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ORIGINAL ARTICLE

Antioxidant and anti-arthritic activity of *Bombax buonopozense* P. Beauv. leaves

Activité antioxydante et anti-arthritique des feuilles de Bombax buonopozense *P. Beauv. feuilles*

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HIGHLIGHTS

- Traditionally used for the treatment of arthritis in Ibadan, Nigeria, *Bombax buonopozense*'s efficacy need to be investigated. Therefore, this study aims to evaluate its antioxidant and anti-arthritic properties.
- The study presented preliminary phytochemicals and brine shrimp lethality was determined. Total phenolic content (TPC), Total flavonoid content (TFC) as well as anti-oxidant activity of the extract and fractions of *Bombax buonopozense* leaves.
- The first data on anti-arthritic activity of crude methanol extract (BBME) at 100, 200 and 400 mg/kg was evaluated in complete Freund adjuvant (CFA) induced arthritis model in rats.
- BBME significantly reduced the paw circumference. BBME (400 mg/kg) prevented biochemical changes to a greater extent than Celecoxib (20 mg/kg). *Bombax buonopozense* leaves could be an effective antiarthritic and holds prospect in the treatment of rheumatoid arthritis.

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KEYWORDS
Bombax buonopozense;
Phytochemical screening;
Antioxidant;
Antiarthritis;
Biochemical parameters

Summary
Background and aim. — *Bombax buonopozense* (Bombacaceae) leaves have been used traditionally for arthritis in south-western Nigeria. Therefore, the aim of the study was to investigate the antioxidant and anti-arthritic activity of *B. buonopozense* in Complete Freund adjuvant-induce arthritic wistar rats.
Experimental procedure. — The plant leaves methanol extract and fractions were screened for preliminary phytochemicals and brine shrimp lethality was determined. Total phenolic content (TPC), Total flavonoid content (TFC) as well as anti-oxidant activity of the extract and fractions were evaluated using 2,2-diphenyl-1-picrylhydrazyl (DPPH). Cyclophosphamide, gallic acid, and ascorbic acid were used as standards respectively. Anti-arthritic activity of crude methanol extract (BBME) at 100, 200 and 400 mg/kg was evaluated in complete Freund's adjuvant (CFA) induced arthritis model in rats. Data were analysed using Graph pad prism version 5, two-way and one-way ANOVA, and Bonferroni *post hoc* test.
Results and conclusion. — Phytochemical screening revealed the presence of flavonoids, alkaloids, and phenolics. The brine shrimp lethality assay of the crude extract and fractions gave LC_{50} value $\geq 1000\,\mu g/mL$, compared to Cyclophosphamide ($LC_{50} = 224.7 \pm 0.35\,\mu g/mL$). The BBME had TPC value of 19.8 ± 0.56 mg GAE/g, while the TFC of ethyl acetate fraction was the highest (173.5 ± 0.05 mg QE/g). The ethyl acetate fraction has the highest antioxidant activity ($IC_{50} = 20.96 \pm 0.23\,\mu g/mL$) as compared to ascorbic acid (2.8 ± 0.01) and rutin ($20.6 \pm 9.26\,\mu g/mL$). BBME significantly reduced the paw circumference. BBME (400 mg/kg) prevented biochemical changes to a greater extent than Celecoxib (20 mg/kg). *Bombax buonopozense* leaves could be an effective antiarthritic and holds prospect in the treatment of rheumatoid arthritis.

MOTS CLÉS
Bombax buonopozense ;
Criblage phytochimique ;
Antioxydant ;
Antiarthrite ;
Paramètres biochimiques

Résumé
Contexte et objectif. — Les feuilles de *Bombax buonopozense* (Bombacaceae) sont traditionnellement utilisées contre l'arthrite dans le sud-ouest du Nigeria. L'objectif de cette étude était donc d'étudier l'activité antioxydante et anti-arthritique de *B. buonopozense* chez des rats wistar souffrant d'arthrite induite par l'adjuvant complet de Freund.
Procédure expérimentale. — L'extrait de méthanol des feuilles de la plante et les fractions ont été examinés pour déterminer les substances phytochimiques préliminaires et la létalité de la crevette de la saumure a été déterminée. Le contenu phénolique total (TPC), le contenu flavonoïde total (TFC) ainsi que l'activité anti-oxydante de l'extrait et des fractions ont été évalués en utilisant le 2,2-diphényl-1-picrylhydrazyl (DPPH). La cyclophosphamide, l'acide gallique et l'acide ascorbique ont été utilisés comme étalons. L'activité anti-arthritique de l'extrait brut de méthanol (BBME) à 100, 200 et 400 mg/kg a été évaluée dans le modèle d'arthrite induite par l'adjuvant complet de Freund (CFA) chez les rats. Les données ont été analysées à l'aide de Graph pad prism version 5, Anova à deux voies et à une voie, et test post hoc de Bonferroni.
Résultats et conclusions. — Le criblage phytochimique a révélé la présence de flavonoïdes, d'alcaloïdes et de composés phénoliques. L'essai de létalité de l'extrait brut et des fractions sur la crevette saumonée a donné une valeur $LC50 \geq 1000\,\mu g/mL$, comparée à la cyclophosphamide ($LC50 = 224{,}7 \pm 0{,}35\,\mu g/mL$). Le BBME avait une valeur TPC de $19{,}8 \pm 0{,}56$ mg GAE/g, tandis que le TFC de la fraction d'acétate d'éthyle était le plus élevé ($173{,}5 \pm 0{,}05$ mg QE/g). La fraction d'acétate d'éthyle a l'activité antioxydante la plus élevée ($IC50 = 20{,}96 \pm 0{,}23\,\mu g/mL$) par rapport à l'acide ascorbique ($2{,}8 \pm 0{,}01$) et à la rutine ($20{,}6 \pm 9{,}26\,\mu g/mL$). Le BBME a réduit de manière significative la circonférence de la patte. Le BBME (400 mg/kg) a prévenu les changements biochimiques dans une plus large mesure que le célécoxib (20 mg/kg). Les feuilles de *B. buonopozense* pourraient être un antiarthritique efficace et offrent des perspectives dans le traitement de l'arthrite rhumatoïde.

Abbreviations

RA	Rheumatoid arthritis
DCM	Dichloromethane
TPC	Total phenolic content
TFC	Total flavonoid content
QE	quercetin equivalent
DPPH	2,2-diphenyl-1-picrylhydrazyl
CFA	Complete Freund's adjuvant
BBME	*Bombax buonopozense* methanol extract
GSH	Glutathione
MDA	malondialdehyde

Introduction

An autoimmune disorder, rheumatoid arthritis (RA) is characterized by symmetrical, inflammatory polyarthritis, which may lead to progressive joint destruction. Toxic compounds that are released into the synovium as a result of inflammation of the joint tissues damage cartilage, cause bone deformities, impair joint function, and finally excruciating pain [1—3]. It is the most prevalent inflammatory arthritis, affecting 20 million individuals worldwide, equivalent to 1—2% of the global population. Women are three times more likely to be affected than males, and the incidence rises with age [4,5].

Medicinal plants are the world's greatest bio-resource for drugs used in traditional medicine, contemporary drugs, functional food components, dietary supplements, folk remedies, pharmaceutical intermediates, and chemical entities for synthetic drugs. Plants are a great source of medicines that are beneficial in the treatment of a variety of disorders, especially in traditional medicine. It has been demonstrated that medicinal plants can be used to treat conditions like HIV/AIDS, malaria, diabetes, sickle-cell anemia, cancer, mental health problems, and microbial infections [6—9]. The primary benefits of using plant-derived medications are that they are typically safer than synthetic equivalents, have substantial therapeutic benefits, and are more affordable than other types of medication [10—12]. Also, the greater dependence on their use in industrialized nations has been attributed to the development of numerous drugs and chemotherapeutics from medicinal plants as well as from widely used rural medicines [13—15]. The World Health Organization recently emphasized the importance of documenting active medicinal plants used in various continents [16,17].

Among many African plants use for treatment of arthritis is *Bombax buonopozense* P. beauv. (Bombacacea). This big tropical tree can reach a height of 40 m and has large buttress roots that can extend six meters [18]. Several African nations, including Ghana, Sierra Leone, Uganda, and Gabon, have a large population of this species. Different parts are used for various uses, and it is known by common vernacular names in various languages, including Vabga (Dagbani) and Kurya (Hausa) [19]. As a galactagogue and to cure menstrual and cardiac issues, the tree's bark is prepared in various ways. In Nupeland, in north-central Nigeria, the stem bark is reportedly used to treat sleeping sickness. Bark infusions are consumed or applied topically to treat fever [20]. The prickly bark powder is used in medications to treat a variety of skin conditions, including river blindness. Diverse components of *Bombax buonopozense* are used for diverse reasons in Nigeria. The young leaves are prepared as an emollient, the ground bark is taken by pregnant women to stimulate lactation, the extract from the bark is drunk or applied to the head to relieve vertigo, and the gum resin from the bark is ground up, combined with oil, and used to treat skin conditions like ''craw-craw'' [21]. Alkaloids, tannins, saponins, steroids, flavonoids, and cardiac glycosides were found in *B. buonopozense* phytochemical investigation [22]. Traditionally used for the treatment of arthritis in Ibadan, Nigeria [23]. *Bombax buonopozense*'s efficacy need to be investigated. Therefore, this study aims to evaluate its antioxidant and anti-arthritic properties.

Material and methods

Drugs, chemicals and reagents

Complete Freund adjuvant (CFA; Santa Cruz Biotech., USA), DTNB (5,5′-dithiobis-2-nitrobenzoic acid; Sigma Aldrich, USA), triochloroacetic acid (Sigma Aldrich, USA), thiobarbituric acid (Sigma Aldrich, USA), sodium carbonate (BDH Poole, England), potassium carbonate (BDH Poole, England), and sodium chloride are some of the substances used (BDH Poole, England)2,2-Diphenyl-1-picrylhydrazyl, sodium bicarbonate, and 4% aluminum chloride (Sigma Aldrich Chemical, Co, USA), Folin-Ciocalteau Reagent, Rutin, Hydrochloric acid, Sodium hydroxide, Potassium Hydroxide, Chloroform, Methanol, Ethyl acetate, Glacial acetic acid, Tween-80, Glycerine, Conc. sulphuric acid, N-Butanol, Dichloromethane, *n*-hexane, Ferric chloride, Iodine, Lead acetate, Magnesium chloride, Nitric acid, Phloroglucinol, Potassium iodide, Safranin O, Sodium acetate, Sodium iodide, Sodium hydroxide.

Collection and identification of plant material

The leaves of *Bombax buonopozense* were collected in large quantity from the environs of the Department of Chemistry, University of Ibadan, Ibadan, Nigeria, in June 2017. The plant was identified by Mr Agwu Patrick of the Department of Pharmacognosy Herbarium, University of Ibadan (DPHUI), Ibadan and authenticated at Bowen University Herbarium, Iwo (voucher number = BUI: 082).

Extraction and partitioning of plant extract

Bombax buonopozense leaves were thoroughly separated from undesirable components. The fresh leaves were stripped from the stem, collected separately, and air-dried under shade for 21 days. An electric blender was used to grind the air-dried leaves. The coarsely pulverized powdered plant material (2 kg) was macerated, using 14 L of distilled methanol for 72 h. It was then filtered through Whatmann (No 1) filter paper. Three times this procedure was carried out. Using a rotary evaporator (Stuart-RE300DB), the filtrates were mixed and concentrated at 45 °C under reduced pressure until a semisolid dark brown crude extract was produced. The weight of the dried extracts was used to

determine the percentage yield, which was then placed in a freezer (4 °C) for storage. After the methanol extract had been dissolved in a 3:1 mixture of methanol and water, it was added to many separating funnels. A 50 mL was partitioned using n-hexane, dichloromethane (DCM), ethyl acetate, and butanol. To create the fractions that were retained in air-tight containers for preliminary testing, each aliquot of the n-hexane, DCM, ethyl acetate, butanol, and aqueous (marc) fractions were pull together and evaporated *in vacuo*. Each fraction's % yield was calculated using the weights that had been assigned to it.

Phytochemical screening

To identify the different kinds of secondary metabolites found in the plant, the extract was subjected to phytochemical screening. With the aid of previously defined standard procedures, tests were carried out on the sample to look for alkaloids, tannins, flavonoids, cardiac glycosides, saponins, steroids, terpenoids, and anthraquinones [24,25].

Estimation of total phenolic content

With a few minor adjustments, the Folin-Ciocalteu technique described by Ogunlakin et al. [26] was used to quantify the total phenolic component concentrations of extracts and fractions. The phenolic contents of the extract were determined using a gallic acid calibration curve that was made by combining 0.5 mL aliquots of 12.5, 25, 50, 100, and 200 μg/mL methanolic gallic acid solutions with 2.5 mL of diluted Follin-Ciocalteu reagent and 2.0 mL of sodium carbonate. After the combination was incubated for 30 minutes, a single beam UV/Visible spectrometer was used to estimate the quantitative amount of phenolics at 765 nm. By plotting the values of the absorbance against concentrations, the calibration curve was created. Determination of activity were made in triplicate for each sample. Using the equation stated below, the total phenolic content was estimated as milligrams of gallic acid equivalent (GAE) per gram of extract.

$$TPC = \left[\frac{Concentration \times Total\ volume}{Weight\ of\ sample}\right]$$

Estimation of total flavonoid content

Utilizing aluminum chloride colorimetry, the total flavonoid concentration was calculated [27]. Five milliliters of methanol was used to reconstitute one milligram of plant extract and its fractions. The samples' flavonoid contents were determined using a quercetin calibration curve that was created by mixing 0.5 mL aliquots of quercetin solutions that were 12.5, 25, 50, 100, and 200 μg/mL in methanol with 0.1 mL of potassium acetate solution, 0.1 mL of aluminum chloride solution, 1.5 mL of methanol, and 2.8 mL of distilled water. The mixture was tested with a single-beam UV/Visible spectrometer at 415 nm after 30 minutes of incubation to determine the quantitative quantity of flavonoids present. The calibration curve was created by showing the value of the absorbance against concentration. A triplicate for each concentration was made. As measured in milligrams of quercetin equivalent (QE) per gram of extract, the overall flavonoid content was determined by applying the following formula:

$$TFC = \left[\frac{Concentration \times Total\ volume}{Weight\ of\ sample}\right]$$

DPPH Free Radical Scavenging Assay

The plant's ability to scavenge free radicals was evaluated in vitro using the 2, 2-diphenyl-1-picrylhydrazyl (DPPH) assay, which was based on minor modifications of the method outlined by Ogunlakin et al. [27]. Rutin and ascorbic acid were the minimum requirements. The stock solutions were made by dissolving 2 mg of the test samples in 20 mL of methanol. The stock solution was then diluted to produce different concentrations (3.125, 6.25, 12.5, 25, 50, and 100 μg/mL). The DPPH reagent was dissolved in methanol to create the working solution (0.004%). Different concentrations of this solution (ranging from 100 to 3.125 μg/mL) were added to the test samples in a 3 mL aliquot. The reaction mixture was vigorously shaken and then incubated for 30 minutes in complete darkness at room temperature. Then, the absorption at 517 nm using a single beam UV/Visible spectrophotometer was recorded. This analysis was in triplicate for each test samples. The DPPH free radical scavenging activity for each sample was calculated using the equation below:

$$\%\ inhibition = \left[\frac{Absorbance\ of\ blank \times Absorbance\ of\ test\ sample}{Absorbance\ of\ blank}\right]$$

Brine shrimp lethality assay

In natural seawater collected from Sultan Beach in Badagry, Nigeria, brine shrimp eggs (Artemia salina (Leach)) was hatched. The eggs hatched after 48 hours in seawater, producing a high number of larva. To test the cytotoxicity of the crude extract and fractions, these microscopic shrimp larvae were utilized. Ten active shrimps (nauplii) each were taken after hatching and subjected to various plant extract's and fractions' concentrations (1, 10, 100, 500, and 1000 μg/mL). A non-linear regression curve was used to determine the 50% lethal concentration (LC_{50} value) at a 95% confidence interval for the plant extract and fractions. This was carried out following the procedure outlined by Ramachandran et al. [28].

In vivo study

Experimental animals

The male Wistar rats used in this study were 120—200 g in weight and were purchased from the animal house, University of Ibadan, Ibadan. The animals were housed in typical housing situations and kept in plastic cages. There was free access to water and basic food. The animals were acclimated for a week in the animal house before the trials began. All of the experimental methods in this investigation were carried out following the guidelines of the NIH Ethical Care and Use

of Laboratory Animals and Bowen University Iwo (BUI) Institutional Animal Ethics Committee (BUI/BCH/2017/0001).

Complete Freund Adjuvant-induced arthritis assay

According to the procedure previously outlined by Lee and Lim [29] and Daram et al. [30], experiments were conducted with slight modifications. The rats' left hind paws were injected with 0.1 mL of CFA (Sigma-Aldrich, MO) containing 10 mg/mL of heat-killed *Mycobacterium tuberculosis*. The six treatment groups, each with six rats, were created randomly from the rats. Group 1 received a 100 μL injection of normal saline and treated with normal saline. Group 2 contains arthritic rat treated with vehicle. Group 3 are arthritic rats, given BBME (100 mg/kg). Group 4 contains arthritic rats given BBME (200 mg/kg). Group 5 rats were arthritic and given BBME (400 mg/kg). Group 6 received celecoxib (20 mg/kg) treatment for arthritis. Different parameters were monitored to track the development of Complete Freund adjuvant-induced Arthritis in rats starting on day 1 following CFA injection. An electronic digital caliper was used to measure the ankle's circumference before and after induction of arthritis, and it was checked every seven days. On day 21, a plethysmometer and an analgesiometer were used to measure the paw volume. Locomotor activity was assessed using an open field maze [31]. The blood Serum was separated and analysed for serum nitrite, GSH, MDA, and serum alkaline phosphatase by standard methods [32—35].

Statistical analysis

The results of all assays obtained were statistically expressed as the mean with the standard deviation (mean ± SD). The collected data were analyzed with GraphPad (Version 9.0). One-way ANOVA followed by Dunnett's Multiple Comparison Test were employed to test for the statistical differences between the groups at $P < 0.05$.

Results

Phytochemical screening, Brine shrimp lethality and antioxidant assays

The distributions of flavonoids, phenolics, alkaloids, tannins, cardiac glycosides, steroids, and saponins in the plants' leaves extract and fractions varied, according to phytochemistry. The lack of anthraquinones was evident (Table 1). The range of the total phenolic content was 3.38 ± 0.26 to 49.88 ± 5.23 mg gallic acid equivalent/g, with the aqueous portions having the highest concentration, as shown. The greatest flavonoid concentrations were found in the ethyl acetate fractions, with total flavonoid levels ranging from 172 ± 0.15 to 173.5 ± 0.05 mg quercetin equivalent/g (Table 2). Fig. 1 displays the IC_{50} values (the concentration of the extract required to scavenge 50% of the DPPH radicals). The IC_{50} value is inversely proportionally to the antioxidant activity. The ethyl acetate fraction highest antioxidant activity followed by methanol extract (IC_{50} value of 20.96 ± 0.23 and 23.15 ± 0.96 g/mL, respectively). The IC_{50} values for ascorbic acid and rutin standards were

Table 1 Preliminary phytochemical screening of powdered sample of *Bombax buonopozense*.
Analyse phytochimique préliminaire de l'échantillon de poudre de Bombax buonopozense.

Test	Inferences
1. Alkaloid	
Mayer's reagent	++
Dragendorff's	+++
Wagner's reagent	+++
2. Saponin	
Frothing	+++
Emulsion	++
3. Anthraquinones	
Free Anthraquinone	—
Combined	—
4. Cardiac glycosides	
Keller-killani's	+++
Kedde's	++
5. Tannin	
Lead acetate test	+++
6. Flavonoid	
Schinoda's	+++
7. Steroids	
Liebermann-Burchard's Reaction	++

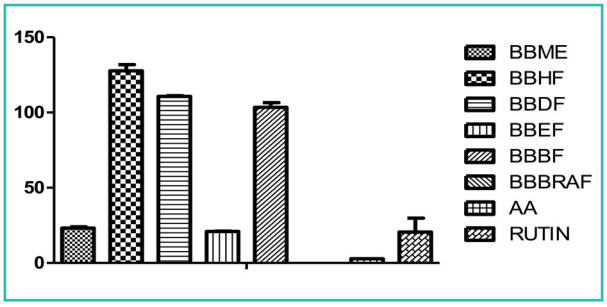

Figure 1. Mean IC_{50} values for DPPH Free Radical activities of *Bombax buonopozense* extract and fractions. BBME, BBHF, BBDF, BBEF, BBBF, BBRAF are Methanol, *n*-Hexane, Dichloromethane, Ethyl acetate, Butanol, and Residual aqueous fractions of *Bombax buonopozense*, respectively.
Valeurs moyennes de l'IC_{50} pour les activités radicales libres DPPH de l'extrait et des fractions de Bombax buonopozense. BBME, BBHF, BBDF, BBEF, BBBF, BBRAF sont respectivement les fractions aqueuses de méthanol, n-Hexane, dichlorométhane, acétate d'éthyle, butanol et résidu de Bombax buonopozense.

2.8 ± 0.01 g/mL and 20.6 ± 9.26 g/mL, respectively. The LC_{50} values of methanol extract, hexane, DCM ethyl acetate, butanol and residual aqueous fraction were 1920 ± 0.10, 1000 ± 0.02, 1000 ± 0.11, 1480 ± 0.18, 1400 ± 0.12, and 1440 ± 0.11 μg/mL, respectively, while cyclophosphamide (standard) had LC_{50} value of 227.35 ± 0.15 μg/mL (Table 3).

Antiarthritic activity of *B. buonopozense*

An increase in ankle thickness was measured to track the progression of arthritis. Rats with arthritis ($n = 6$) were evidently and significantly different from their non-arthritic littermates ($n = 6$) from the first day (Fig. 2). The arthritic

Table 2 Total phenolic content (TPC) and total flavonoid content (TFC) of the plant extracts and fractions.
Teneur totale en phénols (TPC) et teneur totale en flavonoïdes (TFC) des extraits et fractions de plantes.

Samples	TFC (mgQU/g sample)	TPC (mgGAE/g sample)	TFC/TPC ratio
BBME	172 ± 0.15	19.8 ± 0.56	8.68
BBHF	172 ± 0.26	26.38 ± 0.64	6.50
BBDF	173 ± 0.08	3.38 ± 0.26	51.2
BBEF	173.5 ±0.05	14.7 ± 0.44	11.8
BBBF	173.1 ± 0.07	10.23 ± 0.64	16.9
BBRAF	173.3 ± 0.07	49.88 ± 5.23	3.47

Values are expressed as mean ± standard error of the mean (SEM) ($n = 3$), analysed individually in triplicates. BBME, BBHF, BBDF, BBEF, BBBF, BBRAF are Methanol, *n*-Hexane, Dichloromethane, Ethyl acetate, Butanol, and residual aqueous fractions of *Bombax buonopozense*, respectively.

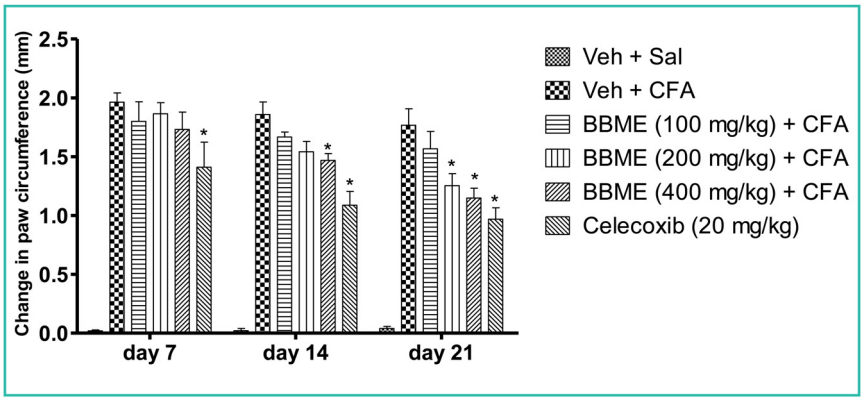

Figure 2. The effect of BBME on the paw swelling in CFA-induced arthritis in rats. Values represents Mean ± SEM ($n = 6$). * $P < 0.05$ vs CFA control group (two-way ANOVA followed by Bonferroni *post hoc* test).
*Effet du BBME sur le gonflement de la patte dans l'arthrite induite par la CFA chez le rat. Les valeurs représentent la moyenne ± SEM ($n = 6$). * $p < 0{,}05$ par rapport au groupe de contrôle CFA (Anova à deux voies, suivie d'un test post hoc de Bonferroni).*

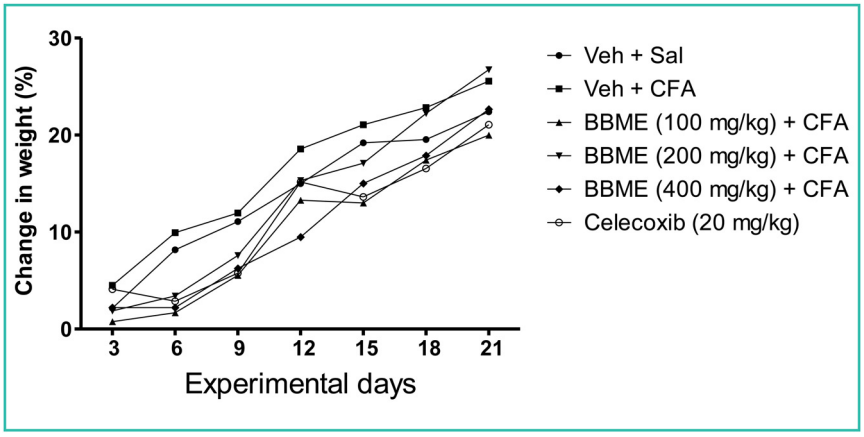

Figure 3. The effect of BBME on body weight gained in CFA-induced arthritis in rats.
Effet du BBME sur le gain de poids corporel dans l'arthrite induite par la CFA chez le rat. Les valeurs représentent la moyenne ± SEM ($n = 6$).

rats' ankle thickness increased throughout the first seven days until reaching a chronic level at around day 12. The following week revealed a little rise in ankle thickness. The non-arthritic littermates barely slightly thicken their ankles. Additionally, in the final seven days of the experiment, interindividual variations in ankle thickness were remarkably modest. As a whole, the arthritic group experienced more fluctuations than the control group. BBME also increase the weight gained in the treatment groups (Fig. 3). Fig. 4 shows the impact of BBME on the walk

Table 3 Brine shrimp lethality assay of crude extract and fractions.
Essai de létalité de l'extrait brut et de ses fractions sur la crevette saumonée.

Samples	LC_{50}(μg/mL)
BBME	1920 ± 0.10
BBHF	1000 ± 0.02
BBDF	1000 ± 0.11
BBEF	1480 ± 0.18
BBBF	1400 ± 0.12
BBRAF	1440 ± 0.11
Cyclophosphamide	227.35 ± 0.15

BBME, BBHF, BBDF, BBEF, BBBF, BBRAF are Methanol, *n*-Hexane, Dichloromethane, Ethyl acetate, Butanol, and residual aqueous fractions of *Bombax buonopozense*, respectively.

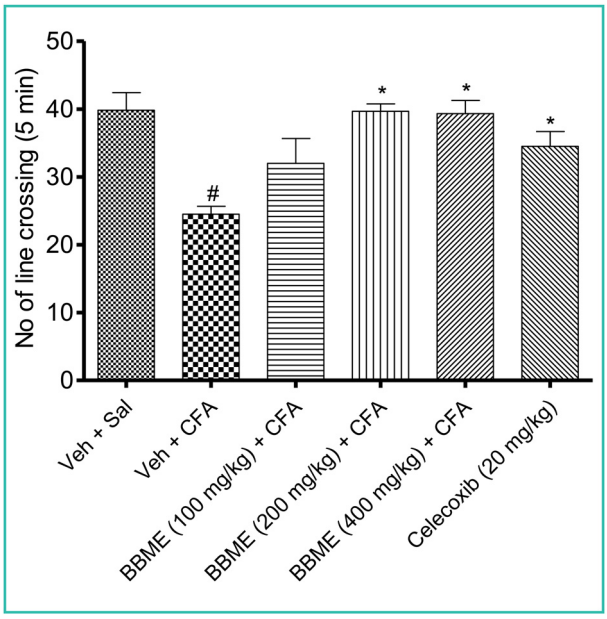

Figure 4. The effect of BBME on the spontaneous locomotory activity in CFA-induced arthritis in rats. Values represents Mean ± SEM ($n = 6$). $^{\#}P < 0.05$ compared to normal saline control group and $^{*}P < 0.05$ vs CFA control alone (one-way ANOVA followed by Bonferroni *post hoc* test).
Effet du BBME sur l'activité locomotrice spontanée dans l'arthrite induite par la CFA chez le rat. Les valeurs représentent la moyenne ± SEM (n = 6). $^{\#}p < 0,05$ par rapport au groupe de contrôle avec solution saline normale et $^{*}p < 0,05$ par rapport au groupe de contrôle avec CFA seul (Anova à sens unique, suivie d'un test post hoc de Bonferroni).

beam paradigm-measured deterioration of motor function brought on by CFA. The results of a one-way ANOVA revealed that the travel distance between treatment groups and time were significantly different. According to posthoc analysis using the Newman-Keuls test, CFA significantly ($P < 0.05$) reduced the distance that rats travelled in the horizontal beam compared to the control and also caused increase in the beam crossing time of affected rats (Fig. 5).

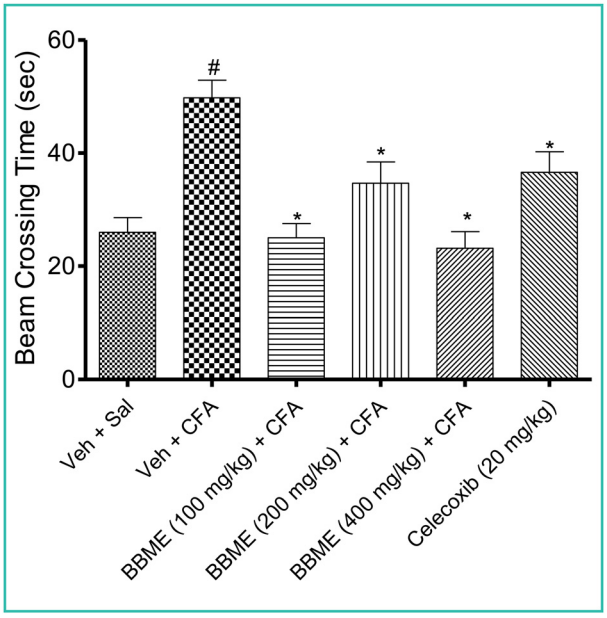

Figure 5. The effect of BBME on the motor coordination test in CFA-induced arthritis in rats. Values represents Mean ± SEM ($n = 6$). $^{\#}P < 0.05$ compared to normal saline control group and $^{*}P < 0.05$ vs CFA control alone (one-way ANOVA followed by Bonferroni *post hoc* test).
Effet du BBME sur le test de coordination motrice dans l'arthrite induite par la CFA chez le rat. Les valeurs représentent la moyenne ± SEM (n = 6). $^{\#}p < 0,05$ par rapport au groupe de contrôle avec solution saline normale et $^{*}p < 0,05$ par rapport au groupe de contrôle avec CFA seul (Anova à sens unique, suivie d'un test post hoc de Bonferroni).

Figs. 6 and 7 displays the impact of BBME on the levels of nitrite and GSH in the serum of groups that received CFA treatment. The depletion of blood GSH concentrations caused by CFA was lessened by oral administration of BBME (100, 200, and 400 mg/kg) or CEL (20 mg/kg).

Fig. 8 displays how BBME affected the levels of MDA in the CFA-rats' serum. The treatment groups varied considerably from one another in terms of MDA serum blood level. MDA levels in the blood serum of CFA-induced rats are reduced by BBME. The amounts of MDA in the blood serum were considerably higher after CFA treatment compared to controls, according to posthoc analysis using the Newman-Keuls test. But when compared to the CFA group, oral administration of BBME or CEL substantially reduced the level of MDA in the blood serum. Rat serum GSH depletion caused by Freund adjuvant is reduced completely by BBME. MDA levels in the blood serum of CFA-induced rats are reduced by BBME. One-way ANOVA revealed that the treatment groups differed significantly from one another: MDA serum blood level. According to posthoc analysis using the Newman-Keuls test, CFA significantly ($P < 0.05$) upsurge the amounts of MDA in the blood serum compared to controls. But when compared to the CFA group, oral treatment of BBME (100, 200, and 400 mg/kg) or CEL (20 mg/kg) considerably decreased the blood serum MDA level. The reductive effect of BBME on serum ALP levels in rats injected with Complete Freund adjuvant (CFA) is concentration dependent (Fig. 9).

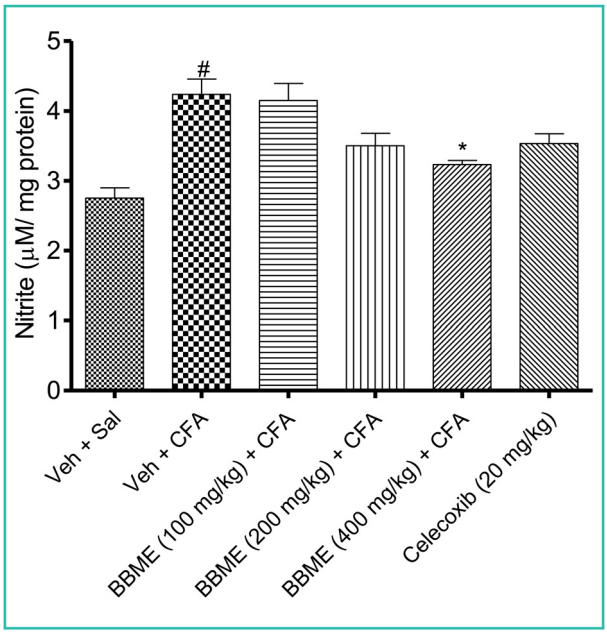

Figure 6. Effect of BBME on nitrite concentrations in the blood serum of rats injected with Complete Freund adjuvant (CFA). Values show the mean and standard error of the mean for 6 animals per category. *$P < 0.05$ compared to Veh + CFA-treated group and #$P < 0.05$ in comparison to the solvent (Veh)-treated group (One-way ANOVA followed by Newman Keuls test).
*Effet du BBME sur les concentrations de nitrites dans le sérum sanguin de rats ayant reçu une injection d'adjuvant complet de Freund (CFA). Les valeurs représentent la moyenne et l'erreur standard de la moyenne pour 6 animaux par catégorie. *$p < 0,05$ par rapport au groupe traité par Veh + CFA et $^{\#}p < 0,05$ par rapport au groupe traité par le solvant (Veh) (Anova à sens unique, suivie du test de Newman Keuls).*

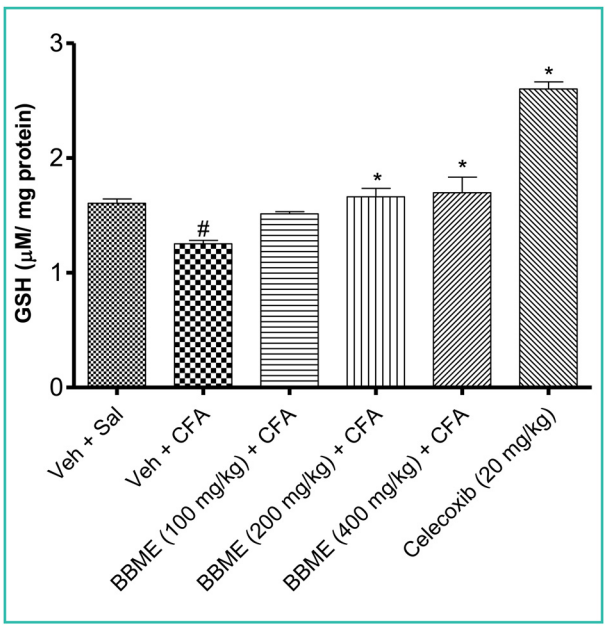

Figure 7. Effect of BBME on glutathione concentrations in the blood serum of rats injected with Complete Freund adjuvant (CFA). Values show the mean and standard error of the mean for 6 animals per category. *$P < 0.05$ compared to Veh + CFA-treated group and #$P < 0.05$ in comparison to the solvent (Veh)-treated group (One-way ANOVA followed by Newman Keuls test).
*Effet du BBME sur les concentrations de glutathion dans le sérum sanguin de rats ayant reçu une injection d'adjuvant complet de Freund (CFA). Les valeurs représentent la moyenne et l'erreur standard de la moyenne pour 6 animaux par catégorie. *$p < 0,05$ par rapport au groupe traité par Veh + CFA et $^{\#}p < 0,05$ par rapport au groupe traité par le solvant (Veh) (Anova à sens unique, suivie du test de Newman Keuls).*

Discussion

Although arthritis is frequently thought to be characterized by joint swelling, many patients also experience inflammation in the subcutaneous tissue, or the membranes surrounding the heart or lungs. A chronic autoimmune condition known as rheumatoid arthritis (RA) usually causes inflammation around the body's synovial joints, resulting in pain and restricted mobility [36—38]. The prevalence of RA is estimated to be 0.5% to 1% in developed nations, with the disease usually manifesting between the ages of 45 and 65 and more frequently affecting women [36—39]. Studies have shown that RA patients' total levels of physical activity are lower than those of healthy individuals in general [40,41]. Both osteoarthritis and rheumatoid arthritis have no known cures. As a result, many types of arthritis can be treated in different ways, including physical therapy, dietary changes, and medication [42,43]. It is highly warranted to look for natural sources of alternative medicines that are efficient and less toxic, which would minimize the load of pills, given the chronic nature of RA and the severe side effects connected with its treatment. Due to their potential application in the treatment and prevention of a variety of chronic diseases, the quest for bioactive chemicals from medicinal plants has increased in recent years [27,28,44—46]. The plant investigated, *Bombax buonopozense*, was part of medicinal plants mentioned as ethnomedicinal plants used to cure inflammation in Ibadan Northwest LGA of Oyo State [23]. The plant's usage in the management of inflammation has not been scientific validated. The results of the phytochemical screening obtained in this study are consistent with the findings of Akuodor et al. [47] for *B. buonopozense*.

Polyphenols, also known as phenols, exhibit a variety of physiological properties, including antioxidant, antimutagenic, anticancer, and gene-modifying expression. The most prevalent and widely present class of plant phenolic compounds or flavonoids are distinguished by a benzo-γ-pyrone structure [15,26,48]. Phenolic compounds contribute significantly to the plant's total antioxidant activity because of their redox properties, which enable them to function as reducing agents, hydrogen donors, and metal chelators and may be linked to their chemical structures [49,50]. Generally, phenolic substances act as antioxidants by scavenging lipid free radicals and preventing hydroperoxides from becoming free radicals [51,52]. The DPPH is a stable nitrogen-centered free radical that is violet in methanol solution; however, it turns yellow (diphenylpicrylhydrazine) when it is reduced by either the gift of an electron or a hydrogen atom [53,54]. The ratio of the test solution's reduced absorbance to that of the DPPH solution without the plant extract is used to calculate the scavenging activity, which is represented as a percentage. The extract and

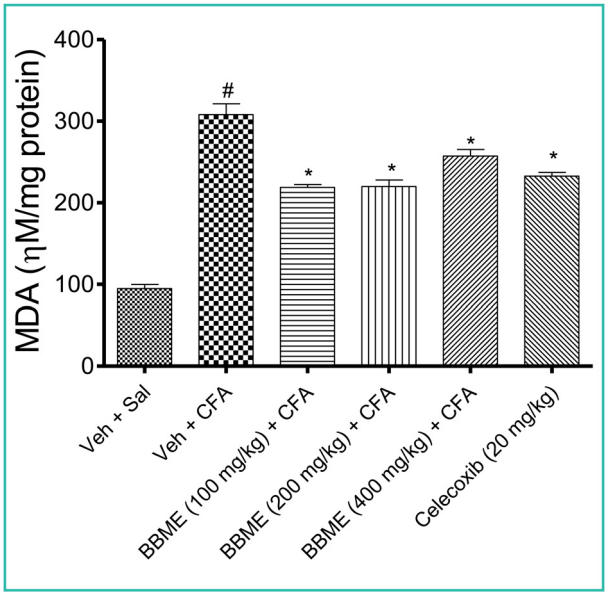

Figure 8. Effect of BBME on MDA levels in the blood serum of injected rats with Complete Freund adjuvant (CFA). Values show the mean and standard error of the mean for 6 animals per category. *$P < 0.05$ compared to Veh + CFA-treated group and #$P < 0.05$ in comparison to the solvent (Veh)-treated group (One-way ANOVA followed by Newman Keuls test).
*Effet du BBME sur les niveaux de MDA dans le sérum sanguin de rats ayant reçu une injection d'adjuvant complet de Freund (CFA). Les valeurs représentent la moyenne et l'erreur standard de la moyenne pour 6 animaux par catégorie. *$p < 0,05$ par rapport au groupe traité par Veh + CFA et #$p < 0,05$ par rapport au groupe traité par le solvant (Veh) (Anova à sens unique, suivie du test de Newman Keuls).*

fractions showed the ability to remove DPPH radicals. *Bombax buonopozense* have been discovered to have antioxidant properties in general [55—57]. The higher levels of phenolics and flavonoids in the leaves extract may be the cause of the antioxidant activity observed in this study. More overall flavonoids and phenolics are often associated with stronger DPPH scavenging action [58,59].

A common bioassay known as the brine shrimp lethality (BSL) assay is dependable, affordable, and quick to run. It requires little in the way of specialized equipment and a small quantity of samples. Since bioactive substances are almost always harmful at large concentrations, it can detect a wide range of pharmacological activities in higher plants as well as evaluate the cytotoxicity to Artemia salina [60]. The fraction with the lowest cytotoxicity is methanol extract, with LC_{50} values of 1920 μg/mL, while cyclophosphamide as reference drug showed the highest cytotoxicity (227.35 μg/mL).

Rats with arthritis induced by Complete Freund adjuvant (CFA) responded favorably to *Bombax buonopozense* methanolic extract. The CFA model induced a proliferative and acute arthritis that resembles clinical arthritis. The intra-plantar surface of the left back paw was given a 0.1 mL injection of CFA to cause arthritis. The MDA, GSH, and ALP concentrations reflect the level of oxidative stress across the animal's entire body. Thus, the levels of MDA, GSH, and ALP in the blood serum of the rats in the various treatment groups were determined. The liver produces glutathione, which serves as the body's first line of defense against oxidative stress and peroxidation [61,62]. Glutathione peroxidase is breaking down the hydrogen peroxide produced during this process. This may also be a factor in the arthritic disorders' reduced activity. A measure of lipid peroxidation is MDA. Reactive oxygen species and the creation of free radicals are also produced by the invading cells, which harm the inflamed joint. *Bombax buonopozense* was effective at preventing the oxidative alterations caused by CFA-induced arthritis.

Paw swelling scores are one metric used to gauge how well different medications combat arthritis. It is used in this investigation to ascertain BBME activity. Comparing the BBME-administered groups to the control group, the paw volume exhibited a significant decrease. After the day the adjuvant was injected, there was a large loss of weight, but there was then a return to normal weight gain in the rats, according to research by Zheng et al. [63] as well as Saleem et al. [64]. The outcome of the current study also suggests a strong correlation between the degree of inflammation and weight loss. The treated rats showed a considerable weight decrease after receiving BBME. It's also critical to remember that the open-field test shows that BBME causes changes in rats' locomotor behaviors. Additionally, it has been noted

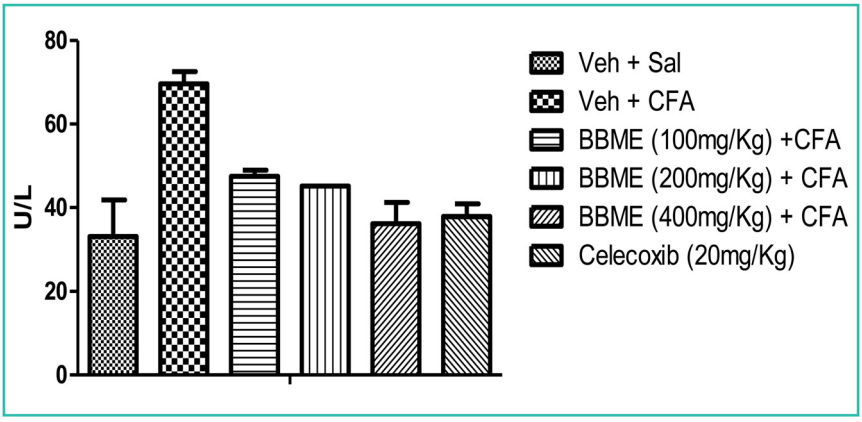

Figure 9. Effect of BBME on serum ALP levels of injected rats with Complete Freund adjuvant (CFA).
Effet du BBME sur les taux sériques d'ALP des rats ayant reçu une injection d'adjuvant complet de Freund (CFA).

that plant extracts from medicinal plants boost the locomotor activity of rats with arthritis brought on by CFA [65,66].

Inflammatory cytokines, chemokines, nitrite, arachidonic acid products, the complement system, endotelin 1, and neutrophil infiltration are all induced by CFA [67,68]. Astaxanthin and monoterpene myrtenol have been shown to reduce inflammation, discomfort, and edema in CFA-induced inflamed joints as well as the synthesis and expression of inflammatory chemicals [69,70]. It takes a certain amount of BBME to reduce nitrite in rats with arthritis induced by CFA. The amount of oxidative stress is influenced by both MDA and GSH. Lipid peroxidation is the primary cause of MDA formation, which also boosts ROS production. GSH is essential in scavenging ROS and preventing oxidative stress [71,72]. Our results, which are consistent with earlier research on medicinal plants, suggested that BBME had an anti-inflammatory effect by reducing MDA levels compared to the negative control and increasing GSH levels in a dose-dependent manner in rats with CFA-induced arthritis [66,73,74]. Elevated ALP typically indicates peri-articular osteoporosis and bone resorption [64,75]. This study demonstrated that the level of ALP in arthritic rats had been restored by BBME at tested doses.

Conclusion

The high potency antiarthritic activity of *Bombax buonopozense* P. Beauv. (Bombacaceae) supports its traditional use as a plant used in the management and/or treatment of a wide range of ailments. *Bombax buonopozense* contains phytochemicals such as phenolics, flavonoids, alkaloids, and saponins. These compounds may also have various degrees of DPPH free radical scavenging activity, which may account for the plant's high antioxidant and anti-arthritic effects.

Ethical statement

All of the experimental methods in this investigation were carried out following the NIH Ethical Guidelines for the Care and Use of Laboratory Animals. In addition, the experiment was approved by Bowen University Iwo (BUI) Institutional Animal Ethics Committee (BUI/BCH/2017/0001).

Data availability

Data will be made available on request.

Authors' contribution

MAS and OAF designed the work. MAS, OAF, AMA, and ADO conducted the study while OAF drafted the manuscript. All authors substantively revised it. All authors contributed to the acquisition, analysis, and interpretation of the data.

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Disclosure of interest

The authors declare that they have no competing interest.

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