Journal of Medicinal Natural Products

Scilight

Article

Check for updates

Pharmacological Investigation of the Active Fractions of *Acacia crassicarpa* Leaf Extract

As-Sazzad Mahmud *, Ariful Islam, Israt Jahan Meem, Md. Rabbi Hasan, Md. Mohiuddin Maruf, Tanvir Ahmed Anik and Mirja Mohammad Niaz Morshed

Department of Pharmacy, Dhaka International University, Satarkul, Badda, Dhaka 1212, Bangladesh
* Correspondence: sazzad.phar@diu.ac; Tel.: +880-1521305611
Received: 15 January 2026; Revised: 5 May 2026; Accepted: 12 May 2026; Published: 22 May 2026

Abstract: Objective: This study explores the biological properties of *Acacia crassicarpa A. Cunn. ex Benth*, a member of the Fabaceae family. Known for its antimicrobial, anti-inflammatory, and antidiarrheal effects, this plant may be beneficial in treating skin infections, diarrhea, wounds, and ulcers. In this study, fractions of ethanolic leaf extracts were analyzed for their analgesic, anti-inflammatory, antipyretic, and acute toxicity effects. Methods: Analgesic, anti-inflammatory, antipyretic, and acute toxicity evaluations were conducted in vivo. The analgesic activity was assessed using the acetic acid-induced writhing method, while the anti-inflammatory effect was measured through the formaldehyde-induced paw edema method. Antipyretic activity was determined by monitoring changes in rectal temperature in mice. Acute oral toxicity was evaluated following the OECD (Organization for Economic Co-operation and Development) guidelines-423 (Fixed Dose Procedure). Results: In the analgesic test, the ethyl acetate fraction exhibited inhibition rates of 35.63% and 45.97% at doses of 250 mg/kg and 500 mg/kg, respectively. In the anti-inflammatory test, inhibition rates were recorded at 43.83% for 250 mg/kg and 58.9% for 500 mg/kg, with the higher dose showing a more significant anti-inflammatory effect. The antipyretic test confirmed that both 250 mg/kg and 500 mg/kg doses demonstrated antipyretic properties. Acute toxicity assessments revealed no toxic effects at doses up to 5000 mg/kg. Conclusion: The *Acacia crassicarpa* leaf extract demonstrated analgesic, anti-inflammatory, and antipyretic effects.

Keywords: *Acacia crassicarpa*; analgesic; anti-inflammatory; antipyretic; acute toxicity

1. Introduction

Natural products remain vital as raw materials for medicine and the creation of new drugs. In recent years, the demand for drug discovery from natural sources has increased, fueled by progress in innovative drug discovery technologies [1]. Traditional medicine is a term used to describe medicines from the earth's natural resources. The majority of people in developing countries continue to use traditional medicine for their basic healthcare needs due to its affordability, accessibility and cultural acceptability [2]. Plants have formed the basis of sophisticated traditional medicine systems that have been in existence for thousands of years and continue to provide mankind with new remedies [3]. In recent years, a tremendous upsurge in the acceptance of plant-based medicines in developed countries has been noted [4]. Many plant-based traditional medicines showed promising potential in efficacy; however, the majority of plant materials used in plant-based traditional medicines and health products remain untested and their use unmonitored [5]. The beneficial effects of these plants arise from phytochemicals, which are non-nutritive compounds that help protect humans from various diseases. Major constituents include alkaloids, flavonoids, saponins, phenolic compounds, phytosterols, proteins, amino acids, gums, mucilage, and lignin. These phytochemicals are crucial in the pharmaceutical industry and play a key role in identifying raw medicinal substances [6].

Medications with anti-inflammatory properties ease pain and curb inflammation by suppressing the COX enzyme. This suppression halts the creation of prostaglandins, compounds that trigger pain and inflammation [7]. Pain-relieving drugs, known as analgesics, work by inhibiting the COX enzyme. This inhibition halts the production of prostaglandins, thereby easing inflammation and alleviating pain [7]. Medications with antipyretic properties generally function by suppressing or decreasing the activity of COX-2. This reduction limits the production of prostaglandin E2 (PGE2), which plays a key role in regulating body temperature, thereby helping to

lower fever [8]. Antipyretic, anti-inflammatory, and analgesic activities exert their effects primarily through the peripheral nervous system [9].

The genus Acacia is comprised of numerous species that are extensively scattered worldwide. *Acacia crassicarpa A. Cunn. ex Benth*, is a tree from the Fabaceae family, native to Australia, Irian Jaya, Indonesia, and Papua New Guinea [10]. It's promising medicinal properties, specifically its anti-inflammatory, analgesic and antipyretic activities. These properties make the plant a potential candidate for developing natural therapeutic agents to address various health conditions, such as pain management, fever, and inflammatory diseases. *Acacia crassicarpa* is known for its rich phytochemical profile, including compounds such as tannins, flavonoids, and alkaloids, which have demonstrated bioactive potential in traditional medicine [11]. It is employed in the treatment of several diseases such as antidiabetic, anti-acetylcholinesterase, antipyretic, and anti-inflammatory properties [12]. Furthermore, this plant has been noted for its antioxidant activity [13], as well as its anti-fungal activity [14] and its anti-inflammatory activities [15]. *Acacia crassicarpa* leaves are an important non-timber forest resource with growing interest in pharmaceutical and nutraceutical applications due to their rich phytochemical composition. Phytochemical analysis of the leaf extract, particularly through GC–MS, has identified a wide range of volatile constituents—up to 61 compounds representing about 95.8% of the essential oil—mainly including aldehydes, sesquiterpenes, alkanes, and oxygenated monoterpenes [16].

This study aims to assess the potential medicinal benefits of *Acacia crassicarpa* leaf extract by investigating its analgesic, anti-inflammatory, antipyretic, and acute toxicity properties. The phytochemistry of this active fraction can be investigated in future studies.

2. Materials and Methods

2.1. Chemical

Analytical grade ethanol and Laboratory-grade reagents, including acetic acid (Merck, Germany), formaldehyde (Merck, Darmstadt, Germany). All standard medications used for pharmacological assessments in vivo were acquired from Square Pharmaceuticals Ltd. and Beximco Pharmaceuticals Ltd. in Bangladesh.

2.2. Plant Collection

In June 2024, Acacia crassicarpa leaves were collected from Madani Avenue, Packhola Moor, Satarkul, Beraid, Dhaka, Bangladesh. The plant specimen was identified by Dr. Mohammad Sayedur Rahman, a senior scientific official at the Bangladesh National Herbarium in Mirpur, Dhaka. The authentication number assigned to the specimen was DACB-94769.

2.3. Extraction and Fractionation

According to the maceration method, after being collected and air-dried in shade, the leaves were ground into a coarse powder and macerated for 14 days using 500 g of powdered leaves and 1000 mL of ethanol, resulting in a 14.7% (*w*/*w*) yield. The ethanol extract was then dissolved in distilled water and fractionated to obtain the ethyl acetate fraction, which yielded 13.21% (*w*/*w*).

2.4. Animals

Young Swiss albino mice (Mus musculus), aged 4 to 6 weeks and weighing between 20 and 25 g, were sourced from Jahangirnagar University, Bangladesh. They were housed in the pharmacology laboratory's animal facility at the Pharmacy Department of Dhaka International University for 2 to 3 weeks to acclimate to their new surroundings. All experiments were conducted in a quiet, controlled, and private environment. The study followed ethical guidelines established by the Committee of Clinical Pharmacy & Pharmacology at the Department of Pharmacy, Dhaka International University, Satarkul, Badda, Dhaka-1212, Bangladesh. [Ref No- CPP/DIU/EC/009].

2.5. Evaluation of Analgesic Activity

As explained by Debnath, the analgesic activity was evaluated using a paradigm in which mice were made to writhing by administering acetic acid [17]. The acetic acid-induced writhing technique is commonly used in animal models to evaluate the analgesic effect of the peripheral nervous system. The test groups received doses of the sample extract at 250 and 500 mg/kg body weight, whereas the positive control group received a dose of the conventional medication Diclofenac Na at 25 mg/kg body weight. Each group of five mice received oral administration of *Acacia crassicarpa* extract and Diclofenac Sodium after receiving an intraperitoneal injection of 0.7% acetic acid, which

caused the mice to writhe (constriction of the abdomen, turning of the trunk, and extension of the hind legs). After fifteen minutes, the number of writhing mice for each mouse was tallied up to five minutes later.

2.6. Evaluation of Anti-Inflammatory Activity

As explained by Debnath, the anti-inflammatory action was evaluated using a model in which mice were given formaldehyde to generate paw edema [17]. In contrast, the positive control group received 100 mg/kg of body weight of the common medication Ibuprofen orally. Oral *Acacia crassicarpa* extract was administered to the test groups at levels of 250 mg/kg and 500 mg/kg body weight. After half an hour, a sliding calliper was used to measure the right hind paw's linear circumference. Then, 0.1 mL of a 2% formaldehyde solution was injected into the right hind paw of each mouse. At intervals of 1, 2, 3, and 4 h, the linear diameter of the injected paw was measured.

2.7. Evaluation of Antipyretic Activity

As explained by Subedi, the antipyretic action was evaluated in a model in which mice were given Brewer's yeast to produce pyrexia [18]. In contrast, the positive control group received 150 mg/kg of body weight of the common medication, paracetamol, orally. Oral *Acacia crassicarpa* extract was administered to the test groups at levels of 250 mg/kg and 500 mg/kg body weight. A digital thermometer was used to record each mouse's normal body temperature. All mice were given a 15% aqueous suspension of Brewer's yeast (10 mL/kg body weight) subcutaneously to produce pyrexia. The animals' body temperatures were then recorded 24 h later.

2.8. Evaluation of Acute Toxicity

Acute oral toxicity was performed by using OECD guidelines-423 (Organization of Economic Co-Operation and Development)–Fixed Dose Procedure [19]. This study aims to determine the appropriate initial dosage for the primary investigation. Swiss Albino mice were used to evaluate the acute oral toxicity of *Acacia crassicarpa*. It was essential to monitor the mice's body weight, as they were fasted for four hours before the experiment. Each mouse received the medication orally based on its body weight. To assess the acute toxicity of the ethyl acetate fraction of *Acacia crassicarpa* leaf extract, oral doses of 300, 2000, and 5000 mg/kg were administered. After the medication was given, food was provided for one to two hours. The mice were closely observed for any noticeable behavioral changes during the first four hours after administration. Following this, regular monitoring continued for the next 24 and 48 h. Behavioral changes, as well as other parameters such as body weight, food intake, temperature, skin and eye color alterations, and urine output, were recorded.

2.9. Statistical Analysis

The means ± standard errors of means were used to express all experimental results. One-way analysis of variance was utilized to evaluate statistical significance using Dunnett's test. With Prism 6.0 (Graph Pad Software Inc., San Diego, CA, USA), statistical analysis was carried out. When $p < 0.05$, the study's results were considered statistically significant.

3. Results and Discussion

3.1. Evaluation of Analgesic Activity

The ethyl acetate fractions of *Acacia crassicarpa* leaf extract demonstrated significant analgesic activity, reducing acetic acid-induced writhing by 35.63% (250 mg/kg) and 45.97% (500 mg/kg) (Figure 1). Pain, also known as algesia, is an uneasy sensation that usually arises from adverse internal or external stimuli. During the analgesic test, intraperitoneal administration of a 0.7% acetic acid solution caused significant body contractions. Analgesic drugs work by inhibiting the COX enzyme, thereby halting prostaglandin synthesis. This reduction in prostaglandin production helps to alleviate pain [7]. The pain-relieving properties of *Acacia crassicarpa* leaf extract might be linked to its ability to inhibit cyclooxygenase, thereby preventing activation of local peritoneal receptors. This aligns with known mechanisms of plant-derived analgesics, where flavonoids and tannins inhibit cyclooxygenase (COX) enzymes, suppressing prostaglandin synthesis [7]. Similar effects were reported for *Acacia nilotica*, where flavonoid-rich extracts reduced pain via peripheral and central pathways [20]. The dose-dependent response suggests cumulative bioactive effects, possibly involving opioid receptor modulation, as seen in other medicinal plants [21]. Further isolation of compounds like quercetin or gallic acid—common in Acacia species—could clarify their specific roles [11,22].

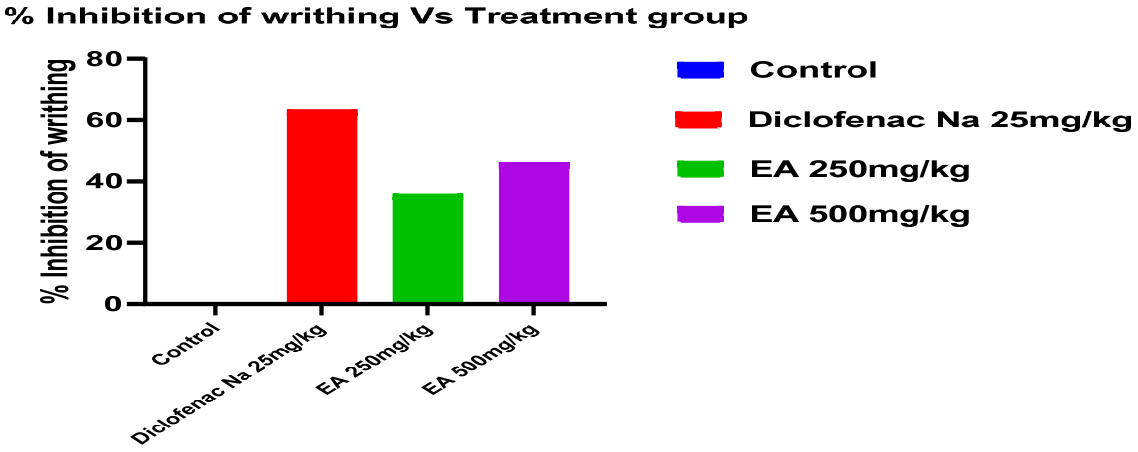

Figure 1. Percentage of inhibition writhing in case of acetic acid-induced writhing. The ethyl acetate fractions of *Acacia crassicarpa* extract, administered at doses of 250 and 500 mg/kg, reduced writhing by 35.63% and 45.97%, respectively. In comparison, Diclofenac Na, used as the standard drug, showed 63.21% inhibition at a dose of 25 mg/kg body weight. Among the two doses, the 500 mg/kg dose exhibited the highest analgesic activity. Experimental data are presented as the mean values along with their standard errors (mean ± SEM).

3.2. Evaluation of Anti-Inflammatory Activity

The ethyl acetate fractions of *Acacia crassicarpa* extract, administered at doses of 250 and 500 mg/kg body weight, reduced inflammation in mice with formaldehyde-induced paw edema. In the evaluation of anti-inflammatory activity, inflammation was induced in the right hind paw of mice by injecting 0.1 mL of a 2% formaldehyde solution. Throughout the observation period, *Acacia crassicarpa* extract fractions at doses of 250 and 500 mg/kg body weight effectively reduced paw edema. After four hours, the ethyl acetate fraction suppressed inflammation by 43.83% and 58.9%, respectively. In comparison, the standard drug Ibuprofen exhibited 59.89% inhibition at a dose of 100 mg/kg body weight. The ethyl acetate fraction exhibited marked anti-inflammatory effects (Figure 2).

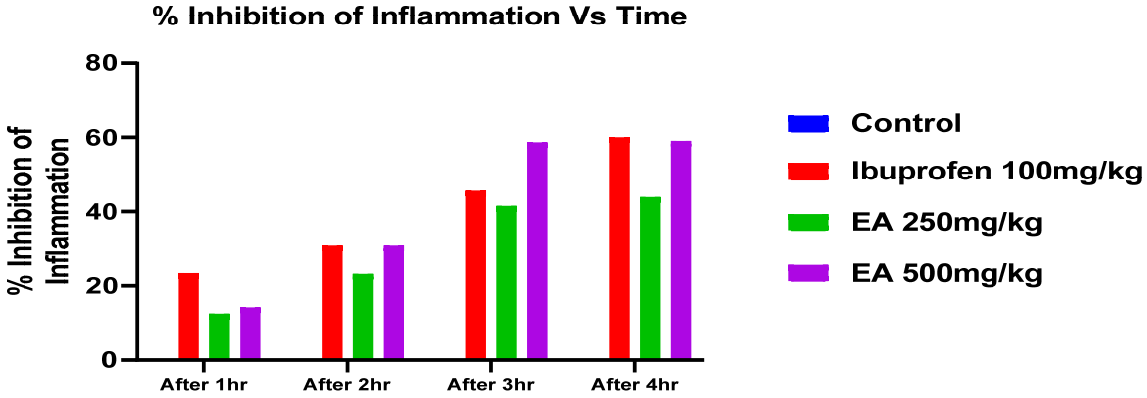

Figure 2. Percentage inhibition of inflammation in the formaldehyde-induced paw edema model. After four hours, EA fractions of *Acacia crassicarpa* (250/500 mg/kg) inhibited inflammation by 43.83% and 58.9% respectively. In comparison, the reference drug Ibuprofen showed 59.89% inhibition at a dosage of 100 mg/kg body weight. In both instances, the 500 mg/kg dose showed enhanced anti-inflammatory efficacy compared to the 250 mg/kg dose. The experimental results are expressed as means ± standard error of the mean (SEM).

The ethyl acetate fractions derived from *Acacia crassicarpa* extract effectively reduced paw edema, with the 500 mg/kg dose showing more pronounced anti-inflammatory effects than the 250 mg/kg dose. Inflammation, a cellular response, is regulated by mediators such as histamine, prostaglandins, bradykinin, cytokines, and leukotrienes [23]. Anti-inflammatory medications work by blocking the COX enzyme, leading to a decrease in prostaglandin production. This reduction helps to reduce both pain and inflammation [7]. Glycine, n-benzyloxycarbonyl-ethyl ester inhibiting COX activity, these compounds reduce prostaglandin production, which

contributes to inflammation [24]. Glycine, n-benzyloxycarbonyl-ethyl ester reduce inflammation so this compound could be responsible for this mechanism.

Inflammation is driven by mediators such as prostaglandins, histamine, and cytokines, which are regulated by COX enzyme activity [23]. The extract's efficacy likely stems from its ability to inhibit COX, reducing prostaglandin production, as supported by studies on *Acacia auriculiformis* where tannins and saponins blocked histamine and prostaglandin release [13,21]. The dose-dependent response suggests a cumulative effect of bioactive compounds, possibly including glycine derivatives, which have been shown to inhibit COX activity [24]. The findings corroborate traditional uses of Acacia species for inflammatory conditions [15]. Further research should quantify inflammatory biomarkers (e.g., TNF-α, IL-6) and explore NF-κB pathway modulation to validate these mechanisms [25].

3.3. Evaluation of Antipyretic Activity

The ethyl acetate fractions of *Acacia crassicarpa* extract, administered at doses of 250 and 500 mg/kg body weight, demonstrated antipyretic effects by lowering pyretic activity (reducing the rectal temperature of mice over a fixed time) induced by yeast-induced pyrexia in a dose-dependent manner. The ethyl acetate fraction of *Acacia crassicarpa* extract reduced pyretic activity by 97.66 ± 0.2400 °F and 96.88 ± 0.5034 °F at doses of 250 mg/kg and 500 mg/kg body weight, respectively. In comparison, the standard medication Paracetamol suppressed pyretic activity by 97.89 ± 0.05831 °F at a dose of 150 mg/kg body weight. Both 250 mg/kg and 500 mg/kg doses of the ethyl acetate fraction demonstrated antipyretic effects by lowering the rectal temperature of the mice over a fixed time period, with the 500 mg/kg dose exhibiting more pronounced antipyretic activity (Figure 3).

The aim of the study was to evaluate the antipyretic properties in mice over a specified period. Pyrexia, a key symptom of fever, was induced in the test by the subcutaneous injection of a 15% Brewer's yeast solution. The antipyretic effect is likely mediated by inhibiting prostaglandin synthesis, similar to the action of paracetamol. This mechanism occurs through the suppression of cyclooxygenase (COX) enzyme activity [26]. Glycine, n-benzyloxycarbonyl-ethyl ester inhibiting COX activity, these compounds reduce prostaglandin production, thus lowering the hypothalamic set point and reducing fever [24]. Glycine, n-benzyloxycarbonyl-ethyl ester reduce temperature so this compound could be responsible for this mechanism.

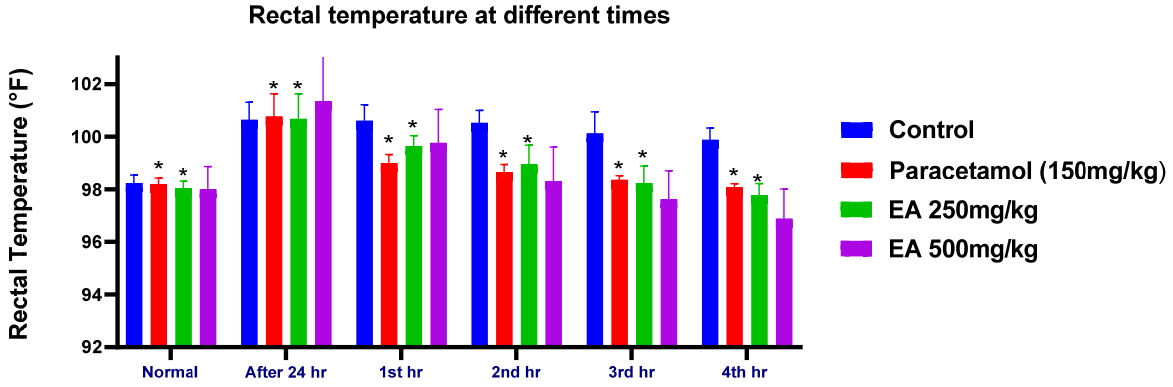

Figure 3. Rectal temperature at different times (for different samples) EA fractions of *Acacia crassicarpa* reduced pyrexia to 97.66 ± 0.2400 °F and 96.88 ± 0.5034 °F, at 250 and 500 mg/kg, respectively. In comparison, the reference drug Paracetamol exhibited 97.89 ± 0.05831 °F inhibition at a dose of 150 mg/kg body weight. Among the two doses tested, the ethyl acetate fraction at 250 mg/kg showed the most pronounced antipyretic activity. The experimental results are expressed as means ± standard error of the mean (SEM). (*$p < 0.05$).

3.4. Evaluation of Acute toxicity

The average weight of mice in the control group (Group I) increased slightly from 30.6 ± 1.89 g to 31.3 ± 1.87 g, indicating normal growth. Likewise, Group II (EA 300 mg/kg) experienced a weight gain similar to the control group. In comparison, Groups III (EA 2000 mg/kg) and IV (EA 5000 mg/kg) showed modest weight increases, ranging from 26.60 ± 3.572 g to 27.80 ± 3.826 g and 30.80 ± 2.154 g to 31.40 ± 2.182 g, respectively. (Figure 4).

Acute toxicity was assessed using the fractions of the *Acacia crassicarpa* extract at dosages of 300, 2000, and 5000 mg/kg. The average body weight of the control group considerably dropped while the *Acacia crassicarpa* leaf extract group showed no visible changes in appearance or behavior and experienced an increase in average

body weight, suggesting no toxic effects. On the second day, the average body weights of mice administered the ethyl acetate fraction of *Acacia crassicarpa* leaf extract at doses of 300 mg/kg, 2000 mg/kg, and 5000 mg/kg were 34.60 ± 1.288 g, 27.80 ± 3.826 g, and 31.40 ± 2.182 g, respectively. Doses up to 2000 mg/kg, suggesting that lower doses would also be non-toxic [27]. Therefore, the absence of toxicity at higher doses, indicates that 250 mg/kg and 500 mg/kg doses are likely safe for experimental use. Although there was a small weight variation behavioral changes and other metrics such urine, food intake, temperature, and changes in the colors of the eyes and skin were all normal. (Table 1) At all administered doses, the test animals exhibited minimal behavioral changes. The acute toxicity study confirmed that the ethyl acetate fraction of *Acacia crassicarpa* leaf extract is safe and non-toxic.

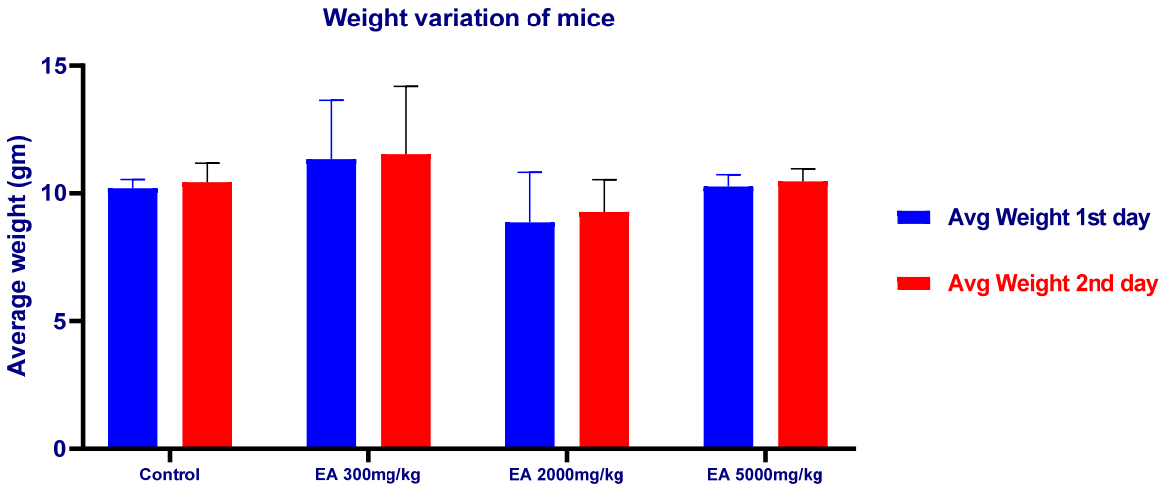

Figure 4. Effects of the EA fractions of *Acacia crassicarpa* extract on the body weight of mice at different doses. All the groups showed slightly increase in body weight after the treatment.

Table 1. General appearance and behavioral observations of the acute toxicity study for control and treated groups. The fractions of *Ficus benjamina* extract showed no behavioral changes, indicating it is safe and non-toxic.

Observation	Group-I (Control)	Group-II EA (300 mg/kg)	Group-III EA (2000 mg/kg)	Group-IV EA (5000 mg/kg)
Food intake	Normal	Normal	Normal	Normal
Skin color	Normal	Normal	Normal	Normal
Temperature	Normal	Normal	Normal	Normal
Drowsiness	Normal	Normal	Normal	Normal
Eye color	Normal	Normal	Normal	Normal
Diarrhea	Normal	Normal	Normal	Normal

4. Conclusions

Acacia crassicarpa has long been valued in traditional medicine, and this study investigated its therapeutic potential through extensive in vivo pharmacological testing. The results demonstrate its potent analgesics, anti-inflammatory and antipyretic effects, with no observed adverse reactions. These findings underscore its potential as a natural treatment for various health conditions, reinforcing its promise for therapeutic use. However, additional research is needed to elucidate its underlying mechanisms and optimize its medical applications.

Author Contributions: A.I., I.J.M., M.R.H., M.M.M., M.M.N.M. and T.A.A. performed the literature review and experiment under the guidance of A.-S.M.; A.I., I.J.M. and A.-S.M. performed the writing—original draft; A.-S.M. performed the review, evaluation, and supervision. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: All animal protocols were reviewed and approved by the Committee of Clinical Pharmacy & Pharmacology, Department of Pharmacy, Dhaka International University (Ref: CPP/DIU/EC/007).

Informed Consent Statement: Not applicable.

Data Availability Statement: All data generated in this study are available from the corresponding author upon request. Results are expressed as mean ± SEM. Statistical analyses were performed using GraphPad Prism (version 9.0), with one-way

ANOVA followed by Tukey's post hoc test (* $p < 0.05$ considered statistically significant). Raw data are securely maintained for verification.

Conflicts of Interest: The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies: No AI tools were utilized for this paper.

References

1. Atanasov, A.G.; Zotchev, S.B.; Dirsch, V.M.; et al. Natural products in drug discovery: Advances and opportunities. *Nat. Rev. Drug Discov.* **2021**, *20*, 200–216.
2. Truter, I. African traditional healers: Cultural and religious beliefs intertwined in a holistic way. *S. Afr. Pharm. J.* **2007**, *74*, 56–60.
3. Gurib-Fakim, A. Medicinal plants: Traditions of yesterday and drugs of tomorrow. *Mol. Asp. Med.* **2006**, *27*, 1–93.
4. Garcia-Alvarez, A.; Egan, B.; De Klein, S.; et al. Usage of plant food supplements across six European countries: Findings from the PlantLIBRA consumer survey. *PLoS ONE* **2014**, *9*, e92265.
5. Ekor, M. The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. *Front. Pharmacol.* **2014**, *4*, 177.
6. Kumar, A.; P, N.; Kumar, M.; et al. Major phytochemicals: Recent advances in health benefits and extraction method. *Molecules* **2023**, *28*, 887.
7. Ghlichloo, I.; Gerriets, V. *Nonsteroidal anti-inflammatory drugs (NSAIDs)*; StatPearls Publishing: Treasure Island, FL, USA, 2019.
8. Timbadiya, M.J.; Nishteswar, K.; Acharya, R.; et al. Experimental evaluation of antipyretic and analgesic activities of Amalakyadi Gana: An Ayurvedic formulation. *AYU* **2015**, *36*, 220–224.
9. Vane, J.R. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. *Nat. New Biol.* **1971**, *231*, 232–235.
10. Wingfield, M.J.; Roux, J.; Wingfield, B.D. Insect pests and pathogens of Australian acacias grown as non-natives–an experiment in biogeography with far-reaching consequences. *Divers. Distrib.* **2011**, *17*, 968–977.
11. Batiha, G.E.-S.; Akhtar, N.; Alsayegh, A.A.; et al. Bioactive compounds, pharmacological actions, and pharmacokinetics of genus Acacia. *Molecules* **2022**, *27*, 7340.
12. Prayogo, Y.H.; Syafii, W.; Sari, R.K.; et al. Pharmacological activity and phytochemical profile of acacia heartwood extracts. *Sci. Pharm.* **2021**, *89*, 37.
13. Prayogo, Y.H.; Batubara, I.; Wahyudi, S.T.; et al. Metabolite profile, antiproliferative, and antioxidant activity of Acacia auriculiformis and Acacia crassicarpa extracts. *J. Saudi Chem. Soc.* **2023**, *27*, 101742.
14. Ali, M.A.; Lou, Y.; Hafeez, R.; et al. Functional analysis and genome mining reveal high potential of biocontrol and plant growth promotion in nodule-inhabiting bacteria within Paenibacillus polymyxa complex. *Front. Microbiol.* **2021**, *11*, 618601.
15. Atiya, A.; Majrashi, T.; Akhtar, S.; et al. The value of Genus Acacia in arid and semi-arid environments for the treatment of chronic inflammatory diseases. *Phytomed. Plus* **2022**, *2*, 100315.
16. Doan, T.Q.; Dinh, T.T.; Matsumoto, T.K.; et al. Chemical composition of essential oil of Acacia crassicarpa Benth. (Fabaceae) from Vietnam. *Bull. Chem. Soc. Ethiop.* **2025**, *39*, 1653–1660.
17. Debnath, S.L.; Kundu, P.; Golder, M.; et al. Phytochemical Characterization and Evaluation of Pharmacological Activities of Leaves of a Mangrove Plant Species-*Aegiceras corniculatum* (L.): Doi. org/10.26538/tjnpr/v4i9. 4. *Trop. J. Nat. Prod. Res.* **2020**, *4*, 516–522.
18. Subedi, N.K.; Rahman, S.A.; Akbar, M.A. Analgesic and antipyretic activities of methanol extract and its fraction from the root of Schoenoplectus grossus. *Evid. -Based Complement. Altern. Med.* **2016**, *2016*, 3820704.
19. Malik, M.K.; Bhatt, P.; Singh, J.; et al. Preclinical safety assessment of chemically cross-linked modified mandua starch: Acute and sub-acute oral toxicity studies in Swiss albino mice. *ACS Omega* **2022**, *7*, 35506–35514.
20. Jame, R.J.S. Phytochemical and pharmacological uses of Acacia nilotica—A review. *Seeds* **2018**, *1*, 15–21.
21. Chaudhary, P.; Sharma, R.; Rawat, S.; et al. Antipyretic medicinal plants, phytocompounds, and green nanoparticles: An updated review. *Curr. Pharm. Biotechnol.* **2023**, *24*, 23–49.
22. World Health Organization. *WHO Expert Committee on Biological Standardization: Seventy-Eighth Report*; World Health Organization: Geneva, Switzerland, 2024.
23. Abdulkhaleq, L.; Assi, M.; Abdullah, R.; et al. The crucial roles of inflammatory mediators in inflammation: A review. *Vet. World* **2018**, *11*, 627.
24. Vane, J.; Botting, R.M. Mechanism of action of anti-inflammatory drugs. *Scand. J. Rheumatol.* **1996**, *25*, 9–21.
25. Liu, T.; Zhang, L.; Joo, D.; et al. NF-κB signaling in inflammation. *Signal Transduct. Target. Ther.* **2017**, *2*, 1–9.

26. Flower, R.; Vane, J. Inhibition of prostaglandin synthetase in brain explains the anti-pyretic activity of paracetamol (4-acetamidophenol). *Nature* **1972**, *240*, 410–411.
27. Gemeda, H.B.; Debella, A.; Endale, M.; et al. Acute and sub-acute toxicity of ethanol extracts of Hagenia abyssinica and Rumex abyssinicus flowers in Swiss albino mice. *PLoS ONE* **2025**, *20*, e0319464.