GSC Biological and Pharmaceutical Sciences
eISSN: 2581-3250 CODEN (USA): GBPSC2
Cross Ref DOI: 10.30574/gscbps
Journal homepage: https://gsconlinepress.com/journals/gscbps/

(RESEARCH ARTICLE)

Check for updates

# Anti-inflammatory Activity of Acutely Administered Methanolic Leaf Extract of *Croton zambesicus Linn* in Laboratory Rats

Bitrus Danladi Pofi [1], Olusayo Moritiwon [1], Timothy Olugbenga Ogundeko [2,*], Ayuba Clagba Sanni [1], Mamzhi Seljul C Ramyil [3], Ndidi C. Ngwuluka [4] and Sunday O. Otimenyin [1]

[1] *Department of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, University of Jos, Nigeria.*
[2] *Department of Pharmacology and Therapeutics, College of Medical Sciences, Bingham University, Jos Campus, Nigeria.*
[3] *Department of Medical Microbiology and Parasitology, College of Medical Sciences, Bingham University, Jos Campus, Nigeria.*
[4] *Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, University of Jos, Nigeria.*

GSC Biological and Pharmaceutical Sciences, 2025, 32(03), 008-014

Publication history: Received on 15 July 2025; revised on 30 August; accepted on 02 September 2025

Article DOI: https://doi.org/10.30574/gscbps.2025.32.3.0334

## Abstract

The present study investigated the acute anti-inflammatory effects of methanolic leaf extract of *Croton zambesicus* (MECZ) in laboratory rats using egg albumin-induced paw oedema and formaldehyde-induced arthritis models. A total of 62 albino rats were used and grouped accordingly to receive varying doses of MECZ (25 mg/kg, 50 mg/kg, and 100 mg/kg), standard drug (Diclofenac 20 mg/kg), and normal saline. Phytochemical screening revealed the presence of alkaloids, triterpenes, saponins, anthraquinones, cardiac glycosides, and steroids. The extract exhibited a dose-dependent and statistically significant ($p < 0.05$) reduction in paw oedema compared to the control. The 100 mg/kg MECZ dose produced effects comparable to diclofenac in both egg albumin-induced paw oedema and formaldehyde-induced arthritis models. The $LD_{50}$ was calculated to be 3807.98 mg/kg, indicating a high margin of safety. These findings suggest that MECZ possesses potent anti-inflammatory properties, supporting its traditional use in managing inflammation-related conditions.

**Keywords:** *Croton zambesicus*; Anti-inflammatory; Phytochemicals; Paw oedema; Herbal medicine; Acute inflammation; Formalin-induced arthritis

## 1. Introduction

Inflammation is a protective immunovascular response that involves immune cells, blood vessels, and molecular mediators [1]. Nonsteroidal anti-inflammatory drugs are used worldwide for the treatment of inflammation [2]. Due to the use of synthetic drugs, many unwanted effects usually appear [3]. When pain is associated with inflammatory conditions, non-steroidal anti-inflammatory or steroidal drugs are administered [4], [1]. The main types of anti-inflammatory medications are the steroidal and non-steroidal drugs. Corticosteroids (steroidal drugs) are used to treat asthma and autoimmune inflammatory response. In addition, non-steroidal drugs are used for mild to moderate pain and as antipyretic through the inhibition of cyclooxygenase enzyme [6].

According to the World Health Organization, approximately 80% of the world population still use plant-based drugs which include the medicinal use of plants as anti-nociceptive drugs in traditional treatment [6]. Examples of some medicinal plants that show anti-inflammatory or analgesic therapeutic properties includes: (Anacardiaceae) could inhibit the production of IgE *in vivo* [7], Magnolia officinalis (Magnoliaceae) that reduce inflammatory arthritis *in vivo* [8], *Clerodendrum phlomidis* L.f (Lamiaceae) that could reduce mediators responsible for synovial inflammation *in vitro*

* Corresponding author: Timothy Olugbenga Ogundeko

*and in vivo* [9], *Arnica montana* topically used as counterirritant to relieve pain [10], *Withania somnifera* and Panax ginseng. (Araliaceae) both modulate COX-2 expression *in vivo* [11],[12], *Erycibe obtusifolia* Benth that prevent paw swelling and articular damage index score [13] *Glycyrrhiza uralensis* which inhibit in vivo arthritis induced by collagen [14], *Lippia dulcis* that inhibit in vitro elastase activity [15] etc. Currently, researchers are using a computational platform to evaluate the potential of plant bioactive compounds towards novel, effective, and affordable drug development candidates to gain a better understanding of drug interactions with the body's biochemical pathways [16]. With a historical foundation in traditional medicine systems, herbal remedies have gained widespread popularity as natural alternatives to conventional treatments.

Herbal medicine has become a good alternative to conventional drugs as it has been used for centuries to treat human diseases [17] as it is mainly based on the idea that plants are a natural means of treatment devoid of any risks. *Croton zambesicus*Muell Arg. (Euphorbiaceae) (syn C. amabilis muell. Arg., C. gratissimus Burch.) is an ornamental tree grown in villages and towns in Nigeria. It is a slender dioecious tree up to 30 feet high, sometimes forming a bowl, with scaly bark. The leaves have a pointed apex and are silvery rusty-scaly below. It is commonly called bushveld, and referred to koriba or ichen maser in Hausa, Ajekobale in Yoruba, mfam in Ekoi and Moramora in Kilba [18]. Different parts of Croton zambesicus (CZ) including the leaf, seed, stem and root are used as antimalaria, laxative, ease menstrual pain, anti-diabetic, cough, dysentery, fever, convulsions, antioxidants, and nephron-protective activities, amongst others in Africa, especially in Nigeria and West African sub-region, [19] - [24]. Ayanniyi *et al*., also reported that aqueous leaf extract of CZ attenuated toxic effects of CCl4 on the heart and thus found to have a protective potential [25]. This highlights the possible effects of naturally derived medicines in tropical illnesses treatment. This development follows the World Health Organization's 2008 ratification of The Beijing Declaration, which promotes the efficacy and safety of folk medicines and claims greater assimilation of these into national health care systems [26].

The therapeutic potential of *Croton zambesicus* from its rich phytochemical profile points to the need to explore the significant biological activities via pharmacological model, as Parveen *et al*., asserted that the conventional treatment of fever and inflammation with synthetic drugs often comes with significant side effects and unpredictable adverse reactions [3]. This study aimed to assess the acute anti-inflammatory effect of methanol leaf extract of *Croton zambesicus* using laboratory rat model.

## 2. Materials and Methods

### 2.1. Plant material collection and Authentication

The leaves of *Croton zambesicus* were collected between April and June, 2011 from Riyom, Plateau State, Nigeria. The plant sample was identified and classified by Mr. Joseph Jeffrey Azila (a plant taxonomist) at the Federal College of Forestry Jos, further authenticated at the Department of Pharmacognosy, University of Jos Nigeria, where it was found to correspond with voucher specimen number UJ/PGPH/HSP/0801.

### 2.2. Preparation of Methanolic Extract of *Croton zambesicus* Leaves (MECZ)

Fresh leaves of Croton zambesicus were rinsed and dried in a well-ventilated portion at the Pharmacology Laboratory, Faculty of Pharmaceutical Sciences, University of Jos, Nigeria for a period of 2 weeks. The dried leaves were ground into powder with mortar and pestle, sieved into fine powder and then stored in air-tight containers. The powdered leaves (300 g) were cold-macerated for 72 hours using methanol and filtered with Whatman filter paper (No.1). The liquid methanolic extract that was obtained by filtration was concentrated in vacuo at 40oC and all the methanol was completely removed, after which the methanolic extract was stored at -4oC in a refrigerator until used [27].

### 2.3. Phytochemical screening

Coloring and precipitation reactions were used to characterize the chemical groups (Anthraquinones, Alkaloids, Steroids, Triterpenes, Cardiac glycosides and Saponins) present in the extract, using the methods described by *Houngbeme et al.,* [28].

### 2.4. Experimental Animals

A total of 62 rats (150-200 g) were obtained from the Animal Experimental Unit of the Department of Pharmacology and Toxicology, University of Jos. The animals were handled in accordance with the Guidelines for Laboratory Procedures laid down by the International Animal Care and Use Committee (IACUC) in Nigeria.

### 2.5. Acute Toxicity Study (Determination of $LD_{50}$)

The Lethal dose ($LD_{50}$) of the MECZ was determined using 12 rats according the method described by Lorke (1983) **as** described by Erhirhie et al., 2018. The $LD_{50}$ value was determined by calculating the geometric mean of the lowest dose that caused death and the highest dose at which all the animal survived. The formula below was however used

$LD_{50} = \sqrt{MLD \times MTD}$ Where $LD_{50}$= median lethal dose MLD=minimum lethal dose, MTD=maximum tolerated dose

### 2.6. Evaluation of Anti-inflammatory Activity of the Extract

*2.6.1. Systemic Acute Inflammation of the Rat Paw*

Twenty-five (25) adult albino rats divided into 5 groups of 5 rats. Fresh egg albumin was used to induce paw oedema in the rats on right hind paw and the oedema formation was monitored in the groups immediately after chemical administration up to 3 hours. Average oedema and its inhibition were assessed at a baseline, 30 minutes, 60 minutes, 120 minutes 180 minutes. This was done according to the method developed by Winter *et al*. (1962) for acute inflammation studies Egg albumin-induced paw oedema as reported by Akindele *et al*., 2015 with slight modification.

*2.6.2. Arthritic-Induced by Formaldehyde in Rats*

The anti-inflammatory activity of *Croton zambesicus* was evaluated by using formalin-induced hind paw edema model using 25 rats. The animals were divided into five groups with five rats in each group. The paw edema induced by injecting 0.1 ml of 2 % formalin into sub- plantar tissues of the rat's paw in all groups, except for the control group that administered normal saline only. After 1 hour of formalin administration, Diclofenac (20 mg/kg), *Croton zambesicus* leaf extract (25 mg/kg, 50 mg/kg and 100 mg/kg) were administered intraperitoneally daily for six days while the volume of oedema paw was measured and recorded according to the method of Seyle, 1947 as reported by Arega *et al*., 2023 with slight modification.

### 2.7. Statistical Analysis

Data obtained were expressed as mean ± standard error of mean (SEM). Graphs were plotted using Microsoft Excel and analyzed using GraphPad Prism 6, Software. Statistical analysis of difference between control and treated groups was carried out using one-way analysis of variance (ANOVA) followed by Bonferroni post-hoc test for multiple comparisons. Statistical significance was taken at $P < 0.05$.

## 3. Results and Discussion

**Table 1** Phytoconstituents in *Croton zambesicus*

| Phytochemicals | Results |
|---|---|
| Anthraquinones | Present |
| Alkaloids | Present |
| Steroids | Present |
| Triterpenes | Present |
| Cardiac glycosides | Present |
| Saponins | Present |

### 3.1. Lethal Dose $LD_{50}$

$LD_{50}$ of *Croton zambesicus* was determined as 3807.98 mg/kg

**Table 2** Effect of MECZ extract on egg albumin Induced Paw Edema in Albino rats

| Treatment | Paw diameter (mm) at time (minutes) of Treatment | | | | | |
|---|---|---|---|---|---|---|
| | **Baseline** | **After Chemical Administration** | **30 minutes** | **60 minutes** | **120 minutes** | **180 minutes** |
| Normal Saline | 3.28 ± 0.14 | 4.65 ± 0.21 | 7.68 ± 0.29 | 7.89 ± 0.13 | 7.99 ± 0.04 | 7.74 ± 0.22 |
| CZ extract 25 mg/kg | 3.01 ± 0.13 | 4.73 ± 0.03 | 7.19 ±0.02 | 7.34 ± 0.04 | 7.12 ± 0.12 | 6.90 ± 0.16 |
| CZ extract 50 mg/kg | 2.96 ± 0.07 | 4.61 ± 0.05 | 6.93 ± 0.06 | 6.75 ±0.09* | 6.30 ± 0.60* | 5.79 ± 0.04* |
| CZ extract 100 mg/kg | 3.03 ± 0.08 | 4.64 ± 0.11 | 6.39 ± 0.14* | 6.18 ±0.10* | 5.79 ± 0.10* | 5.14 ± 0.06* |
| Diclofenac 20 mg/kg | 3.15 ± 0.10 | 4.68 ± 0.04 | 6.43 ± 0.03* | 6.11 ±0.07* | 5.38 ± 0.06* | 4.28 ± 0.05* |

Key: CZ= Croton zambesicus; n = 5; * p<0.05 significant compared to the control group

**Table 3** Effect of MECZ Extract on Formaldehyde Induced Paw Edema in Albino rats

| Treatment (mg/kg) | Day1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 |
|---|---|---|---|---|---|---|
| Normal saline | 0.86 ± 0.03 | 1.82 ± 0.14 | 2.63 ± 0.07 | 3.11 ± 0.06 | 3.34 ± 0.05 | 3.39 ± 0.05 |
| CZ extract 25 mg/kg | 0.39 ± 0.02* | 1.23 ±0.01* | 1.95 ± 0.02* | 2.41 ± 0.02* | 2.08 ± 0.03* | 1.75 ± 0.04* |
| CZ extract 50 mg/kg | 0.47 ± 0.10* | 1.25 ±0.02* | 1.82 ± 0.04* | 1.43 ± 0.03* | 1.23 ± 0.02* | 0.47 ± 0.01* |
| CZ extract 100 mg/kg | 0.94 ± 0.03 | 1.76 ± 0.03 | 1.36 ± 0.02* | 1.02 ± 0.02* | 0.39 ± 0.02* | 0.06 ± 0.03* |
| Diclofenac 20mg/kg | 0.24 ± 0.05* | 0.77 ±0.06* | 1.21 ± 0.05* | 0.83 ± 0.10* | 0.68 ± 0.39* | 0.07 ± 0.01* |

Key: CZ= Croton zambesicus; n = 5; * p<0.05 significant compared to the control group

The study provides compelling evidence for the anti-inflammatory potential of Croton zambesicus methanolic leaf extract (MECZ). The results from both egg albumin-induced paw oedema (Table 2) and formaldehyde-induced arthritis (Table 3) models showed significant inhibition of inflammation, with effectiveness increasing in a dose-dependent manner. The 100 mg/kg dose showed marked anti-inflammatory activity, closely mimicking the effect of the standard NSAID (diclofenac). Our results are similar to earlier reports - In Ghana, bark poultices manage rheumatism. Ethanolic leaf extracts (27–81 mg/kg) reduced carrageenan-induced paw edema by 40% in rats, though less potent than standard drugs like diclofenac [26]. The phytochemical analysis revealed the presence of several bioactive compounds—alkaloids, triterpenes, saponins, steroids, and glycosides—which are known to mediate anti-inflammatory and analgesic effects. These compounds likely act by modulating the release of inflammatory mediators such as prostaglandins and cytokines, or by inhibiting the cyclooxygenase (COX) pathway. Evidence for the anti-inflammatory properties of saponins, flavonoids and other bioactive compounds has been reported by several studies using different models of inflammation [32]-[35]. Essential oils from Croton gratissimus leaves, stem, and roots extracts in Eastern Pretoria (South Africa) had monoterpenoids such as α-phellandrene, α-pinene, and Z- and E-β-ocimene [36]. Interestingly, the most frequent Croton alkaloids are compounds similar to benzylisoquinolines, in fact, crotamide and crotsparsidine (Croton sparsiflorus), crotonamide A (C. pullei), crotonine (C. tiglium), and crotonamide (C. alienus) have been also validated as alkaloids [37].

Notably, the high $LD_{50}$ value (3807.98 mg/kg) suggests that MECZ is relatively safe for acute administration, which aligns with previous studies that have reported the general safety of Croton zambesicus extracts [38], [39]. The dose-dependent nature of the anti-inflammatory effect also provides a promising basis for determining therapeutic dosing regimens in future studies.

Compared to conventional NSAIDs, which are associated with adverse gastrointestinal and renal effects, MECZ offers a potentially safer alternative for managing inflammation. The extract's efficacy in both models used suggests its therapeutic relevance.

These findings support the traditional medicinal use of Croton zambesicus in the treatment of inflammation-related ailments and highlight the importance of further pharmacological and toxicological studies to validate its efficacy and safety in clinical settings. Additional studies could explore its mechanisms of action, bioactive compound isolation, and long-term effects in animal and human models.

## 4. Conclusion

This study concludes that the methanolic leaf extract of *Croton zambesicus* exhibits significant acute anti-inflammatory activity in rat models, with a safety margin supported by a high $LD_{50}$ value. The results validate its traditional use in treating inflammation and suggest that MECZ could serve as a potential alternative or complement to conventional anti-inflammatory drugs. Further studies are recommended to explore its clinical application, mechanism of action, and chronic toxicity profile.

## Compliance with ethical standards

### *Acknowledgments*

Authors wish to thank Mr. Bulus and Mr. Sunday Azi as well as other staff of the Department of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences University of Jos, Nigeria for their assistance.

### *Disclosure of conflict of interest*

Authors declare no conflict of interest of any sort

### *Statement of ethical approval*

Ethical approval was obtained from the Animal Ethics Committee, University of Jos, Nigeria.

## References

[1] Bairy KL, Chogtu B, Nayak V. Effect of fluticasone propionate with biopolymer on skin inflammatory model in wistar rats. *Res J Pharmaceutical, Biol and Chem Sci*. 2015; 6: 721-723.

[2] Narsinghani T, Sharma R. Lead Optimization on Conventional Non-Steroidal Anti-Inflammatory Drugs: An Approach to Reduce Gastrointestinal Toxicity. *Chem Bio & Drug Design*. 2014; 84:1–23.

[3] Praveen KD, Suchita M. Herbal Sources of Anti-inflammatory Potential: A Review. *Int J Phytopharm*. 2013; 4: 158-165.

[4] WebMD, Webster's New World Medical Dictionary, Fully Revised and Updated, Wiley, 2008.

[5] Devillier P. Pharmacology of non-steroidal anti-inflammatory drugs and ENT pathology. *Presse Medicale Paris Fr*. 1983; 30 (39-40 Pt 2) (2001) 70–79.

[6] U. Cm, M. Ct, S. Gd, *et al*., Medicinal plants of the family lamiaceae in pain therapy: a review, Pain Res. Manag. 2018 (2018).

[7] Rivera DG, Balmaseda IH, León AÁ, Hernández BC, Montiel LM, Garrido GG, Hernández RD, Cuzzocrea S. Anti-allergic properties of Mangifera indica L. extract (Vimang) and contribution of its glucosylxanthone mangiferin. Journal of Pharmacy and Pharmacology. 2006 Mar;58(3):385-92.

[8] Munroe ME, Arbiser JL, Bishop GL, Honokiol, a natural plant product, inhibits inflammatory signals and alleviates inflammatory arthritis, J. Immunol. Baltim. Md. 1950 179 (2) (2007) 753–763.

[9] Babu NP, Saravanan S, Pandikumar P, Krishna KB, Raj MK, Ignacimuthu S. Anti-inflammatory and anti-arthritic effects of 3-hydroxy, 2 methoxy sodium butanoate from the leaves of *Clerodendrum phlomidis L.f. Inflamm. Res. Off. J. Eur*. Histamine Res. Soc. Al. 2014; 63 (2): 127–138.

[10] Koenig HG. Chronic Pain: Biomedical and Spiritual Approaches, first ed., The Haworth Pastoral Press, 2003.

[11] Kim JH, Kim SJ, Overexpression of microRNA-25 by withaferin A induces cyclooxygenase-2 expression in rabbit articular chondrocytes, *J. Pharmacol. Sci*. 2014; 125 (1): 83–90.

[12] Shin YW, Bae EA, Kim SS, Lee YC, Kim DH, Effect of ginsenoside Rb1 and compound K in chronic oxazolone-induced mouse dermatitis, *Int. Immunopharm*. 2005; 5 (7-8): 1183–1191.

[13] Pan R, Dai Y, Gao X, Xia Y, Scopolin isolated from Erycibe obtusifolia Benth stems suppresses adjuvant-induced rat arthritis by inhibiting inflammation and angiogenesis, *Int. Immunopharm*. 2009; (7-8): 859–869.

[14] Fu Y, Zhou H, Wang S, Wei Q, Glycyrol suppresses collagen-induced arthritis by regulating autoimmune and inflammatory responses, *PLoS One*. 2014: 9 (7).

[15] Nayal R. Phytochemische und pharmazeutisch-biologische Untersuchungen an der aztekischen Süßpflanze Lippia dulcis Trev, Dissertation. 2009.

[16] Coopoosamy R, Singh, K, Naidoo, K, Nadasan DS, 2023. The role of phytomedicine: Bridging the gap between the past, present, and future', *J Med Plants for Econ Dev*. 2023; 7(1): a197.

[17] Wang H, Chen Y, Wang L, Liu Q, Yang S, Wang C. Advancing herbal medicine: enhancing product quality and safety through robust quality control practices. Front Pharmacol. 2023 Sep 25;14:1265178.

[18] Hutchinson J, Dalziel JM. Flora of West Tropical Africa. In: Hepper, F.N., Ed., 2nd Edition. 1972; Vol. 111, Part 2, 2nd May, Published on Behalf of the Governments of Nigeria, Ghana, Sierra Leone & The Gambia by Crown Agents for Overseas Governments and Administrations, Millbank, London.

[19] Ajibesin KK, Ekpo BAJ, Bala DN, Essien EE, Adesanya SA. 2008. Ethnobotanical survey of Akwa Ibom State of Nigeria. *J. Ethnopharmcol*. 2008; 115: 387-408.

[20] Okokon JE, Nwafor PA. Antiplasmodial activity of root extract and fractions of *Croton zambesicus. J Ethnopharmacol*. 2009;121(1):74-8. DOI: 10.1016/j.jep.2008.09.034, PMID 18996464.

[21] Aderogba MA, McGraw LJ, Bezabih M, Abegaz BM. Isolation and characterization of novel antioxidant constituents of Croton zambesicus leaf extract. *Nat Prod Res* 2011; 25:1224-33.

[22] Shama YA, Ebtihal AS, 2013. Investigations on the Effects of Various Oral Doses of *Croton zambesicus* Seeds' in Wistar Rats. *Journal of Pharmacology and Toxicology, 8: 19-27.*

[23] Ayanniyi RO, Olumoh-Abdul HA, Ojuade FI, Abdullahi AA, Anafi SB. The protective effect of *Croton zambesicus* against carbon tetrachloride-induced renal toxicity in rats. Iran J Toxi 2019; 13:5-8.

[24] Ibrahim MA, Doha EF, Hiba EE, Malak EA, Sahar BA. 2022. "Antioxidant Activity of Croton Zambesicus Muell. Arg Seed Extract". *Asian Journal of Research in Biochemistry*. 2022; 11 (3-4):1-5.

[25] Ayanniyi RO, Olumoh-Abdul HA, Ojuade FI, Asogwa N. Protective effect of Croton zambesicus leaf extract against carbon tetrachloride induced cardiac toxicity in rats.TJPS 2020; 44 (4): 216-219

[26] Ajayi OS, Omomagiowavi AO. Antimicrobial activity of *Croton zambesicus* on *Staphylococcus aureus* and *Streptococcus* species. *J Adv in Microbiology*. 2018; 14(3): 1–10.

[27] Idyu II, Deshi EF, Idyu VC, Ogundeko TO. The Anti-diarrhoeal Effect of Ethanolic-Bark Extract of Sterculia setigera in Mice. Asian J. Sci.Tech. 2015; 6(5): 1397-1400.

[28] Houngbeme AG, Gandonou C, Yehouenou B, Kpoviessi SDS, Sohounhloue D, Moudachirou M, Gbaguidi FA. Phytochemical Analysis, Toxicity and Antibacterial Activity of Benin Medicinal Plants Extracts Used in the Treatment of Sexually Transmitted Infections Associated with HIV/AIDS. *Int. J Pharm Sci and Res*. 2014; 5(5):1739-1745.

[29] Erhirhie EO, Ihekwereme CP, Ilodigwe EE. Advances in acute toxicity testing: strengths, weaknesses and regulatory acceptance. Interdiscip Toxicol. 2018 May;11(1):5-12. doi: 10.2478/intox-2018-0001. Epub 2018 Aug 6. PMID: 30181707; PMCID: PMC6117820.

[30] Akindele AJ, Oladimeji-Salami JA, Usuwah BA. Antinociceptive and Anti-Inflammatory Activities of Telfairia occidentalis Hydroethanolic Leaf Extract (Cucurbitaceae). J Med Food. 2015 Oct;18(10):1157-63.

[31] Arega M, Nardos A, Debella A, Dereje B, Terefe L, Abebe A. Evaluation of Anti-Inflammatory Activity of the Methanol Extracts of *Premna schimperi* Engl (Lamiaceae) Leaves in Rats. J Exp Pharmacol. 2023 Nov 14;15:437-447.

[32] Cheeke PR, Piacente S, Oleszek W. Anti-inflammatory and anti-arthritic effects of Yucca schidigera: a review. *J Inflammation*. 2006; 3:6.

[33] Han N, Bakovic M. (2015). Biologically active triterpenoids and their cardioprotective and anti-inflammatory effects. *J Bioanalysis & Biomed*. 2015; 12:1– 11.

[34] Khan H, Pervaiz A, Intagliata S, Das N, Nagulapalli Venkata KC, Atanasov AG, Najda A, Nabavi SM, Wang D, Pittalà V, Bishayee A. The analgesic potential of glycosides derived from medicinal plants. [30] Daru. 2020 Jun;28(1):387-401.

[35] Mantiniotou M, Athanasiadis V, Kalompatsios D, Bozinou E, Lalas SI. Therapeutic Capabilities of Triterpenes and Triterpenoids in Immune and Inflammatory Processes: A Review. *Compounds*. 2025; 5(1):2.

[36] Sadgrove NJ, Madeley LG, Van Wyk BE. Volatiles from African species of croton (euphorbiaceae), including new diterpenes in essential oil from Croton gratissimus. Heliyon. 2019;5(10) doi: 10.1016/j.heliyon.2019.e02677.e02677

[37] Xu WH, Liu WY, Liang Q. Chemical constituents from croton species and their biological activities. Molecules . 2018;23(9):p. 2333. doi: 10.3390/molecules23092333.

[38] Onwusonye JC, Muritala IK, Odu DA, Uzomba NI, Ogbonnaya M, Duruamaku CC. Oral acute toxicity study of methanol leaf extracts of *Croton zambesicus* in mice. *Merit Res J Pharm and Pharm Sci*. 2016 Feb; 2(1): 001-005.

[39] Magwilu KD, Nguta JM, Mapenay I, Matara D. Phylogeny, Phytomedicines, Phytochemistry, Pharmacological Properties, and Toxicity of *Croton gratissimus* Burch (Euphorbiaceae). *Adv Pharmacol Pharm Sci*. 2022 May 17;2022:1238270.