denaturation assay of *C. mitis* was screened as the protocol outlined by Das *et al.* [20] and their team to estimate the anti-arthritis potential. Different concentrations of MECM (0–400 µg/ml), phosphate-buffered saline (2.8 ml), and egg albumin (0.2 ml) were mixed to form a reaction mixture. The mixture was allowed to incubate for 15 minutes at 37°C. After the incubation, to induce protein denaturation, thermal treatment was given at 70°C for 5 minutes. After cooling, the absorbance was recorded at 660 nm, considering that double-distilled water served as the negative control. The % inhibition of protein denaturation was calculated using the formula; “% inhibition of protein = $(1 - (AT/AC)) \times 100$ ”; Whereas AC = Absorbance of control, AT = Absorbance of test.

2.2.2. Membrane stabilization assay

The potential of *C. mitis* was investigated by the human red blood cell (RBC) membrane stabilization method [20]. Fresh human blood was collected in a heparinised tube, then mixed with Alsever’s solution and centrifuged at $1,000 \times g$ for 10 minutes. The packed erythrocytes were repeatedly washed with isotonic saline (0.85% NaCl). A 10% (v/v) human red blood cells (HRBC) suspension was then prepared in isotonic saline. Thereafter, a reaction mixture was made of 1 ml of MECM extract prepared at different concentrations (0–400 µg/ml), 1 ml of 10% HRBC suspension, 1 ml of phosphate buffer (0.15 M, pH 7.4), and 2 ml of hypotonic saline. The mixture was allowed to incubate for 30 minutes at 37°C. After the incubation, the centrifugation was done, and the absorbance was measured at 560 nm. The percentage hemolysis was calculated using: “% Hemolysis = $(OD_{test} / OD_{control}) \times 100$ ” formula. The percentage of membrane stabilization

was calculated using “% Stabilization = 100 - %Hemolysis”. “ODtest = Optical density of test sample, ODcontrol = Optical density of control”.

2.3. Bioactive study

2.3.1. Animals and diet

Young female Wistar rats (150–170 g weight) (6–8 weeks) were used for evaluating the anti-arthritis effect of the MECM. Prior to the experiment, the animals were acclimatized under standardized room at “23°C ± 2°C with a 12 hours light/12 hours dark” and a relative humidity range between 40% and 70%. The animals were fed a standard laboratory rodent diet and had 24-hour access to drinking water. All procedures involving in experimentation were reviewed, supervised, and authorised by the Institutional Animal Ethics Committee (IAEC) of “SPS, SOA, deemed to be a University, India,” under protocol number “IAEC/SPS/SOA/217/2025.” “CPCSEA” and “ARRIVE” guidelines were followed to carry out this work [21,22].

2.3.2. Drugs and chemicals

Petroleum ether, methanol, Tris-EDTA, Tris-HCl, sodium dodecyl sulfate, phosphate-buffered, and perchloric acid were purchased from Sisco Research Laboratories (SRL) (India). 10 ml of a vial containing CFA Sigma (USA). ELISA kit, such as “Interleukin-6 (IL-6), TNF- α , and IL-10,” were acquired from Thermo Fisher Scientific (India). Anti-oxidant markers such as “Superoxide Dismutase (SOD), Glutathione (GSH), Catalase (CAT),” and oxidative stress markers such as Malondialdehyde (MDA) and Griess Reagent for Nitrite were brought from SRL (India).

2.3.3. Acute toxicity studies

Acute toxicity assessment of methanol extract as per protocol guidelines OECD 423. Healthy male and female rats were used for the study to assess possible sex-dependent differences in toxicity and rule out any serious toxicological properties of the plant extract. The animals were assigned to two groups, each comprising five rats. The test group was given a single successive dosage of “4,000 mg/kg” of the extract after a 12-hour fast, while the control group received only the vehicle for 14 days; both groups were thoroughly monitored for any indications of toxicity [23,24].

2.3.4. RA induction and treatment regimen

The procedure explained by Das *et al.* [20] was used to create the *in-vivo* arthritis model. RA is known to occur more frequently in females than in males, and previous reports suggest that female rats develop a more consistent and reproducible disease course in CFA-induced arthritis models [25]. Therefore, only female rats were selected for this study. The 30 female rats were randomly allotted into five groups in reference to the published CFA-induced arthritis model [5,20]. The group sizes ($n = 6$) for the animals were determined based on a power analysis and in alignment with a previously published CFA-induced arthritis model [20]. Furthermore, A single shot of 0.1 ml of “CFA” was injected into the plantar surface of the right hind paw of all animals except the control group. Throughout the experimental period, animals were maintained under standard laboratory conditions, with free access to food and drinking water, and subjected to a 12 hours light/12 hours dark cycle. The experimental timeline of the current study plan is provided in Figure 1(A). After induction RA, administration of standard drug MTX, tested drug MECM

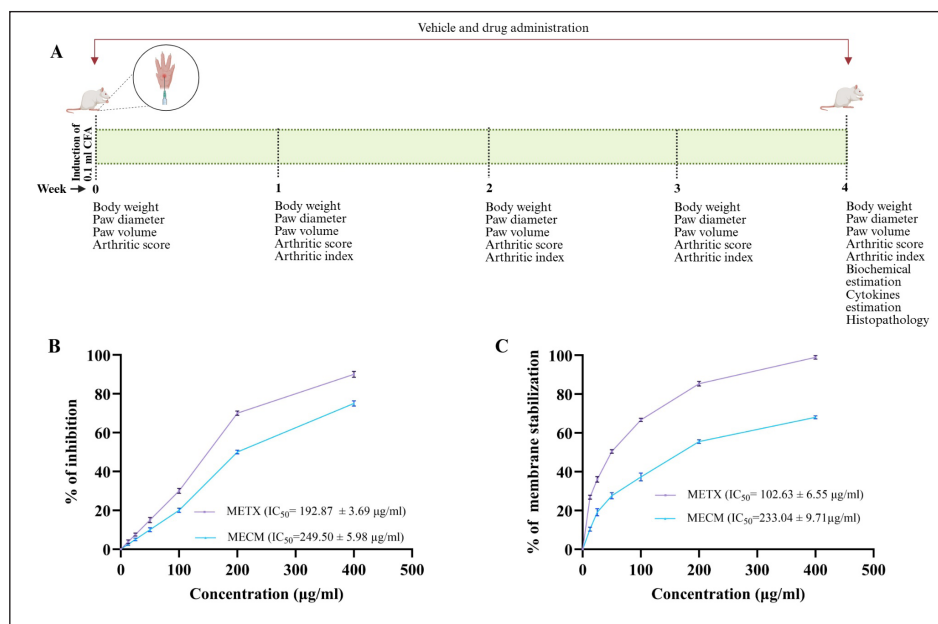


Figure 1. The potential of *C. mitis* in an *in-vitro* model. (A) Experimental timeline; (B) *in-vitro* protein denaturation assay; (C) *in-vitro* membrane stabilization assay. Results are reported as the mean ± SD ($n = 3$).

low dose (MECM-L), and MECM high dose (MECM-H) over a 4-week duration. Treatment allocation was as follows: Group I, normal control receiving vehicle; Group II, arthritic control induced with CFA and administered vehicle; Group III, CFA-induced animals treated with MTX (0.05 mg/kg); Group IV, CFA-induced animals administered MECM-L of 200 mg/kg (MECM-L); and Group V, CFA-induced animals treated with MECM-H of 400 mg/kg (MECM-H).

2.4. Evaluation of arthritis parameters

2.4.1. Body weight, Arthritic index and arthritic score

The body weight (BW) of the animals was also closely monitored as a measure of their general health status and disease progression. The weight was recorded at the baseline (week 0) and then at weekly intervals for a period of up to 4 weeks post-induction of CFA. The level of joint inflammation was measured using the arthritic index scoring technique as described by Das *et al.* [26]. The clinical assessment was done by observing the erythema and swelling of the paw, and the scores were given as follows: “0 for no swelling or erythema;” “1 for mild erythema or swelling of one finger or toe;” “2. Multiple toe or finger erythema and swelling;” “3. Ankle or wrist erythema and inflammation;” “4. Pronounced erythema and inflammation affecting both the digits and the ankle or wrist,” calculated over 4 weeks after arthritis induction. The cumulative score had a maximum of 8, and scores above 1 were considered positive for the onset of arthritis [5]. These scoring evaluations were performed by an investigator who was blinded to the group allocation.

2.4.2. Paw diameter (PD) and paw volume (PV)

Measurements of PV and PD were conducted 4 weeks after CFA was induced. PD was measured using a digital vernier calliper, and PV was measured using a Plethymometer [5].

2.4.3. Pro and anti-inflammatory cytokines

The animals were euthanized by cervical dislocation on day 28. Blood samples were collected by cardiac puncture into Vacutainer tubes: one for serum, one containing EDTA, and one for erythrocyte sedimentation rate (ESR) measurement. The samples were centrifuged at $1,000 \times g$ for 10 minutes to pellet the plasma, which was then preserved at -20°C . Concentrations of anti-inflammatory cytokine “IL-10” and the pro-inflammatory cytokines “IL-1 β ” and “TNF- α ” were measured using ELISA kits that adhere to the protocol of the manufacturer. The expression was represented in pg/ml [27].

2.4.4. Oxidative stress biomarker

Synovial tissue was obtained on 28 days, and the homogenate mixture of this synovial tissue was further analysed to determine levels of oxidative cellular stress. Anti-oxidant enzymes such as SOD, CAT, GSH, and oxidative stress markers such as MDA and Nitrite were quantified [28].

2.4.5. Haematological and biochemical assessment

The blood samples taken were analysed for various biochemical and inflammatory markers such as liver function enzymes [“Aspartate aminotransferase (AST), Alanine

aminotransferase (ALT), and Alkaline phosphatase (ALP)”, kidney function markers (creatinine and urea), and the levels of ESR, “rheumatoid factor” (RF), and “C-reactive protein” (CRP) [20].

2.4.6. Histopathological study

In accordance with the approved ethics guidelines, on day 28 animal were euthanized. Collected ankle joints were fixed in neutral buffered formalin (10%), after which decalcification using formic acid was done. Then the paraffin embedding box was prepared, and 5 μm -thick sections were sectioned with a microtome. Sections were stained with H&E and visualized using a digital microscope system. Histopathological alterations were assessed independently by a blinded pathologist using a validated scoring protocol described by Wang *et al.* [29].

2.5. Statistical analysis

Statistical analysis was conducted with GraphPad Prism version 9.0.0. Results are reported as the mean \pm standard deviation (SD). One-way analysis of variance (ANOVA) followed by Tukey’s multiple comparison tests was made for single-endpoint parameters to assess differences between experimental groups. Two-way repeated-measures ANOVA followed by Tukey’s multiple comparison test was performed for BW, Arthritic index (AI), Arthritic score (AS), PV, and PD. A *p*-value of less than 0.05 was regarded as statistically significant.

3. RESULTS

3.1. Assessment of MECM on protein denaturation and membrane stabilization

MECM was investigated for its inhibition of protein denaturation, a key mechanism involved in causing inflammation. Figure 1(B) reveals that the MECM exhibited remarkable inhibition of protein denaturation across all tested concentrations, with an IC_{50} value of $(249.50 \pm 5.98 \mu\text{g/ml})$. Moreover, a membrane stabilisation assay investigated the ability to protect lysosomal membranes under stress conditions, Figure 1(C). The result suggests that MECM has concentration-dependent membrane-stabilizing capacity, with an IC_{50} value of $(233.04 \pm 9.71 \mu\text{g/ml})$. METX also exhibits a strong percentage of inhibition against protein denaturation with an IC_{50} value of $(92.87 \pm 3.69 \mu\text{g/ml})$, and a membrane stabilisation IC_{50} value of $(102.63 \pm 6.55 \mu\text{g/ml})$.

3.2. MECM suppresses changes in body weight in CFA-induced rats

During the acute toxicity testing, no toxic responses were noted over the 14 days. Based on a maximal tolerable dose of 4,000 mg/kg, the high and low doses were determined to be 1/10th (400 mg/kg) and 1/20th (200 mg/kg), respectively. The observed reduction in body weight may be associated with systemic inflammatory responses. Therefore, the BW of NC and CFA-induced arthritis rats were monitored weekly. Figure 2(A) The disease control (DC) group showed a marked loss of BW compared to the NC group during the 4-week study ($^{***}p < 0.001$). Conversely, METX treatment ($^{###}p < 0.001$), MECM-L ($^{##}p < 0.001$), and MECM-H ($^{###}p < 0.001$) doses

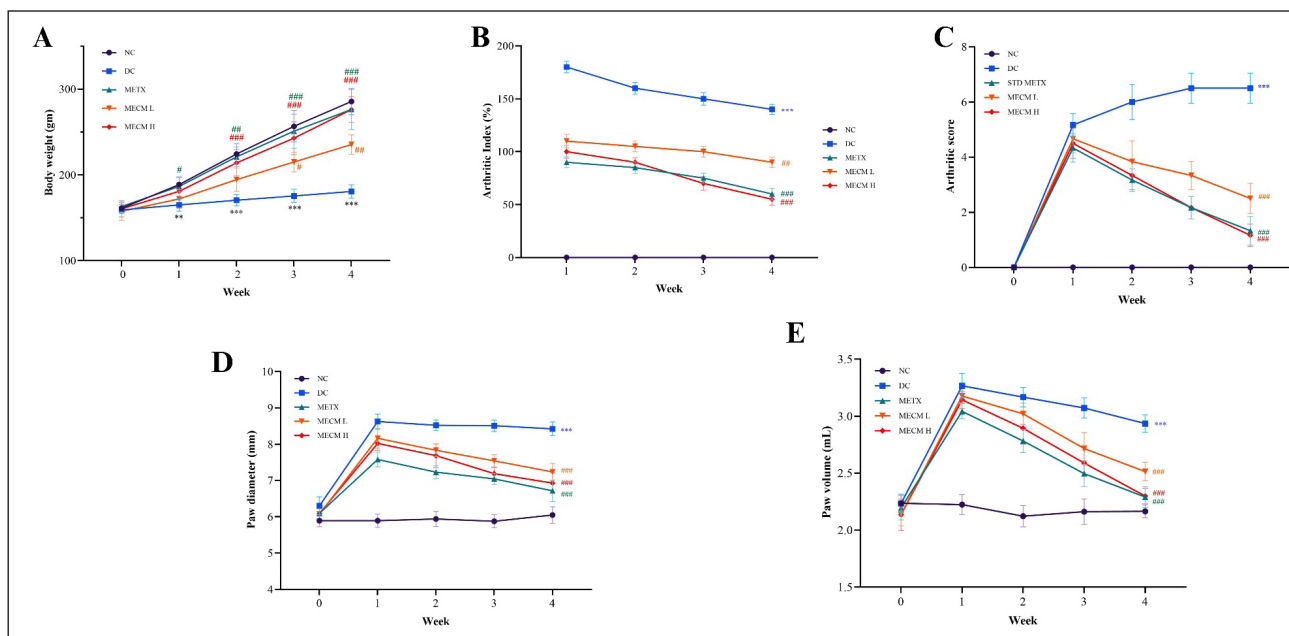


Figure 2. Protective effect of *C. mitis* in a CFA-induced rat model of arthritis. (A) Body weight assessment of all groups; (B) Arthritic index %; (C) Arthritic score; (D) PD; (E) PVs. Results are reported as the mean \pm SD ($n = 6$). Two-way repeated-measures (ANOVA) followed by Tukey's multiple comparison test was employed. The statistical significance, where $**p < 0.01$ and $***p < 0.001$ against to NC and $\#p < 0.05$, $\#\#p < 0.01$ and $\#\#\#p < 0.001$ against to DC.

of MECM led to a significant increase in the BW against DC. These investigations suggest that MECM reduces the systemic wasting effect typically seen with chronic arthritis.

3.3. MECM improved the arthritic score and arthritic index

The evidence suggests that MECM markedly reduces both AI and arthritic scores **Figure 2(B)**. The AI was measured once a week after the CFA induction. In the DC, the AI was found to be increased across the 4 weeks, in contrast to NC ($***p < 0.001$). On the other hand, starting at week 2, the METX and MECM-H treated groups had a statistically significant and gradual decrease in arthritic index compared to DC ($\#\#\#p < 0.001$), indicating protection against joint degradation. Similarly, the arthritis score of DC was markedly higher than that of the NC ($***p < 0.001$), **Figure 2(C)**. In comparison to DC, treatment of MECM results in a substantial concentration-dependent decrease in arthritic score ($\#\#\#p < 0.001$) against DC.

3.4. MECM attenuates paw swelling in CFA-induced rats

It has been shown that administering CFA causes severe inflammation, which results in changes in the paw. Hence, PD and PV were noted for all rats each week to scrutinize the effect of MECM in attenuating the arthritis symptoms. **Figure 2(D)** CFA-induced rat (i.e., DC) ($***p < 0.001$) showed a markedly elevated PD throughout 4 weeks, as shown by vernier calliper measurement. On the other hand, treatment with MECM shows concentration-dependent decreases in PD when against to DC ($\#\#\#p < 0.001$). Likewise, PV was determined by a plethysmometer across the 4 weeks, **Figure 2(E)**. A remarkable PV increase was seen in DC ($***p < 0.001$) compared to NC.

In contrast, METX and MECM exhibit the lower PV ($\#\#\#p < 0.001$) when compared to DC, and show a clear attenuation of paw swelling in CFA-induced rats.

3.5. MECM regulates the pro and anti-inflammatory cytokines

The dysregulation in cytokine balance was clearly seen in the arthritic model group, i.e., DC ($***p < 0.001$), against NC, reflecting that an exaggerated inflammatory response is involved in the disease progression. However, the administration with METX and MECM, both the concentration attenuated the elevated level of "TNF- α ," **Figure 3(A)** and "IL-6," **Figure 3(B)**, remarkably against DC ($\#\#\#p < 0.001$). Similarly, the IL-10 **Figure 3(C)** levels were significantly restored in the treatment groups against the DC ($\#\#\#p < 0.001$). This result indicates that MECM modulates the pro- and anti-inflammatory cytokines.

3.6. MECM diminished oxidative stress and enhanced anti-oxidant defence

The induction of oxidative stress in synovial tissues was validated by measuring major antioxidant and oxidative markers. There was a depletion in the SOD **Figure 3(D)** and CAT **Figure 3(E)**, along with decreased GSH levels **Figure 3(F)**, in the DC group against the NC ($***p < 0.001$), which reflects a compromised antioxidant defence system. Conversely, administration of METX ($\#\#\#p < 0.001$) and MECM ($\#\#p < 0.01$ and $\#\#\#p < 0.001$) at both concentrations prominently reversed levels of these antioxidants against to DC, indicating protection against oxidative damage. In addition, levels of MDA and Nitrite **Figure 3(G and H)**, both well-known indicators of lipid peroxidation and nitrosative stress, were notably increased in the DC ($***p < 0.001$), indicative of widespread oxidative damage. METX and MECM treatment

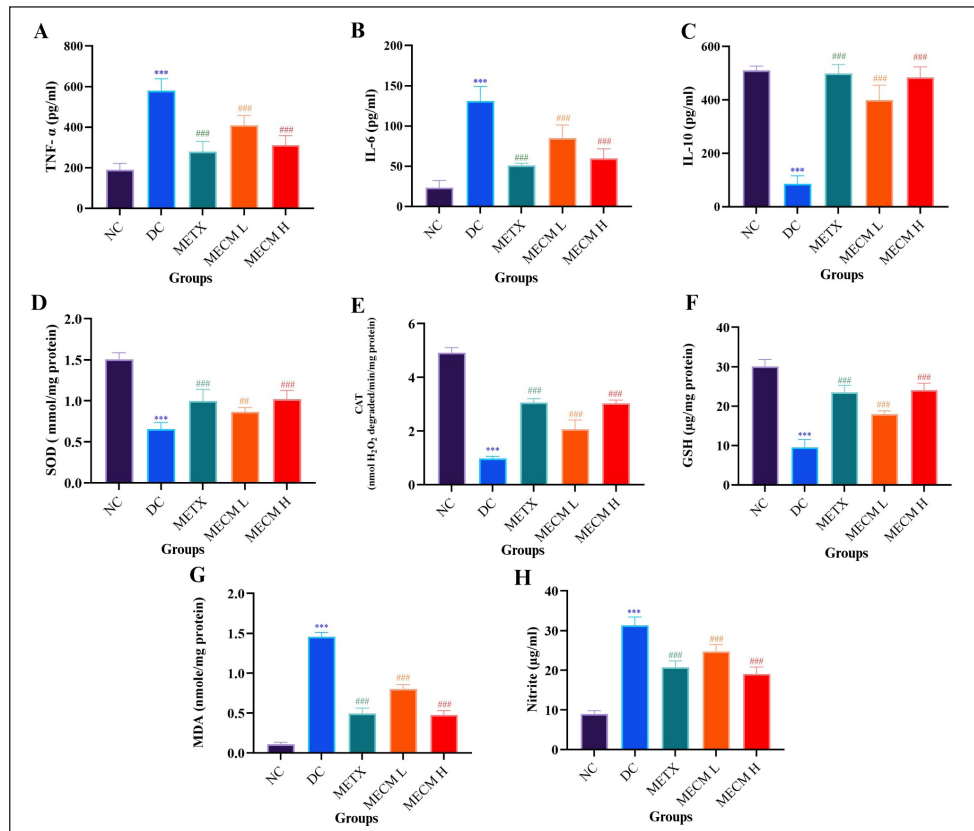


Figure 3. Effect of MECM cytokines levels and oxidative stress. (A) TNF- α levels; (B) IL-6 levels, (C) IL-10 levels; (D) SOD levels; (E) CAT levels; (F) GSH levels; (G) MDA levels; (H) Nitrite levels. Results are reported as the mean \pm SD ($n = 6$). One-way (ANOVA) followed by Tukey's multiple comparison tests was employed for statistical significance, where $***p < 0.001$ against to NC and $###p < 0.01$ and $####p < 0.001$ against to DC.

successfully lowered these high levels in a concentration-dependent manner ($####p < 0.001$) against DC.

3.7. MECM improved the macroscopical and histopathological features on arthritis rats

macroscopic assessment of all animals was conducted prior to the histopathology after different treatments. The findings demonstrated that the DC group exhibited clear signs of arthritis, such as swelling and redness in the paws. However, Treatment with METX and MECM resulted in a noticeable reduction in these arthritic symptoms [Figure 4\(A\)](#). Further, the ankle joints of CFA-induced rats were examined by using H and E staining. [Figure 4\(B\)](#) shows the histopathological results of METX and MECM-treated RA rats. The results reveal that in the NC group, the joint cavity was well preserved with no marked synovial hyperplasia, no obvious cartilage erosion. The hyaline cartilage appears relatively intact. However, in the DC group, the synovial lining is thickened and composed of multilayered synoviocytes. Additionally, it shows high cellular density within the synovium, suggesting the development of pannus tissue, which is a hallmark feature of active RA [30]. This hallmark feature of RA was alleviated upon METX and MECM-H treatment, [Figure 4\(B\)](#). In both groups, hyaline cartilage appeared well-integrated, the synovial line seemed to be moderately thickened, and no sign of cartilage erosion. This examination suggests that

MECM-H extract suppresses pathology upon 28 days of drug induction. [Figure 4\(C\)](#) the histopathological score, where DC was found to have an increased histopathological score against to NC ($***p < 0.001$). This histopathological score remarkably declined by METX and MECM-H ($####p < 0.001$), and MECM-L ($##p < 0.01$) against to DC.

3.8. MECM modulates hematological and biochemical markers

Using hematological and biochemical indicators, the anti-inflammatory and related organ-protective effects of MECM were examined [Figure 5](#). CRP and ESR are the inflammation markers found overexpressed in the DC group against to NC ($***p < 0.001$), confirming systemic inflammation in CFA-induced rats, [Figure 5\(A and B\)](#). Despite being treated with METX and MECM, their levels were significantly reduced. MECM-H showed significant effects comparable to MTX against to DC ($####p < 0.001$). Furthermore, in DC groups, the RF was found to be increased against to the NC ($***p < 0.001$), suggesting that the autoimmune involvement in the CFA-induced model, [Figure 5\(C\)](#). RF levels against DC are dramatically reduced by both METX and MECM therapy ($####p < 0.001$). Liver function tests, such as AST, ALP, and ALT, and kidney function tests, such as urea and creatinine, were investigated for any kind of organ-associated effect

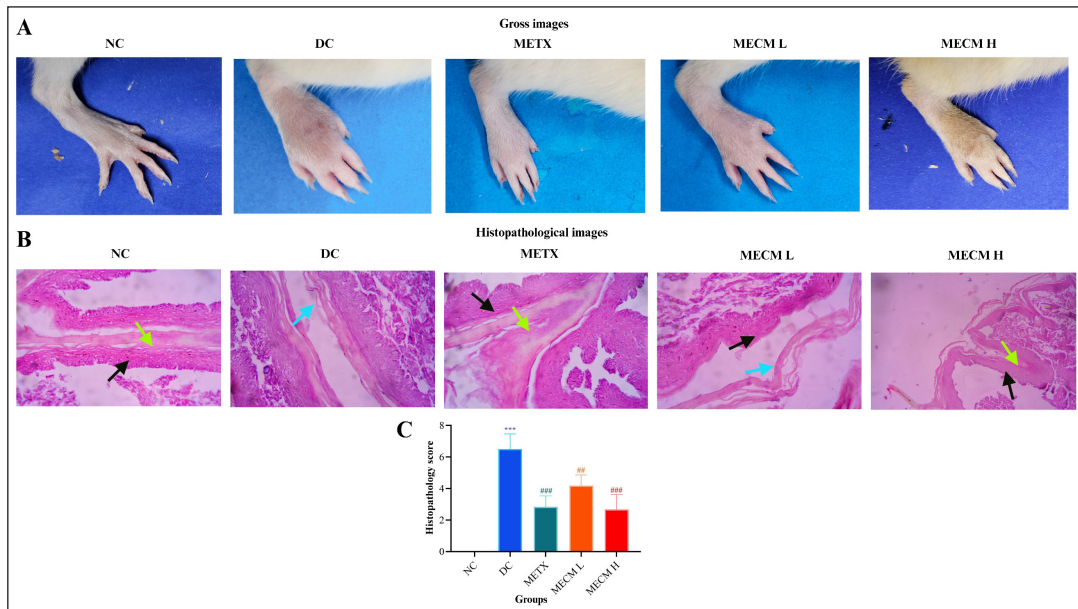


Figure 4. MECM effect on RA physical parameters. (A) Gross images of hind limbs from five experimental groups; (B) Histopathological images. The hyaline cartilage (Green →), synovial hyperplasia (Blue →), synovial lining (Black →); (c) Graphical depiction of X-ray and histopathology scores. Results are reported as the mean \pm SD ($n = 6$). One-way (ANOVA) followed by Tukey's multiple comparison tests was employed for statistical significance, where $***p < 0.001$ against to the NC, $##p < 0.01$, and $###p < 0.001$ against to the DC.

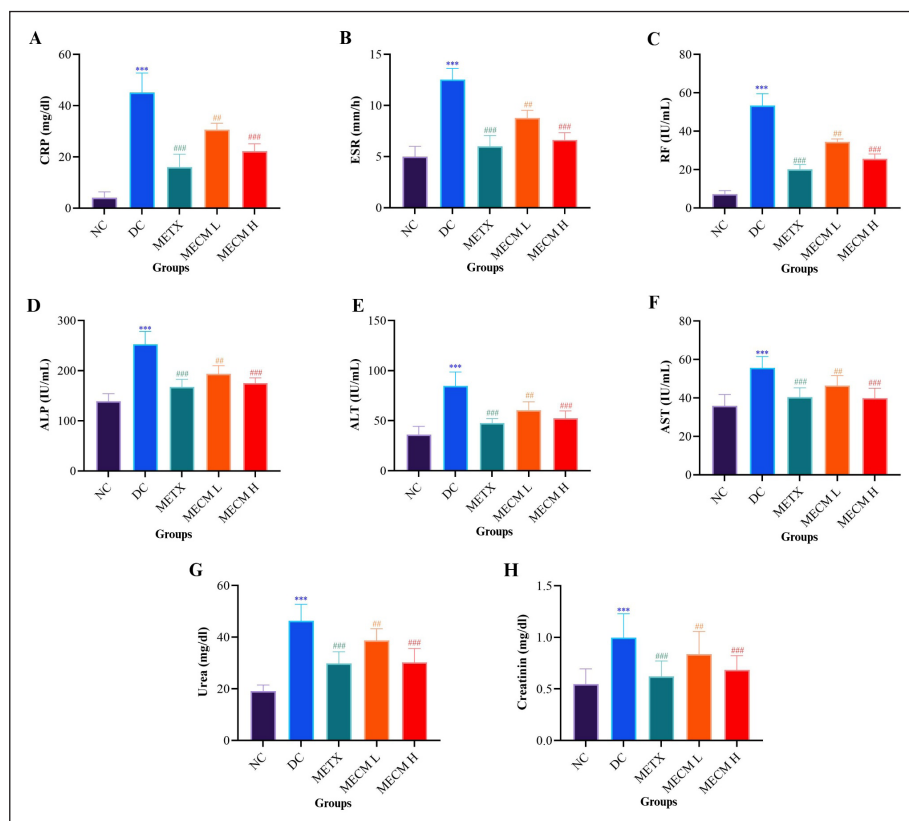


Figure 5. Effects of MECM on hematological and biochemical markers. (A) CRP; (B) ESR; (C) RF; (D) ALP; (E) ALT; (F) AST; (G) Urea; (H) Creatinine. Results are reported as the mean \pm SD ($n = 6$). One-way (ANOVA) followed by Tukey's multiple comparison tests was employed for statistical significance, where $***p < 0.001$ against to NC and $##p < 0.01$ and $###p < 0.001$ against to DC.

Figure 5(D–H). The DC group shows that the levels were significantly increased when against to NC (** $p < 0.001$). When compared to the DC, these levels are significantly reduced to almost normal with the administration of METX and MECM (### $p < 0.001$). While MECM shows concentration-dependent effects. This result suggests MECM has protective effects against organ damage.

4. DISCUSSION

Chronic inflammation is the leading worldwide health issue responsible for more than half of all global deaths. Among diseases with a related condition, RA is especially significant because of its systemic, chronic, and multifactorial etiology [31]. RA is an autoimmune disorder where the immune system targets the protective cover of the joint, which is the synovium, leading to chronic inflammation. This will impact patient's quality of life and places a heavy burden on families, communities, and the healthcare system around the world [32].

Inflammatory components like “TNF- α ” and “IL-6” are a core component of RA's pathophysiology, stimulating inflammation and joint damage [33]. Although conventional therapy is still a mainstay in clinical practice [34]. These therapies also raise some serious risks, including bone marrow suppression, gastrointestinal bleeding, tuberculosis infections of the skin and liver. Nevertheless, there is an urgent unmet need for more effective, safer, and affordable treatment options for RA. Filling this gap entails ongoing research into novel targets, personalized medicine strategies, and integrative approaches that not only control symptoms but also alter the course of the disease more durably. Natural compounds are attracting more and more attention from researchers due to their inexpensive, relatively fewer adverse effects, and potential to target numerous pathways [35,36]. *Caryota mitis*, specifically, fruits from this plant have been employed in ancient practice to control RA symptoms in Bangladesh [19]. Due to its ethnomedicinal significance, this current study seeks to scientifically assess the RA activity of *C. mitis*. While *C. mitis* has been previously reported for its anti-inflammatory and antioxidant properties, its role in autoimmune and inflammatory joint diseases has not been explored. Our results complement earlier findings by confirming its anti-inflammatory and antioxidant potential, and extend the current knowledge by demonstrating that *C. mitis* also modulates pro- and anti-inflammatory cytokines, restores antioxidant defences, and protects joint structure in CFA-induced arthritic rats. This systematic evaluation not only supports its ethnomedicinal applications but also provides a scientific rationale for its use as a supportive or disease-modifying anti-arthritic therapeutic.

Denaturation of protein is a widely accepted indicator of inflammation, as protein denaturation can cause immune responses and the onset of rheumatoid conditions. Protein denaturation inhibition indicates anti-inflammatory action and the possibility of alleviating arthritic symptoms [37]. The percentage inhibition of protein denaturation by MECM was IC₅₀ (249.50 \pm 5.98 μ g/ml), showing considerable protective activity against inflammatory protein denaturation. Membrane

stabilization assay is another significant measure of anti-arthritic potential, as it indicates the potential of a compound to stabilize lysosomal membranes against lysis and thus inhibit the release of inflammatory mediators. RBC membrane stabilization simulates the protection of synovial membranes in arthritic joints. MECM had membrane stabilization value IC₅₀ (233.04 \pm 9.71 μ g/ml), indicating its potential for stabilizing cellular membranes against inflammatory stress.

For our study, we used an adjuvant-induced arthritic model, which induces an immunological reaction that results in joint inflammation and swelling that closely resembles human RA [38]. Since RA occurs more frequently in females than in males, and prior studies indicate that female rats exhibit a more consistent and reproducible disease pattern in CFA-induced arthritis models, we therefore used female rats in the present study [25]. Loss of body weight is often seen in inflammatory conditions, including arthritis, due to decreases in food intake and muscle wasting driven by inflammatory cytokines [39]. Body weight monitoring is an early measure of health and treatment outcome [40]. During the DC group, dramatic body weight loss was noted. But MECM treatment resulted in concentration-dependent recovery of body weight, indicating its potential efficacy in minimizing systemic inflammation and improving recovery. The paw swelling was measured weekly across all groups to assess the progression of arthritis and the therapeutic effect of MECM, and the results suggested that the DC group showed a marked and sustained increase in both PD and PV. In contrast, treatment with MECM led to a clear, dose-dependent attenuation of paw swelling was observed. PD and PV were measured using a digital vernier calliper and a plethysmometer, respectively, and no blinding was employed for these assessments. However, the objective nature of these measurements and the consistent reduction in swelling observed in MECM-treated groups suggest that any potential bias was minimal. Similarly, the DC group showed a progressive elevation of AS and AI. Conversely, MECM treatment significantly reduced AS and AI in a concentration-dependent manner.

In RA, activated immune cells produce an excess of reactive oxygen species, which may trigger pivotal inflammatory mechanisms like NF- κ B that perpetuate synovial inflammation and joint destruction. Thus, the targeting of oxidative stress not only reduces the inflammatory environment but also likely prevents the progression of joint destruction in RA [41]. In this study, in the DC group, there was a significant increase in oxidative stress markers such as MDA, Nitric oxide, and a decrease in antioxidant defence enzymes SOD, CAT, and GSH. However, administration of MECM revealed the abnormalities in RA in contrast to DC. Furthermore, this ROS contributes to the imbalance between pro- and anti-inflammatory cytokines. Our finding shows that upon administration of MECM, the pro- and anti-inflammatory cytokines were markedly balanced.

Elevation of RF, CRP, and ESR indicates active systemic inflammation in RA. The present study demonstrated that MECM treatment resulted in a remarkable decrease in RF, CRP, and ESR levels, suggesting that MECM suppresses

systemic inflammation and autoimmune responses. Raised ALT, AST, ALP, urea, and creatinine levels in the DC group suggest liver and kidney impairment due to chronic inflammation. Administration of MECM decreased these levels, indicating protective activity. Additionally, our macroscopical and histopathological study reveals that enhanced joint structure is achieved by decreasing bone deformity, oedema, and synovial damage, continually restoring joint architecture toward the NC. Our study aligns with the other botanicals that have been extensively evaluated for RA, such as *Curcuma longa* and *Boswellia serata* [42–44]. Both of these plants are well-established and clinically recognised phytomedicines for their anti-inflammatory and antioxidant properties. *Caryota mitis* remains largely unexplored. Our findings therefore position *C. mitis* within this broader pharmacological context, complementing established botanicals while contributing novel evidence for its anti-arthritis efficacy.

Despite its promising findings, the study holds some inherent limitations. Firstly, in this preliminary study, advanced phytochemical analyses such as Gas Chromatography–Mass Spectrometry or Liquid Chromatography–Mass Spectrometry were not performed, as these facilities were not available to us. Identifying and isolating the specific active constituents would provide stronger mechanistic insights. Nevertheless, previous phytochemical studies have already reported the presence of flavonoids, phenolic acids, sterols, and terpenoids in *C. mitis* [18]. These classes of compounds are well recognized for their anti-inflammatory, antioxidant, and immunomodulatory properties, which could plausibly contribute to the observed effects in our study. Future studies should build upon these findings by conducting bioactivity-guided fractionation to isolate and identify the lead phytoconstituents responsible for the observed effects. Secondly, the present work was limited to ELISA-kit-based assessments for cytokine quantification. Although addition of Western blot, Real-time quantitative polymerase chain reaction, and immunohistochemistry would provide deeper mechanistic insights into gene and protein expression changes. The current study's sham control group was not included; however, the control group served as the baseline reference. Future studies should include a sham control group to further strengthen the experimental design. Lastly, this study was conducted using an adjuvant-induced arthritis rat model, which, although widely accepted, may not fully replicate the complexity of human RA. Future work should extend to multiple pre-clinical models, long-term safety evaluations, and eventually clinical validation to translate the therapeutic potential of *C. mitis*.

5. CONCLUSION

The current investigation revealed that the MECM demonstrated anti-inflammatory and anti-arthritis effects in CFA-induced rats, likely mediated through the regulation of cytokine balance and oxidative stress. These findings validate ethnomedicinal claims. Future work should include bioactivity-guided fractionation, identification of active constituents, molecular and cellular pathway analyses,

pharmacokinetics, and formulation strategies to establish translational relevance.

6. LIST OF ABBREVIATIONS

C. mitis: *Caryota mitis*; CFA: Complete Freund's Adjuvant; RA: Rheumatoid Arthritis; ROS: Reactive Oxygen Species.

7. ACKNOWLEDGMENTS

The authors thank the Dean, School of Pharmaceutical Sciences, for his support. Sandesh Kumar Pattanaik was supported in this work by the SOADU Ph.D. fellowship in Pharmacy "Registration No 2381606012".

8. AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

9. CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

10. ETHICAL APPROVAL

The study protocol was approved by the Institutional Animal Ethics Committee (IAEC) of School of Pharmaceutical Sciences, Siksha 'O' Anusandhan, Deemed to be a University, India (Approval No.: IAEC/SPS/SOA/217/2025; Date: 24/01/2025). All experimental procedures were reviewed, supervised, and authorised by the IAEC. The study was conducted in accordance with the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) and the ARRIVE guidelines.

11. DATA AVAILABILITY

All data generated and analyzed are included in this research article.

12. PUBLISHER'S NOTE

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13. USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declare that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript, and no images were manipulated using AI.

REFERENCES

- Goswami TK, Singh M, Dhawan M, Mitra S, Emran TB, Rabaan AA, *et al.* Regulatory T cells (Tregs) and their therapeutic potential against autoimmune disorders - advances and challenges. *Hum Vaccin Immunother.* 2022;18(1):2035117. doi: <https://doi.org/10.1080/21645515.2022.2035117>
- Raj PP, Gopal RK, Sanniyasi E. Investigating the anti-inflammatory and anti-arthritis effects of fucoidan from a brown seaweed. *Curr Res Biotechnol.* 2024;7:100220. doi: <https://doi.org/10.1016/j.crbiot.2024.100220>
- Saleem A, Saleem M, Akhtar MF. Antioxidant, anti-inflammatory and antiarthritic potential of *Moringa oleifera* Lam: an ethnomedicinal plant of Moringaceae family. *South Afr J Bot.* 2020;128:246–56. doi: <https://doi.org/10.1016/j.sajb.2019.11.023>
- Guo X, Wu W, Ran Q, Wang L, Li Y, Chen J, *et al.* Exploring the pharmacological mechanisms of the flower of *Rhododendron molle* in rheumatoid arthritis rats based on metabolomics integrated network pharmacology. *J Ethnopharmacol.* 2024;334:118524. doi: <https://doi.org/10.1016/j.jep.2024.118524>
- Puppala ER, Prasad N, Prakash AN, Abubakar M, Syamprasad NP, Gangasani JK, *et al.* *Mesua assamica* (King & Prain) kosterm. Bark ethanolic extract attenuates rheumatoid arthritis via down-regulating TLR4/NF-kappaB/COX-2/iNOS and activation of Nrf2/HO-1 pathways: a comprehensive study on *in-vitro* and *in-vivo* models. *J Ethnopharmacol.* 2024;335:118671. doi: <https://doi.org/10.1016/j.jep.2024.118671>
- Shekh MR, Ahmed N, Kumar V. A review of the occurrence of rheumatoid arthritis and potential treatments through medicinal plants from an Indian perspective. *Curr Rheumatol Rev.* 2024;20(3):241–69. doi: <https://doi.org/10.2174/0115733971268416231116184056>
- Fang Q, Zhou C, Nandakumar KS. Molecular and cellular pathways contributing to joint damage in rheumatoid arthritis. *Mediators Inflamm.* 2020;1(1):3830212. doi: <https://doi.org/10.1155/2020/3830212>
- Kany S, Vollrath JT, Relja B. Cytokines in inflammatory disease. *Int J Mol Sci.* 2019;20(23):6008. doi: <https://doi.org/10.3390/ijms20236008>
- Liu S, Deng Z, Chen K, Jian S, Zhou F, Yang Y, *et al.* Cartilage tissue engineering: from proinflammatory and anti-inflammatory cytokines to osteoarthritis treatments (Review). *Mol Med Rep.* 2022;25(3):99. doi: <https://doi.org/10.3892/mmr.2022.12615>
- Haddad JJ, Fahlman CS. Redox- and oxidant-mediated regulation of interleukin-10: an anti-inflammatory, antioxidant cytokine?. *Biochem Biophys Res Commun.* 2002;297(2):163–76. doi: [https://doi.org/10.1016/s0006-291x\(02\)02094-6](https://doi.org/10.1016/s0006-291x(02)02094-6)
- Phull AR, Nasir B, Haq IU, Kim SJ. Oxidative stress, consequences and ROS mediated cellular signaling in rheumatoid arthritis. *Chem Biol Interact.* 2018;281:121–36. doi: <https://doi.org/10.1016/j.cbi.2017.12.024>
- Singh JA. Treatment guidelines in rheumatoid arthritis. *Rheum Dis Clin North Am.* 2022;48(3):679–89. doi: <https://doi.org/10.1016/j.rdc.2022.03.005>
- Shokry AA, El-Shiekh RA, Kamel G, Bakr AF, Sabry D, Ramadan A. Anti-arthritis activity of the flavonoids fraction of ivy leaves (*Hedera helix* L.) standardized extract in adjuvant induced arthritis model in rats in relation to its metabolite profile using LC/MS. *Biomed Pharmacother.* 2022;145:112456. doi: <https://doi.org/10.1016/j.biopha.2021.112456>
- Magni A, Agostoni P, Bonezzi C, Massazza G, Mene P, Savarino V, *et al.* Management of osteoarthritis: expert opinion on NSAIDs. *Pain Ther.* 2021;10(2):783–808. doi: <https://doi.org/10.1007/s40122-021-00260-1>
- Pattanaik SK, Anil MP, Jena S, Rath D. A mechanism-based perspective on the use of flavonoids in the treatment of diabetes and its complications. *Curr Diabetes Rev.* 2024;22(2):1–22. doi: <https://doi.org/10.2174/0115733998335480241022084655>
- Kumar SS, Bhosle D, Janghel A, Deo S, Raut P, Verma C, *et al.* Indian medicinal plants used for treatment of rheumatoid arthritis. *Res J Pharm Technol.* 2015;8(5):597–610. doi: <https://doi.org/10.5958/0974-360X.2015.00099.2>
- Lu S, Wang Q, Li G, Sun S, Guo Y, Kuang H. The treatment of rheumatoid arthritis using Chinese medicinal plants: from pharmacology to potential molecular mechanisms. *J Ethnopharmacol.* 2015;176:177–206. doi: <https://doi.org/10.1016/j.jep.2015.10.010>
- Pattanaik SK, Jena S, Rath D. Pharmacology and phytochemistry of *Caryota mitis*: a brief. *Int Res J Multidiscip Scope.* 2025;6(1):1168–80. doi: <https://doi.org/10.47857/irjms.2025.v06i01.02369>
- Mollik M, Hassan AI, Paul TK, Mariz Sintaha MS, Khaleque HN, Noor FA, *et al.* A survey of medicinal plant usage by folk medicinal practitioners in two villages by the Rupsha River in Bagerhat district, Bangladesh. *Am -Eurasia Sustain Agric.* 2010; 4: 349–57. Available from: <https://api.semanticscholar.org/CorpusID:129530852>
- Das C, Kar P, Dash P, Pradhan D, Rai VK, Rajwar TK, *et al.* Protective effect of *Tecoma stans* (L.) Juss.ex Kunth in CFA-induced arthritic rats. *J Ethnopharmacol.* 2025;337:118944. doi: <https://doi.org/10.1016/j.jep.2024.118944>
- Percie Du Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, Baker M, *et al.* The ARRIVE guidelines 2.0: updated guidelines for reporting animal research. *PLoS Biol.* 2020;18(7):e3000410. doi: <https://doi.org/10.1371/journal.pbio.3000410>
- Singh VP, Yadav S. Ethics, animal welfare and regulation: the Indian perspective. In: Nagarajan P, Gudde R, Srinivasan R, editors. *Essentials of laboratory animal science: principles and practices.* Singapore: Springer Singapore; 2021. 39 p
- Rath D, Kar DM, Panigrahi SK, Maharana L. Antidiabetic effects of *Cuscuta reflexa* Roxb. in streptozotocin induced diabetic rats. *J Ethnopharmacol.* 2016;192:442–9. doi: <https://doi.org/10.1016/j.jep.2016.09.026>
- Pattanaik SK, Pattanaik S, Dash M, Sahoo S, Ray A, Jena S, *et al.* Exploring anti-diabetic activity of *Caryota mitis* Lour. through modulation of PPAR- alpha/gamma, GLUT-4, using *in-vitro*, *in-vivo* and *in-silico* approaches. *J Ethnopharmacol.* 2025;352:120215. doi: <https://doi.org/10.1016/j.jep.2025.120215>
- Patel R, Kadri S, Gohil P, Deshpande S, Shah G. Amelioration of complete Freund's adjuvant-induced arthritis by *Calotropis procera* latex in rats. *Future J Pharm Sci.* 2021;7(1):213. doi: <https://doi.org/10.1186/s43094-021-00361-w>
- Das C, Ghosh G, Rath G, Das D, Kar B, Pradhan D, *et al.* Chemometric profiling and anti-arthritis activity of aerial parts of *Glinus oppositifolius* (L.) Aug. DC. *J Ethnopharmacol.* 2024;328:117991. doi: <https://doi.org/10.1016/j.jep.2024.117991>
- Das C, Ghosh G, Bose A, Das D. Prophylactic efficacy of bioactive compounds identified from GC-MS analysis of Balarista formulation on adjuvant induced arthritic rats by inhibiting COX-2 inhibitor. *South Afr J Botany.* 2021;141:200–18. doi: <https://doi.org/10.1016/j.sajb.2021.04.033>
- Pattanaik S, Paidsetty SK, Pakeeraiah K, Prusty SK, Sahu PK. Design and synthesis of phyto-Saxagliptin conjugates: targeting DPP IV, AChE, and β -amyloid in cognitive impairment. *J Mol Struct.* 2025;1322:140386. doi: <https://doi.org/10.1016/j.molstruc.2024.140386>
- Wang F, Liu M, Tang Q, Sun H, Yang G, Sun J. Anti-rheumatic arthritis efficacy of *Pueraria montana* extract against type-II collagen-induced rheumatoid arthritis rat model an *in vitro* and *in vivo* assessment. *J Ethnopharmacol.* 2025;340:119175. doi: <https://doi.org/10.1016/j.jep.2024.119175>
- Cajas LJ, Casallas A, Medina YF, Quintana G, Rondón F. Pannus and rheumatoid arthritis: historic and pathophysiological evolution. *Revista Colombiana De Reumatología (English Ed).* 2019;26(2):118–28. doi: <https://doi.org/10.1016/j.rcreue.2018.10.005>
- Finckh A, Gilbert B, Hodgkinson B, Bae SC, Thomas R, Deane KD, *et al.* Global epidemiology of rheumatoid arthritis. *Nat Rev Rheumatol.* 2022;18(10):591–602. doi: <https://doi.org/10.1038/s41584-022-00827-y>

32. Fazal SA, Khan M, Nishi SE, Alam F, Zarin N, Bari MT, *et al.* A clinical update and global economic burden of rheumatoid arthritis. *Endocr Metab Immune Disord Drug Targets.* 2018;18(2):98–109. doi: <https://doi.org/10.2174/1871530317666171114122417>
33. Haleagrahara N, Hodgson K, Miranda-Hernandez S, Hughes S, Kulur AB, Ketheesan N. Flavonoid quercetin-methotrexate combination inhibits inflammatory mediators and matrix metalloproteinase expression, providing protection to joints in collagen-induced arthritis. *Inflammopharmacology.* 2018;26(5):1219–32. doi: <https://doi.org/10.1007/s10787-018-0464-2>
34. Satapathy T, Minj A, Verma M. Impact of NSAIDs corticosteroids DMARDs biologics and their comparisons with natural products in C-reactive proteins (CRP) linked cardiovascular disorders. *Inflammopharmacology.* 2025;2025:1–27. doi: <https://doi.org/10.1007/s10787-025-01767-1>
35. Pattanaik SK, Anil PM, Jena S, Rath D. Interlinking diabetes and Alzheimer’s disease: a pathway through medicinal plant-based treatments. *J Ethnopharmacol.* 2025;351:120092. doi: <https://doi.org/10.1016/j.jep.2025.120092>
36. Pattanaik SK, Sahoo S, Acharya SK, Barad PK, Pattanaik S, Rath D. *Crateva magna* (Lour.) DC ameliorates rheumatoid arthritis via TNF-signalling pathways: an integration of *in-silico*, *in-vitro* and *in-vivo* approach. *J Ethnopharmacol.* 2026;356:120854. doi: <https://doi.org/10.1016/j.jep.2025.120854>
37. Esho BA, Samuel B, Akinwunmi KF, Oluyemi WM. Membrane stabilization and inhibition of protein denaturation as mechanisms of the anti-inflammatory activity of some plant species. *Trends Pharm Sci.* 2021;7(4):269–78. doi: <https://doi.org/10.30476/tips.2021.93160.1118>
38. Adefegha SA, Bottari NB, Leal DB, De Andrade CM, Schetinger MR. Interferon gamma/interleukin-4 modulation, anti-inflammatory and antioxidant effects of hesperidin in complete Freund’s adjuvant (CFA)-induced arthritis model of rats. *Immunopharmacol Immunotoxicol.* 2020;42(5):509–20. doi: <https://doi.org/10.1080/08923973.2020.1814806>
39. Klingberg E, Bilberg A, Björkman S, Hedberg M, Jacobsson L, Forsblad-D’Elia H, *et al.* Weight loss improves disease activity in patients with psoriatic arthritis and obesity: an interventional study. *Arthritis Res Therapy.* 2019;21(1):17. doi: <https://doi.org/10.1186/s13075-019-1810-5>
40. Hu Y, Cardounel A, Gursoy E, Anderson P, Kalimi M. Anti-stress effects of dehydroepiandrosterone: protection of rats against repeated immobilization stress-induced weight loss, glucocorticoid receptor production, and lipid peroxidation. *Biochem Pharmacol.* 2000;59(7):753–62. doi: [https://doi.org/10.1016/s0006-2952\(99\)00385-8](https://doi.org/10.1016/s0006-2952(99)00385-8)
41. Fonseca LJSD, Nunes-Souza V, Goulart MOF, Rabelo LA. Oxidative stress in rheumatoid arthritis: what the future might hold regarding novel biomarkers and add-on therapies. *Oxidative Med Cellular Longevity.* 2019;1(1):7536805. doi: <https://doi.org/10.1155/2019/7536805>
42. Mahto K, Kuwar OK, Maloo A, Kumar A. Therapeutic potential of *Boswellia serrata* in arthritis management: mechanistic insights into COX-2, 5-LOX, and NFκB modulation. *Inflammopharmacology.* 2025;2025:1. doi: <https://doi.org/10.1007/s10787-025-01912-w>
43. Zeng L, Yang T, Yang K, Yu G, Li J, Xiang W, *et al.* Efficacy and safety of curcumin and *curcuma longa* extract in the treatment of arthritis: a systematic review and meta-analysis of randomized controlled trial. *Front Immunol.* 2022;13:891822. doi: <https://doi.org/10.3389/fimmu.2022.891822>
44. Kim H, Jung J, Lee M, Kim M, Kang N, Kim OK, *et al.* *Curcuma longa* L. extract exhibits anti-inflammatory and cytoprotective functions in the articular cartilage of monoiodoacetate-injected rats. *Food Nutr Res.* 2024;68:10402. doi: <https://doi.org/10.29219/fnr.v68.10402>

How to cite this article:

Pattanaik SK, Pattanaik S, Pattanaik S, Jena S, Rath D. Modulation of inflammatory pathways by *Caryota mitis* in rheumatoid arthritis: *In-vitro* and *in-vivo* insights. *J Appl Pharm Sci.* 2026;16(05):176-186. DOI: 10.7324/JAPS.2026.286618