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Original Research Article

Antiinflammatory Appraisal of *Bidens pilosa* (Asteraceae) Leaf Extract in Rodent's model

Olayemi. K. Wakeel[1],*, Mathew K. Bello[2], Damola. O. Komolafe[3], Oyetunji T. Kolawole[1], Akeem A. Ayankunle[4].

[1]*Department of Pharmacology and Therapeutic, Faculty of Basic Clinical Sciences, College of Health Sciences, LadokeAkintola University of Technology Ogbomoso, Nigeria.*
[2]*Department of Pharmacology and Therapeutics, Faculty of Basic Clinical Sciences, University of Ilorin, Ilorin Kwara State.*
[3]*Department of Mental Health Nursing, Faculty of Nursing Sciences, Osun State University Osogbo, Osun State.*
[4]*Department of Pharmacology and Therapeutics, Faculty of Basic Clinical Sciences, Osun State University Osogbo, Osun State.*

ABSRTACT

The ongoing search for safe antiinflammatory agents is crucial, considering the role of proinflammatory factors in diseases such as asthma, rheumatoid arthritis, cancer, and neurodegenerative disorders. The flora of Nigeria is abundant in medicinal plants used in traditional folk medicine for various inflammatory disorders. Therefore, we evaluates the antiinflammatory activity of the aqueous leaf extract of *Bidens pilosa* (ALEBP). The antiinflammatory activity was evaluated using egg albumin, agar-induced paw edema models for acute inflammation, complete Freud Adjuvant (CFA)-induced arthritis and cotton pellets granuloma models for chronic inflammation in rats. In each of the experimental models, animals in groups 2, 3, 4, and 5 received doses of the extract at 40, 80, and 160 mg/kg, along with Indomethacin at a dose of 5 mg/kg. Group 1 was administered 10 ml/kg of normal saline. All treatments were given one hour before the induction of inflammation. ALEBP produced significant ($P<0.05$) and dose-dependent (40-160 mg/kg) reduction of paw edema volume in rats. In chronic inflammation (CFA-induced arthritis), the extract significantly ($p< 0.05$) inhibited edematous response in a dose-related manner, provoking an inhibitory effect (59.1%, maximum inhibition) at 160 mg/kg on day 21. ALEBP also significantly ($p<0.05$) and dose-dependently reduces the granuloma weight in a chronic model of granuloma pouch in rats. The findings of the present study indicate that ALEBP possesses antiinflammatory activity, lending pharmacological credence to the suggested use of the plant as a natural remedy in the management of inflammatory conditions in some rural communities of Nigeria.

Keywords: *Bidens pilosa*, Aqueous Extract, indomethacin, Antiinflammatory Activity

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Introduction

Inflammation involves a wide range of physiological responses to viruses, dust particles, human pathogens, irritants and damaged cells.[1] Acute and chronic inflammation are the two primary classifications of inflammation based on various inflammatory processes and cellular mechanisms [2]. Pain is described as an uncomfortable sensory and emotional experience related to actual or potential tissue damage.[1] Many illnesses, including cancer, autoimmune disorders, cardiovascular disease, arthritis, diabetes, eye disorders and neurological illnesses, are all associated with inflammation.[2] Vasodilation (redness, heat, and swelling), inflammation, and pain are the primary indicators of inflammation. All of these signs are triggered by the production and physiological activity of prostaglandins, which are produced when tissue is damaged.[3] Nonsteroidal anti-inflammatory drugs (NSAIDs) such as indomethacin, piroxicam aspirin, ibuprofen, and naproxen, along with opioids and steroids, are commonly employed to manage inflammatory conditions.[4] The acute inflammatory reaction consists of two stages: the vascular phase and the cellular phase, which can also be reproduced in experimental animal models.[5]

*Corresponding author. mail: okwakeel@lautech.edu.ng
Tel: +2348034241692

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Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

Bidens pilosa, a species of plant in the Asteraceae family, has been utilized in traditional medicine for various purposes. It is an annual plant that originated in South America but is now widely distributed in most pan-tropical areas of the world.[6] It is a branched annual forb of refined habit, growing up to 1.8 meters tall and is characterized by its elongated budlike achene that bears recurred or hooked bristles, which ensures its dissemination. The plant has numerous ridged branches, reaching over two meters under favourable conditions, and produces 3,000-6,000 seeds, many of which germinate readily at maturity, facilitating three or four generations in some areas per year.[7] During the Vietnam War, soldiers began using the herb as a vegetable, which resulted in it being called the "soldiers' vegetable".[8] Recent research has highlighted its potential for neuroprotection, cognitive enhancement, and anti-inflammatory treatment. *Bidens pilosa* contains a diverse range of phytochemicals, including flavonoids (quercetin, kaempferol, and phenolic acids (caffeic acid, ferulic acid, and sinapic acid),[9] terpenoids (α-pinene, β-pinene, and limonene),[10] alkaloids (bidensine and pilosine).[11] It has been traditionally used to treat fever, rheumatism, and digestive issues.[11] It is also being used as a vegetable and in traditional soups. Additionally, it has been used to treat skin conditions and wounds, serving as an antiseptic and antibacterial agent.[9,10] *Bidens pilosa* has shown anxiolytic and antidepressant effects, indicating its potential as a natural remedy for anxiety and depression.[12] At the same time, its anticancer properties have been shown to inhibit the growth of cancer cells.[13] Furthermore, its neuroprotective effects may help prevent or treat neurodegenerative diseases, such as Alzheimer's and Parkinson's.[14] Additionally, its anti-ageing properties can reduce oxidative stress and improve skin health.[15] Anti-inflammatory and antioxidant activities,[16] antimicrobial and antiviral

properties,[17] anti-diabetic and anti-hypertensive effects,[18] anticancer properties,[19] hepatoprotective effects,[20] cardiovascular protection,[19] anti-ageing, anti-wrinkle effects,[21] and anti-amnesic.[22] Overall, *Bidens pilosa* has shown promise in modern medicine, warranting further research into its potential uses. Therefore, we aim to evaluate the antiinflammatory activity of the aqueous leaf extract of *Bidens pilosa*

Materials and Methods

Plant Collection, Identification and Preparation

The leaves of *B. pilosa* were collected on March 19 2024, at Medicinal Herbarium, Obafemi Awolowo University, IIe Ife, Osun state, Nigeria. The plant was identified at the Department of Pharmacognosy, Faculty of Pharmacy, Obafemi Awolowo University, Ile Ife, Nigeria, by taxonomist Mr Ogunlowo I.I., where a voucher specimen was deposited, and the voucher (FPI 2536) number was given. The collected materials were allowed to air-dry in the shade for two weeks. After drying, the leaves were ground into a powder using a pestle and mortar. The powdered leaves were weighed and then extracted with absolute ethanol using cold maceration techniques. The resulting extract was evaporated to dryness using a rotary evaporator, yielding a black residue of 10.7% w/w, which was then stored in a desiccator for further use.

Animal Material

Male and female Wistar rats, weighing between 220 and 250 grams, were used in this study. They were housed in a well-ventilated room in clean plastic cages with wood shavings as bedding at the animal facility of the Department of Pharmacology and Therapeutics, Faculty of Basic Clinical Sciences, Ladoke Akintola University of Technology (LAUTECH), Ogbomoso, Oyo State, Nigeria. The animals were kept under standard conditions, with a temperature of 25°C and a 12-hour light/dark cycle. They had free access to standard animal feed produced by the animal house at LAUTECH and were provided with clean water ad libitum in hygienic conditions. Before conducting any experiments, the animals were given time to acclimate to the laboratory environment. Each experimental group in this study consisted of six rats. The investigation adhered to the guidelines for the care and use of laboratory animals published by the U.S. National Institutes of Health (NIH No. 85-23, revised 1996).

Egg albumin-induced paw edema in rats

The rat paw edema method[23] was utilized to measure acute inflammation by assessing the change in volume of the rat's hind paw.[24] which was induced by a subplantar injection of egg albumin.[25,26] A 0.1 mL dose of fresh, undiluted egg albumin (0.01 g/mL) was injected into the subplantar region of the right hind paw one hour after administering intraperitoneal doses of ALEBP (40, 80, or 160 mg/kg. oral). Control animals received either 10 mL/kg of distilled water or 5 mg/kg of indomethacin, also administered intraperitoneally. Inflammation was evaluated by calculating the difference between the initial volume of the treated paw (Vo) and the volume at various time points after the injection of the phlogistic agent (egg albumin). The percentage inhibition of edema was then calculated using the appropriate formula.[27,28]

% Inhibition = [(Vo –Vt) x 100]/ Vo
Vo = paw volume of control; Vt = paw volume of treated group

Agar-induced paw edema in rats

The rat paw edema method[23] was employed as described earlier. Groups of six animals received ALEBP (40, 80, 160 mg/kg, i.p). One hour later, edema was induced by injecting 0.1 mL of a freshly prepared colloidal suspension of 2 % agar into the subplantar region of the right paw of the rats. The distilled water volume displaced by the treated paw was measured before the injection and at 1, 2, 3, and 4 hours after edema induction. Control groups received 10 mL/kg of distilled water (as vehicle) or 5 mg/kg of indomethacin orally. Inflammation was assessed using the egg albumin-induced edema method, as previously described.

Adjuvant-Induced Arthritis in Rats

The effect of ALEBP on chronic inflammation was evaluated using the Complete Freund's Adjuvant (CFA) arthritis test in rats.[29] Rats divided into five groups randomly (n=6) and were treated daily for 21 days. The treated groups received ALEBP 40, 80, or 160 mg/kg, oral). In comparison, the control groups received either 10 mL/kg of distilled water (as the vehicle) or 5 mg/kg of indomethacin (as the standard drug). All animals were injected with CFA (0.1 mL) in the left hind paw of the subplantar region. The volume of distilled water displaced was measured on day 1 (before CFA injection) and days 5, 12, and 21 (after induction of edema). The percentage inhibition[30] of each group was calculated as follows:

[(Vo –Vt) x 100]/ Vo
Vo = paw volume of control; Vt = paw volume of treated group

Cotton-pellet granuloma test in rats.

The effect of ALEBP on chronic inflammation was evaluated using the cotton-pellet granuloma test in rats [31]. On day 1, the rats received ALEBP at the doses of 40, 80, or 160 mg/kg, (oral). Control animals received either prednisolone (5 mg/kg) or vehicle control group (10ml/kg) orally. Thirty minutes later, autoclaved cotton pellets (weighing 50 ± 1 mg) were implanted in the dorsal part of the rats under diethyl ether anesthesia. The rats administered the drugs daily for seven consecutive days. On the 8th day, the animals were euthanized with an overdose of ether. The pellets were then removed, dried in an oven at 60°C, and weighed to determine the level of inhibition of granuloma development. The difference between the initial and post-implantation weight was considered to be the dry weight of granuloma tissue[31] and was calculated using the relation:

[(Tc – Tt) x 100]/ Tc
Tc = weight of the wet pellet
Tt = weight of the dry pellet

Data and Statistical Analysis

The data obtained are presented as means (± SEM) for each group of animals (n=6). Data from distilled water or normal saline-treated 'control' rats were utilized as the baseline. In all cases, the results from the extract- and reference drug-treated 'test' animal groups were compared to those from the distilled water or normal saline groups. A one-way analysis of variance (ANOVA) was used to examine the differences between the 'test' animal groups and the vehicle-treated 'control' groups, using a 95% confidence interval. Following this analysis, Dunnett's post-hoc test was applied. A statistical significance level of $P \leq 0.05$ was set for all tests.

Results and Discussion

The study on the inflammatory effect indicated that the extract significantly ($p < 0.05$) reduced or inhibited paw edema induced by egg albumin in a dose-dependent manner. The effect produced by the extract (80 and 160 mg/kg) was comparable to that of indomethacin at 5 mg/kg (see Table 1). However, in the agar-induced paw edema, the effect produced by the extract at the maximum dose (160 mg/kg) was lower than that of indomethacin at 5 mg/kg (Table 2). In the experiments, egg albumin-induced edema peaked at 1 hour and decreased over time. In contrast, agar-induced edema showed a progressive increase in paw swelling over time. The early inhibition of the acute phase of edema caused by egg albumin and the progressive increase in edema induced by agar suggest that the extract may suppress both the early and later phases of the acute inflammatory response. During acute inflammation, chemical mediators known as pro-inflammatory mediators are released, including histamine, serotonin (5-HT), kinins, and prostanoids, which mediate inflammation-induced responses.[32,33] The findings from this study demonstrate that the aqueous leaf extract of *Bidens pilosa* effectively inhibited edema caused by both egg albumin and agar, indicating its potential role in modulating inflammatory responses through the inhibition of these pro-inflammatory mediators.

In the case of chronic inflammation caused by CFA-induced arthritis, the extract demonstrated a significant ($p<0.05$) inhibition of the edematous response in a dose-dependent manner. The maximum

inhibition produced by the ALEBP (160 mg/kg) was 59.1 % on day 21, while indomethacin (5 mg/kg) a non-steroidal anti-inflammatory drug produced 63.6 % (see Table 3). It was reported that arthritis, modified macrophages are typically clustered in small formations or surrounded by lymphocyte cuffs.[34] This event is a consequence of cell-mediated immunity.[35] However, these activated macrophages at the site of inflammation or injury are known to secrete peptide growth factors that partly mediate the healing and repair processes.[34] The current study found that the aqueous leaf extract of *Bidens pilosa* reduced edema caused by Complete Freund's Adjuvant (CFA)-induced arthritis. This implies that the extract may promote tissue repair through the pro-healing actions of these secretions, primarily since tissue necrosis worsens the later stages of arthritis. Necrotic tissue produces a factor known as tumour necrosis factor (TNF), which can perpetuate inflammation through various mechanisms, including releasing mediators from dead tissues or dying leukocytes.[36]

Table 1: Effect of ALEBP on egg albumin-induced acute inflammation.

Treatment	Dose (mg/kg)	Edema (ml) – 1 hr	2 hrs	3 hrs	4 hrs
Control	0	0.32 ± 0.01	0.27 ± 0.23	0.25 ± 0.14	0.19 ± 0.54
ALEBP	40	0.23 ± 0.04	0.20 ± 0.03	0.18 ± 0.03	0.13 ± 0.14
ALEBP	80	0.20 ± 0.03	0.18 ± 0.03	0.14 ± 0.02	0.07 ± 0.10*
ALEBP	160	0.18 ± 0.03	0.16 ± 0.02	0.12 ± 0.02	0.06 ± 0.23*
Indomethacin	5	0.29 ± 0.06	0.20 ± 0.10	0.13 ± 0.08	0.06 ± 0.01*

**Values are recorded as means±SEM (n=5).
*Values are statistically significant ($p<0.05$) in relation to control. One way ANOVA followed by Dunnett'post-hoc Multiple Comparison tests

Table 2: Effect of ALEBP on agar-induced acute inflammation

Treatment	Dose (mg/kg)	Edema (ml) – 1 hr	2 hrs	3 hrs	4 hrs
Control	0	0.25 ± 0.01	0.35 ± 0.03	0.38 ± 0.14	0.52 ± 0.45
ALEBP	40	0.40 ± 0.04	0.34 ± 0.03	0.26 ± 0.03	0.19 ± 0.45*
ALEBP	80	0.30 ± 0.03	0.24 ± 0.03	0.19 ± 0.02	0.13 ± 0.05*
ALEBP	160	0.18 ± 0.03	0.16 ± 0.02	0.12 ± 0.05	0.08 ± 0.01*
Indomethacin	5	0.21 ± 0.01	0.15 ± 0.02	0.10 ± 0.01	0.05 ± 0.02*

**Values are recorded as means±SEM (n=5).
*Values are statistically significant ($p<0.05$) in relation to control. One way ANOVA followed by Dunnett'post-hoc Multiple Comparison tests

However, in the cotton pellet granuloma test, the extract was not as effective as the standard anti-inflammatory steroid drug, prednisolone, in inhibiting the growth of granuloma tissue as the percentage inhibition is much higher than that of the extract (see Table 4). In the cotton pellet-induced granuloma, the effectiveness of this model is evaluated by measuring the increase in the dry weight of the implanted cotton pellet, which indicates granuloma formation at the implantation site. This model is known for its reliability in studying chronic inflammatory conditions, such as those present in the synovium of patients with rheumatoid arthritis.[37] In the current study, pretreatment with ALEBP demonstrated a dose-dependent reduction in granuloma formation; However, its efficacy was not comparable to that of the standard drug prednisolone.

Table 3: Effect of ALEBP on Complete Feud adjuvant-induced arthritis in rats

Treatment	Dose (mg/kg)	Edema (ml) – Day 5	Day 12	Day 21	Inhibition (%) Day 21
Control	0	0.35 ± 0.12	0.28 ± 0.09	0.22 ± 0.04	0
ALEBP	40	0.34 ± 0.02	0.27 ± 0.04	0.17 ± 0.02	22.7*
ALEBP	80	0.34 ± 0.06	0.21 ± 0.07	0.13 ± 0.02	41.0*
ALEBP	160	0.32 ± 0.09	0.19 ± 0.03	0.09 ± 0.01	59.1*
Indomethacin	5	0.32 ± 0.02	0.16 ± 0.02	0.08 ± 0.02	63.6*

**Values are recorded as means±SEM (n=5).
*Values are statistically significant ($p<0.05$) in relation to control. One way ANOVA followed by Dunnett'post-hoc Multiple Comparison tests

Table 4: Effect of ALEBP on cotton pellet granuloma

Treatment	Dose (mg/kg)	Granuloma Weight (mg)	Inhibition (%)
Control	0	201.34 ± 2.30	0
ALEBP	40	196.14 ± 1.27	2.58
ALEBP	80	151.21 ± 1.02*	25.00*
ALEBP	160	115.32 ± 1.24*	42.72*
Prednisolone	5	78.25 ± 1.13*	61.14*

**Values are recorded as means±SEM (n=5).
*Values are statistically significant ($p<0.05$) in relation to control. One way ANOVA followed by Dunnett'post-hoc Multiple Comparison

In addition to modulating arthritis events by inhibiting mediator release, the extract may also prevent CFA-induced arthritis and the resulting tissue damage associated with the condition. Although this study did not establish the exact chemical component or components responsible for the anti-inflammatory activity of ALEBP, previous research has shown that tannins, saponins, and alkaloids possess anti-inflammatory properties in various experimental animal models. *Bidens pilosa* has been reported to contain saponins, alkaloids, and tannins.[38] Therefore, it is reasonable to speculate that these phytochemical constituents contribute to the observed anti-inflammatory effects of the plant's leaf extract. However, further studies are necessary to clarify this speculation.

Conclusion

The experimental evidence obtained from this laboratory study indicates that the aqueous leaf extract of *Bidens pilosa* possesses anti-inflammatory activity. These findings provide pharmacological support for the ethnomedical use of *Biden pilosa* as a natural remedy for the treatment, management, and control of various inflammatory conditions in rural communities of Nigeria.

Conflict of interest
The authors declare no conflict of interest

Authors' Declaration
The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them

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