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MINI REVIEW

# A perspective on anti-inflammatory properties of *Cleome gynandra*

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**Abstract**

*Cleome gynandra* L. is a widely consumed leafy vegetable. This plant is grown as a weed and widely distributed in tropical and subtropical regions such as Africa, South Asia, and Southeast Asia. In Malaysia, this plant is known as 'maman' and is commonly consumed in stew and pickles. *Cleome gynandra* contains various natural bioactive including flavonol, glycoside, flavonoids, essential oils, bicyclic diterpenes, triterpenoids, coumarinolignoids and dipyridodiazepinone substances that have nutritional values and health-promoting characteristics. Numerous investigations have shown this plant exhibited significant pharmacological activities, including antioxidant, anticancer, anti-arthritic, antiparasitic, antimalarial, antifungal, and anti-inflammatory. Various reports showed that the *C. gynandra* extracts significantly reduced paw edema in adjuvant arthritis-induced rats. Nonetheless, a comprehensive review investigating the anti-inflammatory attributes of this plant has not yet been conducted. This paper aimed to explore the anti-inflammatory activities of *C. gynandra* and its potential mechanism of action.

## 1. Introduction

Inflammation is the body's defence mechanism response to factors such as bacteria, viruses, fungi, damaged cells, cell death, cancer, ischemia, and toxic substances (Ferrero-Miliani *et al*., 2007; Zhao *et al*., 2021). This response can generate acute and chronic inflammation in a variety of organs, including the heart, kidney, liver, pancreas, brain, lung, and reproductive system, resulting in tissue damage and diseases (Chen *et al*., 2018). Chronic inflammatory diseases are a leading cause of death worldwide, with the World Health Organization (WHO) ranking them as the greatest threat to human health (Pahwa and Jialal, 2019). Chronic diseases like stroke, chronic respiratory diseases, heart disorders, cancer, obesity, and diabetes cause 3 out of 5 deaths globally. Cardiovascular diseases account for 31% of all deaths, with coronary heart disease (CHD) being the most common (Al-Mawali, 2015; Pahwa and Jialal, 2019). One possible way to combat chronic inflammation is by using anti-inflammatory agents, which can be found in various sources, including natural products from plants, many of which have yet to be studied chemically or biologically (Dinarello, 2010; Nunes *et al*., 2020; Liu *et al*., 2022).

*Cleome gynandra* (Figure 1), for instance, is a plant that has the potential to exhibit anti-inflammatory properties (Mishra *et al*., 2011; Chandradevan *et al*., 2020; Mashamaite *et al*., 2022; Moyo and Aremu, 2022). Reports claim this plant contains high nutrients and health-promoting characteristics including antioxidant, anticancer, anti-arthritic, antiparasitic, antimalarial,

Figure 1. *Cleome gynandra* leaves.

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antifungal, and anti-inflammatory (Mashamaite *et al*., 2022; Moyo and Aremu, 2022). This plant can be found widely distributed in tropical and subtropical regions (Moyo and Aremu, 2022). This leafy plant is known as 'maman' in Malaysia and is widely consumed in stew, curries and pickles (Muhialdin *et al*., 2018). Various reports have demonstrated the anti-inflammatory activities of *C. gynandra*, although the precise mode of action of these activities is not yet fully understood. This study aims to provide a closer perspective on the anti-inflammatory activities of *C. gynandra.*

## 2. Pharmacological and traditional uses

The Cleome genus plants are important as a source of nutrition and food. The plant contains a significant amount of phenolic compounds (Moyo and Aremu, 2022). The aerial parts of *C. gynandra* and other Cleome species are effective in treating different fungal and bacterial infections (Singh *et al*., 2018; Chand *et al*., 2022; Moyo and Aremu, 2022). According to Ayurveda, *C. gynandra* is recognized for its anthelmintic properties and can be used to alleviate gastrointestinal infections, pruritus, and ear infections (Mishra *et al*., 2011; Adhikari and Paul, 2018). In traditional medicine, the whole plant of *C. gynandra* is utilized to manage diverse medical conditions such as inflammatory diseases, tumours, parasitic infections, and diabetes, and also exhibits antioxidant properties and enhances lysosomal stability (del Carmen Juárez-Vázquez and Jiménez-Arellanes, 2019; Chand *et al*., 2022). Multiple studies have shown that the leaves and seeds of *C. gynandra* are used in various countries to treat conditions such as earache, constipation, inflammation, and epileptic fits, and as a disinfectant (Lokesha, 2018).

## 3. Nutritional values

The Cleomaceae family of plants are consumed as a type of vegetable, and the leaves and shoots of these plants have a sharp, mustard-like flavour. Proteins, fatty acids, dietary amino acids, and lipids are all present in high concentrations in the seed oil of Cleome species like *C. gynandra*. These vegetables also contain a lot of fibre with little fat. Minerals, proteins, and important vitamins, including vitamins A and C, are abundant in *C. gynandra*. High calcium, iron, and zinc concentrations are also present (Jinazali *et al*., 2017). Other compounds found in this plant include luteolin, β-cryptoxanthin, violaxanthin, ascorbic acid, β-carotene, and y-tocopherol. These plants can be utilized as dietary supplements or added to various products to increase their shelf life. Additionally, they can serve as colouring and flavouring agents (Moyo and Aremu, 2022).

## 4. Anti-inflammatory properties

Chronic inflammatory diseases, which include eight of the leading causes of death globally according to the World Health Organization's World Health Statistics 2019, are closely linked to the presence of inflammation (Liu *et al*., 2022). Inflammation is recognized as a significant contributing factor in the development and progression of these diseases. Chronic inflammation is a complex physiological response that occurs when the immune system remains constantly activated, leading to persistent inflammation (Pahwa and Jialal, 2019). Unlike acute inflammation, which serves as a necessary defence mechanism against injury and infection, chronic inflammation can be detrimental and contribute to the development of various diseases. Conditions associated with chronic inflammation include cardiovascular diseases, rheumatoid arthritis, type 2 diabetes, Alzheimer's disease, Parkinson's disease, and cancer. Researchers have recognized natural products, particularly plant-derived compounds, as valuable novel immunomodulators that possess potent anti-inflammatory properties. The anti-inflammatory characteristics displayed by plant-based therapeutics have attracted significant attention as alternative approaches for managing infectious and debilitating diseases (Oguntibeju, 2018; Nunes *et al*., 2020).

Table 1 provides a compilation of studies highlighting the anti-inflammatory activity of *C. gynandra*. In an *in vivo* study conducted by Narendhirakannan *et al*. (2005), it was found that the methanolic extract of *C. gynandra* leaves contained biologically active components such as steroids, flavonoids, saponins, carbohydrates, phenols, and glycosides, which exhibited the potential to reduce arthritis induced by Freund's adjuvant in rats. Notably, the extract-treated rats displayed a significant decrease in paw volume starting from the third week, comparable to normal rats. Moreover, weight loss associated with arthritis was significantly reversed after treatment with the extract. Haematological and biochemical parameters related to arthritis, including haemoglobin, white blood cells, and erythrocyte sedimentation rate, were restored to normal levels following *C. gynandra* extract treatment. Similarly, another study by Narendhirakannan *et al*. (2007) demonstrated that the ethanolic extract of *C. gynandra* caused a reduction in paw swelling in treated rats starting from the third week. The elevated activity of lysosomal enzymes and inflammatory cytokines observed in arthritis-induced rats, such as lactate dehydrogenase, alkaline phosphatase, aspartate transaminase, alanine transaminase, ß-glucuronidase, cathepsin-D, N-acetyl-ß-glucosaminidase, acid phosphatase, and TNF-alpha, experienced a significant reduction after treatment with C*. gynandra* extract.

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Table 1. Anti-inflammatory activity of *C. gynandra* left extract.

| Extract | Subject | Dose | Key findings | References |
|---|---|---|---|---|
| Ethanolic extract | RAW 264.6 cells | 15.63 - 500 µg/mL | 100% ethanolic extract of *C. gynandra* tends to inhibit nitric oxide production better than it scavenges DPPH free radicals. | Chandradevan *et al*. (2020) |
| Chloroform water extract | Carrageenan-induced paw oedema Wister rats | 100 mg/kg | A significant reduction of rat paw oedema was observed with a maximum inhibition of 46.93% comparable to the standard drug which showed an inhibition of 51.75%. | Mule *et al*. (2008) |
| Ethanolic extract | Male albino rats of Wister strain induced with adjuvant arthritis | 150 mg/kg | The lysosomal activity was significantly reduced in *C. gynandra*-treated rats | Narendhirakannan *et al*. (2007) |
| Methanolic extract | Male albino rats of Wister strain after the induction of adjuvant arthritis | 150 mg/kg | A significant reduction in paw volume from the third week onward in *C. gynandra*-treated rats. | Narendhirakannan *et al*. (2005) |

Chronic inflammation and the development of inflammatory disorders are closely linked to the overstimulation of TNFA signalling. Therefore, it is crucial to focus on this protein as a key target when creating therapeutic agents to combat these diseases. TNF-alpha, in particular, is implicated in the pathological mechanism of rheumatoid arthritis and its levels were restored to normal upon treatment with *C. gynandra* extract (Narendhirakannan *et al*., 2007). In another study, carrageenan-induced paw oedema was used as a model of the exudative phase of acute inflammation. The extract caused a significant reduction of rat paw oedema with a maximum inhibition of 46.93% after 2 hrs of treatment (Mule *et al*., 2008). Nitric oxide (NO), produced by various cell types, has gained significant attention due to its multifaceted role in the inflammatory cascade. NO can exert pro-inflammatory effects by modulating key processes in inflammation, such as vasodilation, leukocyte recruitment, and the production of other inflammatory mediators. It acts as a signalling molecule to promote the activation of immune cells, including macrophages and neutrophils (Papi *et al*., 2019; Cyr *et al*., 2020; Guo *et al*., 2020). The 20% ethanolic extract of *C. gynandra* was found to display the best anti-inflammatory activities in metabolomics studies (Chandradevan *et al*., 2020).

These reports indicate the potential of *C. gynandra* to possess bioactive molecules that could act as anti-inflammatory agents. Nonetheless, there is neither a comprehensive *in vitro* nor *in vivo* study carried out to unravel the mechanism of action. Certain pathways like the vascular endothelium pathway or arachidonic acid pathway can be used to further investigate the mechanistic effect of the plant extracts.

## 5. Future prospect of *Cleome gynandra* as anti-inflammatory agent

Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most frequently prescribed drug classes for pain and inflammation. They belong to a group of drugs that have analgesic, antipyretic, and anti-inflammatory properties (Wong, 2019; Nunes *et al*., 2020). NSAIDs offer pain relief for numerous symptoms which include osteoarthritis, sprains and strains, lower back pains, gout, and rheumatoid arthritis. The main therapeutic effects of NSAIDs are principally achieved by their capability to inhibit the cyclooxygenase enzymes (COX-1 and COX-2) involved in the synthesis of prostaglandins (PGs). Arachidonic acid is converted to PGs, which are crucial regulators of inflammation, by the enzymes COX-1 and COX-2 (Papi *et al*., 2019; Faki and Er, 2021). The gastrointestinal tract, kidneys, and platelets normally express COX-1, a "housekeeping" enzyme (Faki and Er, 2021). It appears to be in charge of modulating the thromboxane A2 and prostaglandin synthesis (Hanna and Hafez, 2018; Faki and Er, 2021). Prostaglandins preserve the integrity of the stomach mucosa, facilitate appropriate platelet function, and control renal blood flow under the control of COX-1 (Ornelas *et al*., 2017). The isoenzyme COX-2 is mainly linked to inflammation. The synthesis of prostaglandins, which are key mediators of inflammation, pain, and fever, is induced by cytokines and growth factors and occurs mostly at inflammatory sites (Jahnavi *et al*., 2019). By inhibiting both COX isoforms, traditional NSAIDs to variable degrees prevent prostaglandin synthesis (Ferrer *et al*., 2018). Plants are the primary source of molecules for the development of new drugs, which amplifies transnational interest in finding substances derived from plants, particularly since a large proportion of species are yet to be studied

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chemically or biologically, particularly in terms of anti-inflammatory activity. There exists a gap in our current understanding regarding the precise mechanisms through which *C. gynandra* exerts its anti-inflammatory activities, particularly concerning the COX pathway (Figure 2). To bridge this knowledge gap, further research is warranted to identify and isolate the specific bioactive compounds present in *C. gynandra* that are responsible for their anti-inflammatory effects. By isolating these compounds, researchers can conduct detailed studies to unravel their chemical composition and establish a structure-activity relationship. Such investigations will help determine the specific molecular interactions between these compounds and the COX pathway, shedding light on their mechanisms of action. Moreover, understanding the potential synergistic interactions between the bioactive compounds of *C. gynandra* and the COX pathway is of significant interest. Investigating how these compounds work in concert to modulate the pathway can provide a comprehensive understanding of the plant's anti-inflammatory potential. It may also unveil novel therapeutic approaches, as synergistic interactions can enhance the efficacy and potency of anti-inflammatory interventions.

## 6. Conclusion

In conclusion, the paper highlights the abundant opportunities for further exploration and investigation into the anti-inflammatory properties of *C. gynandra*. Despite the limited attention given to this plant, the significant potential exhibited by this plant warrants continued research and development in order to fully harness its therapeutic benefits. By delving deeper into the mechanisms and bioactive compounds responsible for the anti-inflammatory effects of *C. gynandra*, we can unlock new possibilities for its application in the treatment and management of various inflammatory conditions. These promising prospects open doors for future studies and pave the way for the development of innovative therapeutic strategies that harness the natural potential of *C. gynandra* as a valuable anti-inflammatory agent.

## Conflict of interest

The authors declare no conflict of interest.

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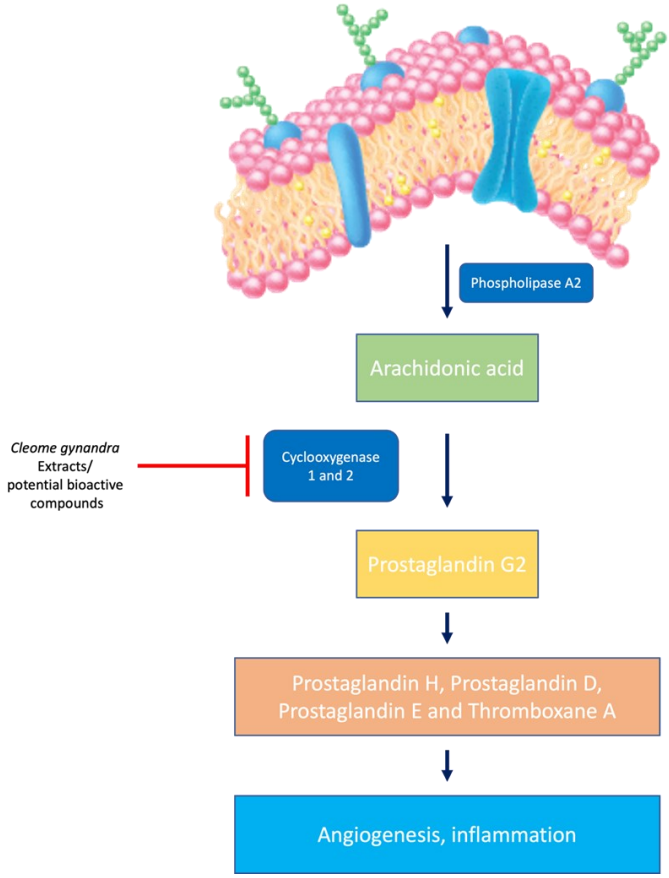


Figure 2. Illustration on the possible anti-inflammatory mechanism exerted by *Cleome gynandra* extracts or bioactive constituents.

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