



IN VITRO ANTI-INFLAMMATORY POTENTIAL OF MEDICINAL PLANTS AND PLANT-DERIVED BIOACTIVE COMPOUNDS: A COMPREHENSIVE REVIEW

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How to cite this Article: N. Tulasi Uma Rani*¹, SK. Sarma Sree, G. Mugibunnisa, M. Hasini Praveena, T.K. Karthikeya (2026). In Vitro Anti-Inflammatory Potential Of Medicinal Plants And Plant-Derived Bioactive Compounds: A Comprehensive Review. World Journal of Advance Pharmaceutical Sciences, 3(10), 1-6.



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Article Info

Article Received: 04 August 2026,

Article Revised: 24 August 2026,

Article Accepted: 14 Sept. 2026.

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DOI: <https://doi.org/10.5281/zenodo.23066829>

ABSTRACT

Inflammation is a complex biological response that plays a vital role in protecting the body against pathogens, tissue injury, and harmful stimuli. However, persistent or uncontrolled inflammation is associated with the development of numerous chronic diseases, including arthritis, cardiovascular disorder, diabetes, neurodegenerative diseases, and cancer. Although conventional anti-inflammatory drugs are effective, their long-term use is often limited by adverse effects, creating a need for safer and more effective therapeutic alternatives. Medicinal plants have emerged as promising sources of anti-inflammatory agents due to their rich content of bioactive phytochemicals such as flavonoids, phenolics, alkaloids, terpenoids, tannins, and glycosides. This review summarizes recent in vitro studies on the anti-inflammatory potential of medicinal plants, plant-derived compounds, and green synthesized nanoparticles. The reviewed studies demonstrate that these natural products exert anti-inflammatory effects through multiple mechanisms, including inhibition of protein denaturation, stabilization of cellular membranes, suppression of pro-inflammatory cytokines, reduction of nitric oxide production, inhibition of cyclooxygenase and lipoxygenase pathways, modulation of NF-κB signaling, and attenuation of oxidative stress. Furthermore, a strong relationship between antioxidant and anti-inflammatory activities was observed among many plant extracts. Overall, the findings highlight the therapeutic potential of medicinal plants as valuable sources of novel anti-inflammatory agents and support further in vivo and clinical investigations for the development of safe and effective treatments for inflammatory disorders.

KEYWORDS: Anti-inflammatory activity, medicinal plants, phytochemicals, cytokines, NF-Kb, oxidative stress, natural products.

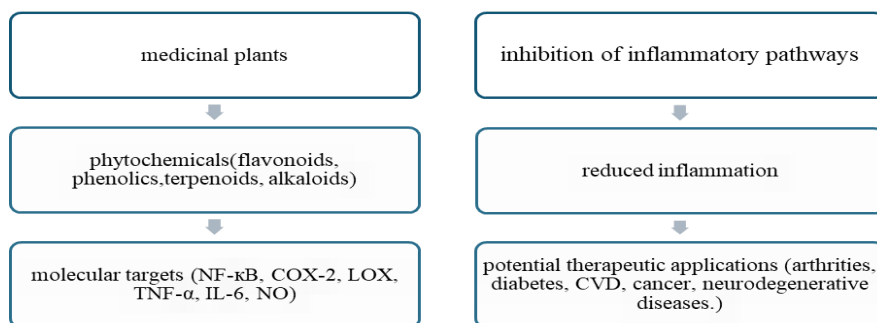
INTRODUCTION

Inflammation is part of the body's defense mechanism.^[1] Inflammation is an ancient medical term initially referring to classic signs and symptoms, including edema, erythema (redness), warmth, pain, and loss of function (stiffness and immobility).^[2] It is the process by which the immune system recognizes and harmful and foreign stimuli and begins the healing process.^[1] Inflammation is a second-line defense against infectious

agents.^[3] Chronic inflammatory diseases are the, most significant cause of death in the world. The world health organization (WHO) ranks chronic diseases as the greatest threat to human health. Worldwide, 3 of 5 people die due to chronic inflammatory diseases like stroke, chronic respiratory diseases, heart disorders, cancer.^{[4][5][6]} The magnitude of global plant diversity is estimated at more than 50,000 species.^{[7][8]} Medicinal plants continue to be an interesting source of natural

products for treating various health conditions. It is estimated that more than 150,000 plant species have been studied, many of which contain valuable therapeutic agents.^{[9][10]} Plants have played an important role in human health care since ancient times. Plants produce several substances that exert biological activities.^[11] The world health organization (WHO) estimates approximately 65% of the world population incorporates traditional medicine into medical care. The use of medicinal plant-based natural compounds to treat many illnesses has become a great trend in clinical research.^[12] Thus, plants have become the first source of substances

for the development of new drugs, and a considerable part of the drugs prescribed in the world are derived from them.^{[13][14][15][16]} The epidemiology of inflammatory diseases and their growing impact on global health, it highlights that chronic inflammation contributes to the development of major disorders such as obesity, diabetes, kidney disease.^[17] This study was conducted to know about the inflammation and the use of the natural herbs and plants for treating the inflammation. To create the awareness about the inflammation and about using the natural herbs to treat the inflammation.



Pathophysiology of inflammation

Inflammation is initiated when immune cells recognize pathogens or damaged tissues through pattern recognition receptors. Activation of macrophages, neutrophils, and other immune cells leads to the release of inflammatory mediators including:

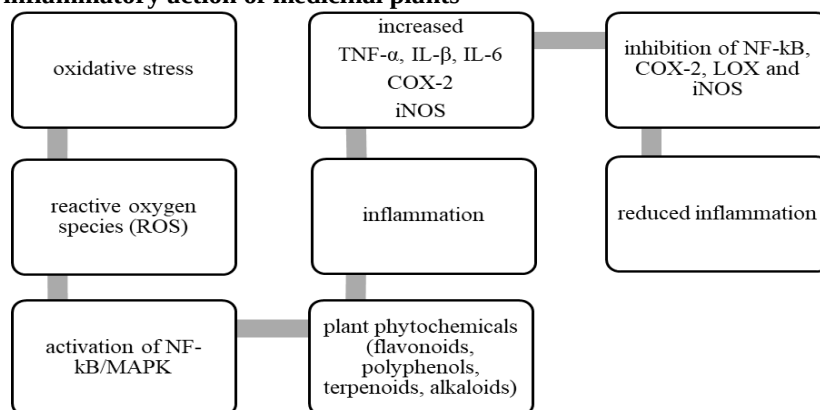
- Tumor necrosis factor-alpha (TNF- α)
- Interleukin-1 β (IL-1 β)
- Interleukin-6 (IL-6)
- Prostaglandins
- Leukotrienes
- Reactive oxygen species (ROS)

These mediators activate intracellular signaling pathways such as:

- Nuclear factor-kappa B (NF-Kb)
- Mitogen-activated protein kinase (MAPK)
- Cyclooxygenase (COX) pathway
- Lipoxygenase (LOX) pathway

Persistent activation of these pathways contributes to chronic inflammation and tissue damage. Therefore, inhibition of inflammatory mediators and signaling pathways is considered an important therapeutic strategy.

Mechanism of anti-inflammatory action of medicinal plants



3. mechanisms of anti-inflammatory action of medicinal plants

Medicinal plants exert anti-inflammatory effects through multiple mechanisms:

3.1 Inhibition of pro-inflammatory cytokines

Many phytochemicals suppress TNF- α , IL-1 β , IL-6, and IL-8 production, thereby reducing inflammatory responses.

3.2 suppression of NF- κ B signaling

NF- κ B regulates numerous inflammatory genes. Several plant compounds inhibit NF- κ B activation and nuclear translocation.

3.3 reduction of nitric oxide production

Over production of NO by inducible nitric oxide synthase (iNOS) contributes to inflammation. Plant extracts frequently suppress NO generation.

3.4 COX and LOX inhibition

inhibition of cyclooxygenase and lipoxygenase enzymes decreases production of prostaglandins and leukotrienes.

3.5 Membrane stabilization

Plant extracts protect lysosomal and erythrocyte membranes, preventing release of inflammatory mediators.

3.6 Antioxidant activity

Many phytochemicals neutralize ROS and reduce oxidative stress, thereby interrupting inflammation-associated tissue damage.

Table 1: Molecular targets affected by plant-derived anti-inflammatory agents.

Target	Role in inflammation	Plants/compounds affecting target
NF- κ B	Cytokine transcription	Naringin, 17-o-acetylacuminolide
TNF- α	Pro-inflammatory cytokine	Ajunga iva, neoandrographolide
IL-6	Inflammatory mediator	Muraglitazar, naringin
COX-2	Prostaglandin synthesis	Ficus benghalensis, scrophularia scorodonia
LOX	Leukotriene synthesis	Enicostemma axillare, isolona dewevrei

4. Medicinal plants and bioactive compounds with in vitro anti-inflammatory activity

4.1 plant-mediated nanoparticles

Pomegranate peel nanoparticles

Pomegranate peel extract-mediated calcium sulphate nanoparticles exhibited strong inhibition of protein denaturation, comparable to diclofenac sodium. Bioactive constituents such as punicalagin, ellagic acid and gallic acid contributed significantly to anti-inflammatory effects.^[18]

Aspalathus linearis selenium nanoparticles

Green-synthesized selenium nanoparticles demonstrated potent anti-inflammatory activity through albumin denaturation inhibition and membrane stabilization assays.^[19]

4.2 medicinal plants

Centella asiatica

Centella asiatica demonstrated remarkable membrane stabilization activity with protection exceeding 94% attributed to asiaticoside, madcassoside, and flavonoids.^[20]

Enicostemma axillare

The methanolic extract exhibited significant inhibition of protein denaturation and lipoxygenase activity due to flavonoids, tannins, and phenolic compounds.^[21]

Basella alba

Leaf extracts showed notable HRBC membrane stabilization, indicating potential for reducing inflammatory tissue damage.^[22]

Rhizophora mucronate

Methanolic leaf extract effectively inhibited protein denaturation and membrane lysis while displaying anti-arthritis potential.^[23]

Calendula officinalis

Marigold flower tea formulation showed strong anti-inflammatory and antioxidant activities through anti-protease and albumin denaturation inhibition assays.^[24]

Pedalium murex

Hydro-alcohol extracts demonstrated substantial membrane stabilization and protein denaturation inhibition effects.^[25]

Camellia sinensis

Green tea exhibited greater anti-inflammatory activity than black tea due to higher catechin concentrations and antioxidant capacity.^[26]

4.3 bioactive phytochemicals

17-o-acetylacuminolide

This diterpenoid isolated from neouvaria foetida suppressed TNF- α , IL-1 β , IL-6, nitric oxide production, and NF- κ B signaling.^[27]

Neoandrographolide

A major constituent of Andrographis paniculata, neoandrographolide reduced macrophage activation and inhibited NO, TNF- α and ROS Production.^[28]

Naringin

Naringin suppressed NF- κ B activation and reduced expression of TNF- α , IL-6, IL-8, COX-2, and iNOS, making it a promising anti-inflammatory agent.^[29]

Muraglitazar

Muraglitazar effectively reduced inflammatory cytokine production and nitric oxide synthesis through PPAR-mediated pathways.^[30]

Table 2: Medicinal plants and plant-derived compounds with in vitro anti-inflammatory activity.

S.No	Plant/compound	family	Bioactive constituents	In vitro model	Key findings
1	Pomegranate peel	lythraceae	Punicalagin, ellagic acid	BSA, egg albumin denaturation	Significant inhibition of protein denaturation
2	Centella asiatica	apiaceae	Asiatocside, madecassoside	HRBC membrane stabilization	94.97% membrane stabilization
3	Enicostemma axillare	gentianaceae	Flavonoids, phenols.	Protein denaturation LOX inhibition	Significant anti-inflammatory activity

Table 3: Major phytochemicals and their anti-inflammatory mechanisms.

Phytochemical	Source plant	Molecular target	Mechanism of action
naringin	Citrus species	NF- κ B, Nrf2	Suppresses cytokines and oxidative stress
neoandrographolide	Andrographis paniculata	TNF- α , NO	Inhibits macrophage activation
Asiaticoside	Centella asiatica	Inflammatory enzymes	Membrane stabilization
kaempferol	Nerium oleander	iNOS, MAPK	Reduce NO production

Table 4: Anti-inflammatory screening assays used in reviewed studies.

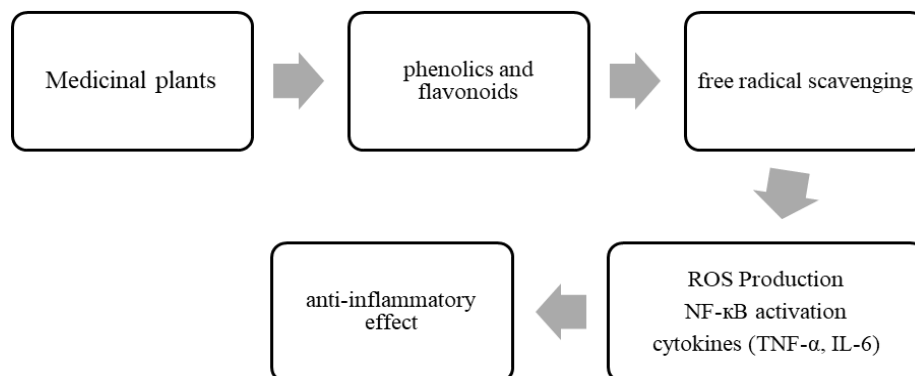
Assay	principle	Marker evaluated	significance
Protein denaturation assay	Prevention of protein denaturation	Inflammation inhibition	Widely used screening method.
HRBC membrane stabilization	Protection of RBC membrane	Lysosomal stabilization	Indicated anti-inflammatory activity.
NO inhibition	Reduction of nitric oxide	iNOS activity	Measures inflammatory mediator suppression.
LOX inhibition assay	Inhibition of lipoxygenase	Leukotriene synthesis	Reduces inflammation.
COX inhibition assay	Inhibition of cyclooxygenase	Prostaglandin synthesis	Anti-inflammatory action.

5. Relationship between antioxidant and anti-inflammatory activities

Oxidative stress and inflammation are closely interconnected biological processes. Excessive production of ROS activates inflammatory signaling pathways such as NF- κ B, resulting in increased cytokine release and tissue injury. Many medicinal plants reviewed here in process both antioxidant and anti-inflammatory activities.

Phenolic compounds, flavonoids, tannins, and terpenoids act as free radical scavengers, reducing oxidative stress and preventing activation of inflammatory cascades. Plants such as *acalypha indica*, *mimusops elengi*, *wedelia trilobata*, *camellia sinensis*, and *ajuga iva* demonstrated strong antioxidant effects alongside anti-inflammatory activity. These findings suggest that antioxidant activity contributes significantly to the anti-inflammatory potential of medicinal plants.

Relationship between antioxidant and anti-inflammatory activities



6. Future perspectives

Despite encouraging in vitro findings, several challenges remain:

- Standardization of plant extracts.
- Pharmacokinetic and toxicological evaluations.
- Validation through animal studies.
- Identification of active phytoconstituents.
- Large-scale clinical trials.

- Development of nano formulations to improve bioavailability.

Future research should focus on elucidating molecular mechanisms and translating laboratory findings into clinically useful anti-inflammatory therapies.

Table 5: Future prospects and research gaps.

Current findings	limitation	Future direction
Strong in vitro evidence	Lack of clinical studies	Human trails
Multiple bioactive compounds identified	Poor standardization	Standardized extracts
Nano particles show enhanced activity	Limited toxicity data	Safety studies
Molecular mechanisms elucidated	Limited pharmacokinetic data	ADME studies

CONCLUSION

Medicinal plants and plant-derived bioactive compounds represent a valuable source of potential anti-inflammatory agents. The reviewed studies demonstrate that numerous plant extracts, phytochemicals and nanoparticles formulations effectively inhibit inflammatory mediators, suppress cytokine production, regulate NF- κ B signaling, stabilize cellular membranes, reduce oxidative stress. Plants such as *Centella asiatica*, *Andrographis*, *paniculata*, *calendula officinalis*, *enicostemma axillare*, *mimusops elengi*, and *camellia sinensis* exhibited particularly anti-inflammatory properties. The close association between antioxidant and anti-inflammatory activities further supports the therapeutic value of phytochemicals in managing chronic inflammatory disorders. Although the current evidence is largely based on in vitro investigations, these findings provide a strong foundation for future in vivo studies and clinical trials. Continued research into medicinal plants may facilitate the development of safer, effective, and affordable anti-inflammatory therapies for a wide range of inflammatory diseases.

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