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Research Article

EVALUATION OF THE ANTI-ARTHRITIC ACTIVITY OF THE AQUEOUS EXTRACT OF THE LEAVES OF *ANNONA SENEGALENSIS* PERS. (ANNONACEAE)

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ABSTRACT

Objectives: Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting the joints, with symptoms such as edema, pain, and joint deformities. This study aimed to evaluate the effect of the aqueous extract of the leaves of *Annona senegalensis* on arthritis in rats.

Methods: Arthritis was induced by injecting 0.1 mL of Complete Freund's Adjuvant (CFA) into the left hind paw of the rats. The extract was administered orally at daily doses of 40, 100, and 200 mg/kg body weight. Assessments included paw edema volume, joint structure, oxidative stress markers, and the activity of major antioxidant enzymes. Preliminary phytochemical analysis showed significant levels of polyphenols (224.71±8.42 mg EAG/g extract), flavonoids (26.16±2.09 mg EQ/g extract), and tannins (107.06±5.19 mg EAT/g). The extract significantly reduced paw edema volume ($p<0.001$), with inhibition rates reaching up to 44.74%. Biochemical analyses showed a reduction in oxidative stress, indicated by decreased malondialdehyde levels and increased activities of antioxidant enzymes, particularly superoxide dismutase and catalase. Histological examination of paw tissue from treated and control animals showed improved joint architecture following extract administration.

Conclusion: *A. senegalensis* exhibits significant anti-arthritic potential, supporting its use as a promising therapeutic agent for the management of RA.

Keywords: *Annona senegalensis*, Arthritis, Oxidative stress, Rat.

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INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune inflammatory disease with a prevalence estimated at 1% of the world's population [1]. It is characterized by systemic inflammation of joints, affecting the cartilage and bone around the joints. In severe cases, it can result in significant destruction of bone and cartilage [2,3]. RA can likewise affect different segments of the body in like manner joints and even delivers diffuse disease or irritation in the lungs, pericardium, pleura, and sclera, nodular sores, and in subcutaneous tissue [4]. The focal point in the treatment of RA is pain reduction, reduction of inflammation, and damage to joints [5]. Conventional synthetic anti-inflammatory drugs used in managing RA often show limited efficacy and are associated with long-term adverse effects [6]. This situation has stimulated interest in exploring alternative treatments based on medicinal plants, which are known for their tolerability and ability to act on multiple biological targets [7].

Annona senegalensis is a medicinal plant widely used in various regions of the world to treat multiple conditions, including joint pain and inflammation. It has been reported to possess antioxidant, antimicrobial, antidiarrheal, anti-inflammatory, antiparasitic, anticonvulsant, antimalarial, and antinociceptive properties [8]. The Complete Freund's Adjuvant (CFA)-induced arthritis model is commonly employed to simulate the characteristics of human arthritis, such as joint edema, oxidative stress, and alterations in the antioxidative system [9]. This model is linked to a significant increase in oxidative stress, contributing to cartilage destruction and the progression of inflammation [10].

This study aimed to evaluate the effect of the aqueous extract of the leaves of *A. senegalensis* (AEAS) on CFA-induced arthritis in rats through analysis of clinical, biochemical, and histopathological parameters.

METHODS

Plant material

The leaves of *A. senegalensis* were collected during the winter season in the Hauts-Bassins region (11°9'53.7"N, 04°18'18.6"W), situated more than 300 km from Ouagadougou, the capital of Burkina Faso. They were stored in plastic bags and transported to the Laboratory of Animal Physiology at Université Joseph KI-ZERBO (Ouagadougou), where they were washed and dried in a ventilated area. Botanical identification was conducted at the Department of Plant Biology and Ecology of the same university, where a sample was deposited under the identification number 18049.

Animal material

Male and Female Wistar rats weighing an average of 132.5 g from Université Joseph KI ZERBO were used. They were housed under standard laboratory conditions (22±3°C, relative humidity 50±10%, 12-h light/dark cycle) and had free access to food and water. All animal experiments were conducted by the Animals (Scientific Procedures) Act 1986 and the European Directive 2010/63/EU on the protection of animals used for scientific purposes. The study also complied with the ARRIVE 2.0 guidelines [11].

Preparation of the aqueous extract

The cleaned and dried leaves of *A. senegalensis* were ground into a fine powder. One hundred grams (100 g) of the powder were macerated in 1000 mL of distilled water for 24 h. The filtrate was centrifuged at 2000 rpm for 10 min. The supernatant was frozen at −23°C and subsequently lyophilized at 25°C for 24 h. The AEAS was obtained and stored in an airtight container. The extraction yield was 24.23%. It was calculated using the following formula: $\frac{\text{mass of extract obtained}}{\text{initial powder mass}}$

Quantitative phytochemical assays

Total polyphenols were measured using the colorimetric method with Folin–Ciocalteu reagent, as described by George *et al*. [12]. The flavonoid content of the extract was measured using the aluminum chloride ($AlCl_3$) method outlined by Lamien-Meda *et al.* [13]. Tannin levels in the extract were quantified following the method described by Sombie *et al*. [14].

Anti-arthritic activity of AEAS on CFA-induced arthritis

The methods described by Pearson and Wood [15] and Fotio *et al*. [16] were used to assess the effect of EAAS on chronic inflammation induced by CFA. Inflammation was induced in twenty-five (25) male and female rats by injection of 0.1 mL CFA into the subplantar surface of the hind paw of the rat. Rats were divided into five groups of 5 animals each. Group I received orally distilled water (10 mL/kg) and served as the control; group II received prednisolone (5 mg/kg); and groups III, IV, and V received the aqueous extract at doses of 40, 100, and 200 mg/kg, respectively. Treatment with extract and prednisolone began on day 9 after induction and was orally for 12 days. A further group of 5 rats served as a normal control and received neither inflammation induction nor treatment. Inflamed joint volume was measured before injection of the adjuvant (Vo) and on day 9, then every 3 days until day 21, using the UGO BASILE plethysmometer. At the end of the experiment, the animals were anesthetized by ether inhalation and then sacrificed. Blood was collected for complete blood count and serological analysis. Liver, kidneys, and spleen were collected for analysis of tissue oxidative stress parameters. Three inflamed joints were harvested per group and fixed in formalin (10%) for histological sections.

Biochemical and tissue oxidative stress parameters analysis

Blood collected in dry tubes was centrifuged at 3000 rpm for 15 min. The resulting serum was used to measure levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin, triglycerides, creatinine, and urea using colorimetric kits (Atlas Medical, UK), according to the manufacturer's instructions.

The liver, kidneys, and spleen were homogenized for oxidative Stress analysis. Malondialdehyde (MDA) levels were determined according to Lefevre *et al.* [17]. Catalase (CAT) activity was measured using Sinha's colorimetric method [18]. Superoxide dismutase (SOD) activity was evaluated following the method of Misra and Fridovich [19].

Histopathological analysis

Excised hind paws were fixed in 10% formalin for 1 week, then decalcified using 15% nitric acid. They were dehydrated in a graded ethanol series, cleared in xylene (1 h and 1.5 h), and embedded in paraffin. Histological sections were obtained and mounted on glass slides, stained with hematoxylin and eosin, and examined under a light microscope for morphological assessment.

Statistical analysis

Data were entered using Microsoft Excel 2016 and used to calculate joint volume differences and inflammation inhibition percentages. Results are expressed as mean ± standard error of the mean. Statistical analyses and graph generation were performed using GraphPad Prism version 8.3.4. One-way analysis of variance followed by Tukey's multiple comparison *post hoc* test was used to determine statistical significance. A $p<0.05$ was considered statistically significant.

RESULTS

Quantitative phytochemical analysis

Table 1 shows the estimated contents of total phenols, total flavonoids, and tannins in the extract. The contents were expressed per gram of dry extract and are 224.71±8.42 mg EAG/g for total polyphenols, 26.16±2.09 mg EQ/g for flavonoids, and 107.06±5.19 mg EAT/g for tannins.

Table 1: Quantitative phytochemical

Phytochemical components	Concentration (per g of dry extract)
Total polyphenols	224.71±8.42 mg GAE/g
Total tannins	107.06±5.19 mg TAE/g
Total flavonoids	26.16±2.09 mg QE/g

Effect of EAAS on paw edema

Subplantar injection of 0.1 mL of CFA into the right hind paw induced paw edema in rats, reaching a peak volume of 0.91±0.08 mL on day 15 post-induction. Treatment with EAAS at a dose of 200 mg/kg resulted in a significant ($p<0.001$) reduction in paw volume throughout the experimental period, with a maximum inhibition of 44.74% observed on day 18. At doses of 100 and 40 mg/kg, EAAS also significantly ($p<0.01$) reduced paw edema on day 15, with maximum inhibition percentages of 29.48% and 21.76%, respectively. The reference drug, prednisolone (5 mg/kg), exhibited the highest anti-inflammatory effect with a maximum inhibition of 68.05% recorded on day 21 (Table 2).

Effects of the AEAS on hematological parameters

Table 3 shows the effects of the AEAS on selected hematological parameters. A significant increase in white blood cell (WBC) count ($p<0.01$) was observed in rats treated with CFA alone (negative control group) compared to the normal control group. However, a significant decrease ($p<0.001$) in hemoglobin concentration, red blood cell (RBC) count, and platelet count was observed in the same animals compared to the normal control. Treatment with AEAS at doses of 200 and 100 mg/kg significantly reduced ($p<0.01$) the elevated WBC counts compared to the negative control group. At the same doses, the extract significantly increased RBC count, hemoglobin concentration ($p<0.01$), and platelet count ($p<0.001$ and $p<0.05$, respectively) compared to the control.

Effects of the AEAS on hepatic and renal biomarkers

Figs. 1 and 2 show the effects of the AEAS on hepatic and renal function biomarkers. A significant increase in serum levels (ALT; $p<0.001$), bilirubin ($p<0.05$), creatinine, and urea ($p<0.001$) was observed in CFA-treated rats compared to the normal control group. However, the levels of AST and ALP did not show significant changes ($p>0.05$) relative to the normal control. Treatment with EAAS at doses of 200 and 100 mg/kg led to a significant reduction in ALT levels ($p<0.05$ and $p<0.01$, respectively) compared to the CFA control group. The same doses also significantly reduced urea concentrations ($p<0.01$ and $p<0.05$, respectively).

Effect of the AEAS on oxidative stress parameters

The effects of AEAS on MDA concentrations, SOD, and CAT activities are presented in Table 4. These results show a significant increase ($p<0.001$) in MDA concentration in the liver, kidneys, and spleen of rats treated with CFA alone compared to the normal control. Conversely, SOD and CAT activities were significantly decreased ($p<0.001$) in these organs in rats treated with CFA alone compared to the normal control. The dose of 200 mg/kg extract produced a significant reduction ($p<0.001$) in MDA concentration, as did the doses of 100 and 40 mg/kg ($p<0.01$) compared to the negative control. CAT activity increased significantly ($p<0.001$) at all doses of the extract, as did SOD activity ($p<0.001$; $p<0.01$ and $p<0.05$ for doses of 200, 100, and 40 mg/kg, respectively) compared to the control.

Effect of AEAS on the histological structure of the rat ankle joint

Fig. 3 shows photographs of sections of the rat ankle joint. CFA induced WBC infiltration, joint space erosion, granuloma formation, and synovial pannus in rats. Rats treated with prednisolone 5 mg/kg and different doses of the extract showed protection of the joint structure with slight white cell infiltration, reduced erosion characterized by a decrease in joint space and synovial membrane thickening.

Table 2: Effect of AEAS on CFA-induced arthritis in rats

Day	CFA (Control)	Prednisolone (5 mg/kg) (%)	AEAS (200 mg/kg) (%)	AEAS (100 mg/kg) (%)	AEAS (40 mg/kg) (%)
9	0.80±0.03	0.55±0.04 (31.66)***	0.67±0.03 (15.67)**	0.70±0.05 (11.91)	0.72±0.07 (10.03)
12	0.84±0.06	0.41±0.02 (51.04)**	0.66±0.03 (21.66)*	0.68±0.05 (19.58)*	0.76±0.05 (10.09)
15	0.91±0.08	0.36±0.06 (60.61)***	0.57±0.03 (37.74)**	0.64±0.03 (29.48)*	0.71±0.04 (21.76)*
18	0.86±0.06	0.34±0.05 (60.17)***	0.48±0.03 (44.74)***	0.62±0.02 (27.91)**	0.68±0.04 (20.93)*
21	0.78±0.04	0.25±0.11 (68.05)***	0.46±0.02 (41.21)***	0.59±0.02 (24.92)**	0.64±0.05 (18.53)**

The values are expressed as mean±standard error of the mean. The values in parentheses represent the mean percentage of inhibition; n=5, *p<0.05, **p<0.01, ***p<0.001, significant differences compared to the control. EAAS: Aqueous extract of the leaves of *Annona senegalensis*, CFA: Complete Freund's adjuvant

Table 3: Effects of the aqueous extract of the leaves of *Annona senegalensis* on selected hematological parameters

Parameter	Control	CFA	Prednisolone 5 mg/kg	AEAS 200 mg/kg	AEAS 100 mg/kg	AEAS 40 mg/kg
WBC (10≥/µL)	6.10±0.73	9.57±0.58**	6.02±0.51$^{\#\#}$	7.02±0.24$^{\#}$	7.24±0.18$^{\#}$	8.46±0.26
RBC (10^6/µL)	9.47±0.11	7.90±0.16***	9.04±0.11$^{\#\#}$	8.95±0.19$^{\#}$	8.83±0.18$^{\#}$	8.69±0.26
HGB (g/dL)	16.31±0.06	14.80±0.05***	16.04±0.08$^{\#\#}$	15.73±0.13$^{\#}$	15.69±0.27$^{\#}$	15.40±0.20
PLT (10≥/µL)	912.67±44.86	770.00±39.8***	974.67±17.70$^{\#\#\#}$	924.67±19.8$^{\#\#\#}$	843.67±31.8$^{\#}$	814.67±28.76

Data are expressed as mean±standard error of the mean; n=5. *p<0.05, **p<0.01, ***p<0.001: Significant differences compared to normal group. $^{\#}$p<0.05, $^{\#\#}$p<0.01, $^{\#\#\#}$p<0.001: significant differences compared to control group (CFA). AEAS: Aqueous extract of the leaves of *Annona senegalensis*, CFA: Complete Freund's adjuvant

Table 4: Effect of aqueous extract of the leaves of *Annona senegalensis* on oxidative stress parameters in liver, kidney, and spleen

Tissue	Parameters	Treatment (mg/kg)					
		DW	CFA	Pred 5	AEAS 200	AEAS 100	AEAS 40
Liver	SOD (U/mg protein)	4.05±2.02	1.47±3.23***	3.68±2.24$^{\neq\neq\neq}$	3.08±2.67$^{\neq\neq}$	2.77±2.91$^{\neq\neq}$	2.21±2.79
	CAT (U/mg protein)	21.13±0.2	16.01±0.07***	19.67±0.2$^{\neq\neq\neq}$	18.01±0.31$^{\neq\neq\neq}$	17.80±0.2$^{\neq\neq\neq}$	18.72±0.23$^{\neq\neq\neq}$
	MDA (mmol/L)	0.29±0.01	0.52±0.03***	0.32±0.01$^{\neq\neq\neq}$	0.35±0.02$^{\neq\neq\neq}$	0.36±0.01$^{\neq\neq\neq}$	0.43±0.01
Kidney	SOD (U/mg protein)	2.41±0.4	0.44±0.2***	2.17±0.06$^{\neq\neq}$	2.03±0.05$^{\neq}$	1.18±0.13$^{\neq}$	0.98±0.07
	CAT (U/mg protein)	38.26±1.11	26.27±1.3***	36.26±0.83$^{\neq\neq\neq}$	33.02±0.33$^{\neq\neq}$	28.62±1.19	29.01±0.9
	MDA (mmol/L)	0.39±0.004	0.55±0.01***	0.46±0.003$^{\neq\neq\neq}$	0.49±0.004$^{\neq}$	0.53±0.02	0.52±0.009
Spleen	SOD (U/mg protein)	6.74±0.22	3.21±0.16***	6.51±0.27$^{\neq\neq\neq}$	5.65±0.06$^{\neq\neq\neq}$	5.08±0.18$^{\neq\neq}$	4.99±0.21$^{\neq}$
	CAT (U/mg protein)	27.18±0.41	21.12±0.01***	24.83±0.93$^{\neq\neq}$	24.72±0.71$^{\neq\neq}$	22.51±0.22	23.08±0.56
	MDA (mmol/L)	0.62±0.01	0.78±0.02***	0.63±0.01$^{\neq\neq\neq}$	0.64±0.01$^{\neq\neq\neq}$	0.66±0.02$^{\neq\neq}$	0.67±001$^{\neq\neq}$

Values represent mean±standard error of the mean; n=5; *p<0.05, **p<0.01, ***p<0.001, significant differences from the normal control; $^{\neq}$p<0.05, $^{\neq\neq}$p<0.01, $^{\neq\neq\neq}$p<0.001, significant differences from CFA control group. EAAS: Aqueous extract of the leaves of *Annona senegalensis*, CFA: Complete Freund's adjuvant, Pred: Prednisolone, ED: Distilled water, MDA: Malondialdehyde, SOD: Superoxide dismutase, CAT: Catalase

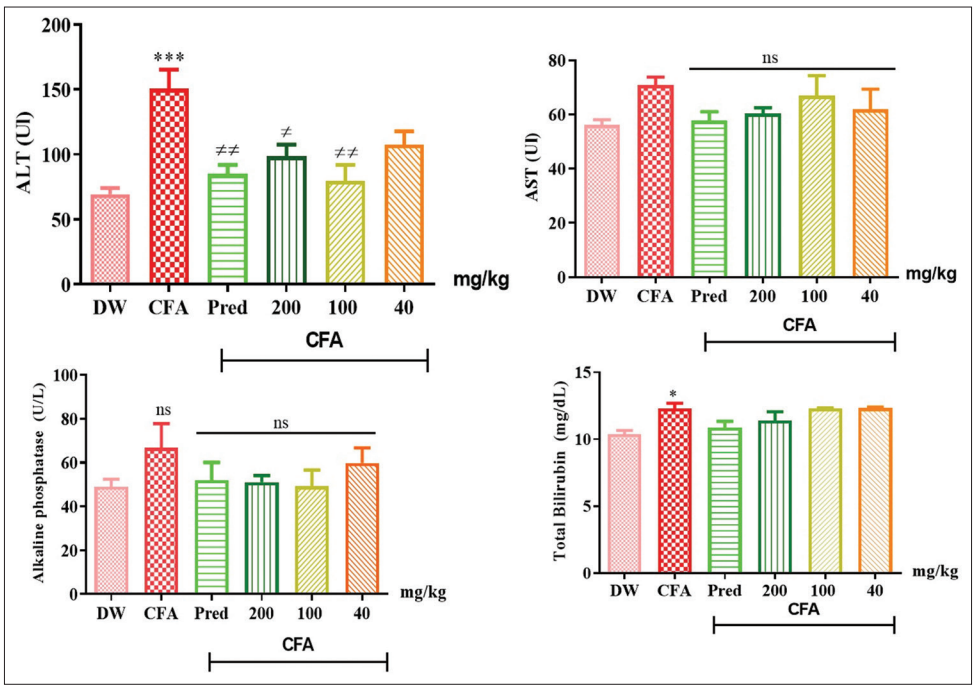

Fig. 1: Effects of aqueous extract from the leaves of *Annona senegalensis* on markers of liver function in rats

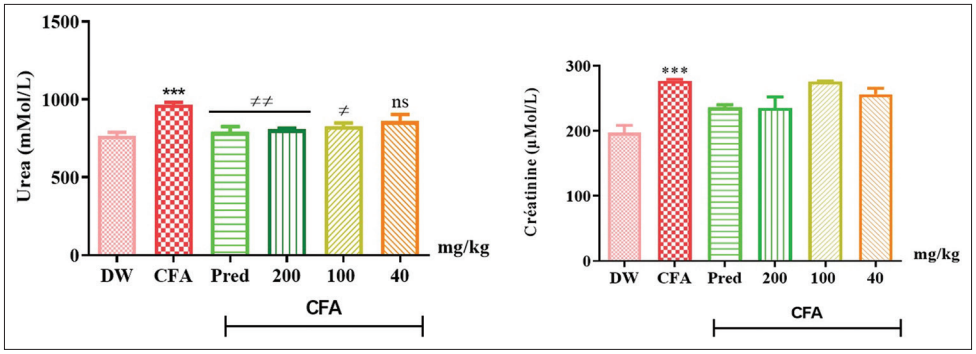

Fig. 2: Effects of the aqueous extract of the leaves of *Annona senegalensis* on renal function markers in rats. Each bar represents the mean±standard error of the mean (n=5); *p<0.05; ***p<0.001 indicate a significant difference compared to the normal control group. *p<0.05; **p<0.01 indicate a significant difference compared to the complete Freund's adjuvant control group

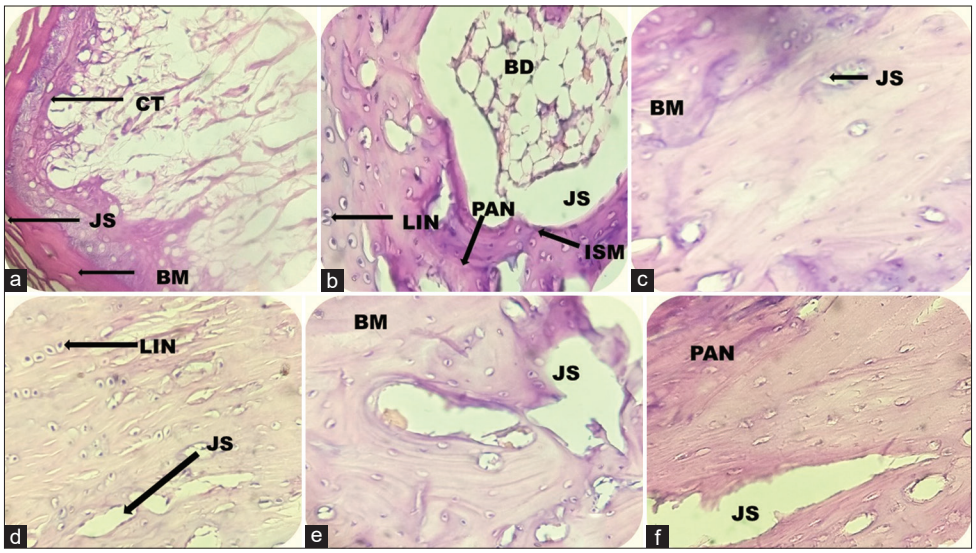

Fig. 3: Sections of the rat ankle joint. (a) Normal control, (b) CFA control, (c) Prednisolone 5 mg/kg, (d-f) Animals treated with aqueous extract of the leaves of *Annona senegalensis* at doses of 200, 100, and 40 mg/kg, respectively, CT: Cartilage tissue, PAN: Pannus, JS: Joint space, LIN: Leukocyte infiltration, BM: Bone matrix, BD: Bone destruction, ISM: Inflamed synovial membrane, CFA: Complete Freund's adjuvant

DISCUSSION

Chronic inflammation induced by CFA is associated with arthritis and constitutes one of the most widely used experimental models for studying RA [20]. This model replicates the symptoms observed in human arthritis, including joint edema, lymphocyte infiltration, and cartilage degradation [21]. The CFA, composed of immunostimulants derived from bacterial constituents (*Mycobacterium tuberculosis* or inactivated butyricum), sensitizes immune cells, triggering the local release of chemotactic factors that attract leukocytes. The inflammatory process is characterized by the infiltration of immune cells (macrophages, neutrophils, T, B, and NK lymphocytes) into inflamed joints, leading to fibroblast proliferation, such as synoviocytes [22]. The infiltration of immune cells and synovial cell proliferation leads to the formation of an invasive inflammatory tissue, known as a pannus, which destroys cartilage and bone. Synoviocytes produce chemokines, matrix metalloproteinases (MMPs), prostaglandin E2, and cyclooxygenase-2, which amplify inflammation, hyperplasia, and destruction of cartilage and bone tissue [23].

Injection of 0.1 mL CFA into the plantar joint of rats induced edema that peaked on the 15th day of the experiment. The extract, as well as prednisolone (used as a reference drug), significantly reduced edema volume throughout the experiment. These findings suggest that the extract possesses anti-inflammatory properties and can modulate immune responses. The anti-inflammatory activity of the extract may be attributed to the presence of chemical compounds with anti-inflammatory potential. Phytochemical assays showed the presence of polyphenols, flavonoids, and tannins at levels of 224.71±8.42 mg EAG/g, 26.16±2.09 mg EQ/g, and 107.06±5.19 mg EAT/g, respectively. These phytochemicals are known to possess therapeutic activity [24]. Nisar *et al.* [25] reported that certain phytochemical compounds such as polyphenols can suppress the expression of pro-inflammatory genes (interleukin [IL]-1A, IL-1B, tumor necrosis factor [TNF]) and upregulate the expression of anti-inflammatory genes such as IL10A and TGF-β1. Zhu *et al.* [26] demonstrated that kaempferol, a flavonoid, reduces pro-inflammatory cytokines while increasing IL-10, an anti-inflammatory cytokine. Kaempferol decreases the release of pro-inflammatory cytokines by inhibiting the activation of nuclear factor Kappa B (NF-κB), a key regulator of inflammation [27]. Flavonoids can also act on signal transduction through protein kinases, inducing the expression of antioxidant and anti-inflammatory genes and inhibiting oxidative and inflammatory genes [28]. The phytochemical compounds in the extract may also prevent leukocyte immunoproliferation at the inflammatory site and exert immunostimulatory effects on inflammatory cells. Gallic acid (a tannin) and vanillic acid (a phenolic acid) may inhibit leukocyte migration by suppressing adhesion molecules in vascular endothelial cells through inhibitory modulation of IL-1, TNF-α, and NF-κB [29].

Hematological analysis revealed a significant increase in WBC count accompanied by a decrease in hemoglobin levels, RBCs, and

circulating platelets in the CFA control group. The elevated levels of leukocytes indicate stimulation of immune defenses against invading pathogens [30]. The reduction in RBCs may be due to increased destruction and decreased synthesis [31]. Exposure of RBCs to harmful substances causes membrane lysis, hemolysis, and hemoglobin oxidation [32]. Platelets play a significant role in inflammation and immune response. They aggregate at the injury site and release cytokines and chemokines that attract neutrophils and monocytes [33]. They also adhere to WBCs to enhance their effects and form aggregates, leading to a decrease in circulating thrombocytes [34]. In animals treated with AEAS, these parameters showed notable improvement. At doses of 100 and 200 mg/kg, a significant reduction in leukocyte count was observed, along with an increase in RBCs, hemoglobin levels, and platelet count compared to the negative control group. These results indicate a potential immunomodulatory effect of the extract, which may also stabilize RBC membranes. Kitadi *et al.* [35] also demonstrated that the aqueous extract of *A. senegalensis* significantly prevents RBC hemolysis.

Serum ALT and urea levels were significantly increased in CFA control group, reflecting hepatocellular damage and renal insufficiency in these rats [36]. This increase was significantly inhibited by the extract, indicating its hepatoprotective and nephroprotective activities. Flavonoids, saponins, sterols, and triterpenes are known for their liver and kidney protective properties [37]. The presence of these metabolites in the extract may explain the observed effects.

During arthritis development, excessive accumulation of neutrophils in the affected area promotes free radical production [38]. CFA induced a significant increase in MDA levels and a decrease in CAT and SOD activity in the liver, kidneys, and spleen. The extract significantly increased CAT and SOD activity and significantly decreased MDA levels compared to the CFA control group. These results show that our extract reduced the deleterious effects of ROS accumulation. Flavonoids can react with most free radicals capable of abstracting hydrogen from CH2 groups between double bonds in polyunsaturated fatty acids, thereby effectively preventing lipid peroxidation. Several studies have shown that administration of polyphenol-rich extracts significantly increases CAT activity [39]. Histological analysis of the tibio-tarsal joint revealed severe synovial hyperplasia, massive leukocyte infiltration, cartilage degeneration, and synovial tissue thickening. Rats treated with *A. senegalensis* aqueous extract showed dose-dependent improvement in joint architecture, characterized by reduced severity of bone and cartilage destruction, decreased infiltration of inflammatory cells, and inhibition of cartilage and bone degradation. Our results demonstrate that *A. senegalensis* aqueous extract has anti-arthritic activity. Yoon *et al.* [40] showed that gallic acid, a natural polyphenolic acid, inhibits the expression of pro-inflammatory genes such as TNF-α, iNOS, ICAM-1, and MMPs in fibroblast-like synoviocytes of RA, thereby reducing inflammatory responses and slowing joint degradation and tissue damage progression. Gallic acid blocks pro-inflammatory signaling pathways (NF-κB, JAK/STAT, MAPK) and reduces the expression of tissue-degrading enzymes (MMPs), reducing inflammation and protecting tissues against damage caused by inflammation and oxidative stress in RA synoviocytes. Kaempferol, a flavonoid, inhibits the migration, invasion, and proliferation of fibroblast-like synoviocytes, which are key players in cartilage destruction. It also reduces TNF-α expression, thereby decreasing synovial inflammation [41,42].

CONCLUSION

The results obtained in this study demonstrate that the aqueous leaf extract of *A. senegalensis* exerts significant anti-arthritic activity in the CFA-induced arthritis model in rats. The extract significantly reduced paw edema, improved joint tissue architecture, and favorably modulated oxidative stress, as evidenced by decreased MDA levels and increased activities of SOD and CAT enzymes. The extract appears to act through a mechanism combining anti-inflammatory and antioxidant effects, attributable to the secondary metabolites it contains. Based on these findings, *A. senegalensis* could represent a potential alternative for the management of RA. However, further investigations are required to elucidate its molecular targets and better assess its efficacy.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally from conceptualization to quality control of the document.

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CONFLICT OF INTEREST STATEMENT

We declare that we have no conflict of interest.

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