

Medicinal Plants as Potential Sources of Analgesic and Anti-Inflammatory Agents: A Review

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Abstract

Pain and inflammation are complex biological phenomenon that occurs in association with tissue damage, infection, and chronic wounds. Treatment of these includes non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroid drugs, and opioid analgesics, but these treatments can have severe side effects such as gastrointestinal side effects, kidney damage, and other cardiovascular risks, tolerance, and dependency. In recent years, there has been increasing interest in using bioactive compounds from plants as alternative strategies for pain and inflammation management, with improved efficacy and safety. The therapeutic activities of medicinal plants are mediated through a variety of phytochemicals and they interact with various inflammatory pathways such as COX, LOX, NF- κ B, MAPK and cytokine signaling pathways. In this review, the ethnopharmacological importance, phytochemical constituents and pharmacological activity of the medicinal plants that exhibit anti-inflammatory and analgesic activities have been discussed. A special focus is placed on the anti-inflammatory effects of plant secondary metabolites, including their mechanisms of action that inhibit pro-inflammatory mediators, and on their antioxidant properties. Moreover, this review covers experimental evidence for the efficacy of herbal extracts in pain and inflammation models using in vitro, in vivo, and in silico approaches. While the findings are promising, there are still a number of issues to overcome, including low bioavailability, a lack of standardization and limited clinical trials to aid clinical translation. In conclusion, medicinal plants are a potential source of novel, alternative and multi-target therapeutic agents for pain and inflammatory disorders with less side effects.

The plant-based anti-inflammatory and analgesic effects of medicinal plants can be attributed to the presence of phytochemicals such as flavonoids, alkaloids, terpenoids, and non-steroidal anti-inflammatory drugs (NSAIDs) which inhibit the NF- κ B pathway and/or COX pathway. Medicinal plants possess anti-inflammatory and analgesic properties due to the presence of phytochemicals such as flavonoids, alkaloids, terpenoids and non-steroidal anti-inflammatory drugs (NSAIDs) that inhibit the NF- κ B pathway and/or COX pathway.

Keywords: Pain, Inflammation, Medicinal plants, Phytochemicals, Flavonoids, Alkaloids, Terpenoids, NSAIDs, COX pathway, LOX pathway, NF- κ B signaling, MAPK pathway, Cytokine signaling, Antioxidant activity, Ethnopharmacology, Herbal medicine, Bioactive compounds, In vitro, In vivo, In silico

Introduction to Ethnopharmacology

The synergy between ethnopharmacology and pharmacological screening is a powerful approach for discovering new therapeutic possibilities from traditional medicinal plants (Farzeen and colleagues, 2024). The traditional uses, which are traditionally made use of in ethnobotanical surveys, have already provided a solid basis for the discovery of important pharmaceutical agents, avoiding the limitations of high throughput

screening (HTS) assays (Gu et al., 2014, p. 903). The systematic approach is a key link between traditional medicinal knowledge and contemporary drug discovery, aiding the discovery of bioactive secondary metabolites with therapeutic promise (Agnihotri et al., 2025; Kori et al., 2025). Additionally, continued research in phytochemical profiling and molecular biology enables more than just an ethnomedicinal description; it can facilitate a more rigorous experimental assessment of phytochemicals in medicinal plants (Gireesh et al., 2025). High-resolution strategies such as metabolomics and network-based drug design have shed light on the molecular interactions between complex phytochemical scaffolds and validated pharmacologic targets, thus increasingly supporting this translational continuum (Thalachandra et al., 2025; Wenhao, 2024).

Historical Medicinal Context

Historically, herbs and botanicals have been used in ancient medical texts such as the Rigveda and the Sushruta Samhita to treat complex health issues, and contemporary research confirms their efficacy in treating several ailments. (Taher et al., 2025, p. 2). The foundational practices are currently guiding research to find cost-effective and accessible solutions for the use of synthetic pharmaceuticals, especially in view of the increasing global demand for therapeutic molecules with minimal side effects (Rauf et al., 2017, p.1). The renewed interest is supported by pioneering research by early 19th-century chemists, including the extraction of morphine from *Papaver somniferum*, which led to the development of methods and technologies for isolating individual bioactive components.

Modern Therapeutic Need

The increasing prevalence of chronic diseases and the many negative effects of traditional non-steroidal anti-inflammatory drugs (NSAIDs) and opioids (Oxycodone) require new approaches to pharmacology, particularly in the context of chronic diseases (Lisa et al., 2020; p. 207; Alshehri et al., 2024; p. 1328129). Therefore, it is crucial to explore global biodiversity and the chemical diversification of natural products to identify new leads for therapeutic applications with improved safety profiles, addressing the increasing demand for new therapeutic leads (Chaachouay & Zidane, 2024). Nowadays, with the aid of emerging computational platforms and bioinformatic tools, these complex herbal mixtures are systematically identified for their mechanisms of actions, thus bridging the translational gap between ethnomedicinal reports and applications (Makunga et al., 2022, p. 1066875).

List the biological mechanisms that cause inflammation

Inflammation is a complex series of molecular signals that involve activation of the NF- κ B, MAPK, and JAK-STAT pathways, leading to the release of pro-inflammatory mediators (Shahrezaei et al., 2025). Phytochemicals like flavonoids, terpenoids and alkaloids break into these cascades by affecting the enzymatic activities and by inhibiting the expression of cytokines (Patil et al., 2019, p. 4393). The mechanisms are mainly related to inhibition of the enzymes cyclooxygenase and lipoxygenase which interrupt the metabolic pathway of arachidonic acid, responsible for the maintenance of inflammatory responses (Moualek et al., 2026; Pal et al., 2025). Moreover, the antioxidant activity of these enzymes against specific phenolic compounds can be used as a therapeutic approach to reduce tissue damage and relieve pain in chronic inflammatory diseases (Dilshad et al., 2023, p. 1273192).

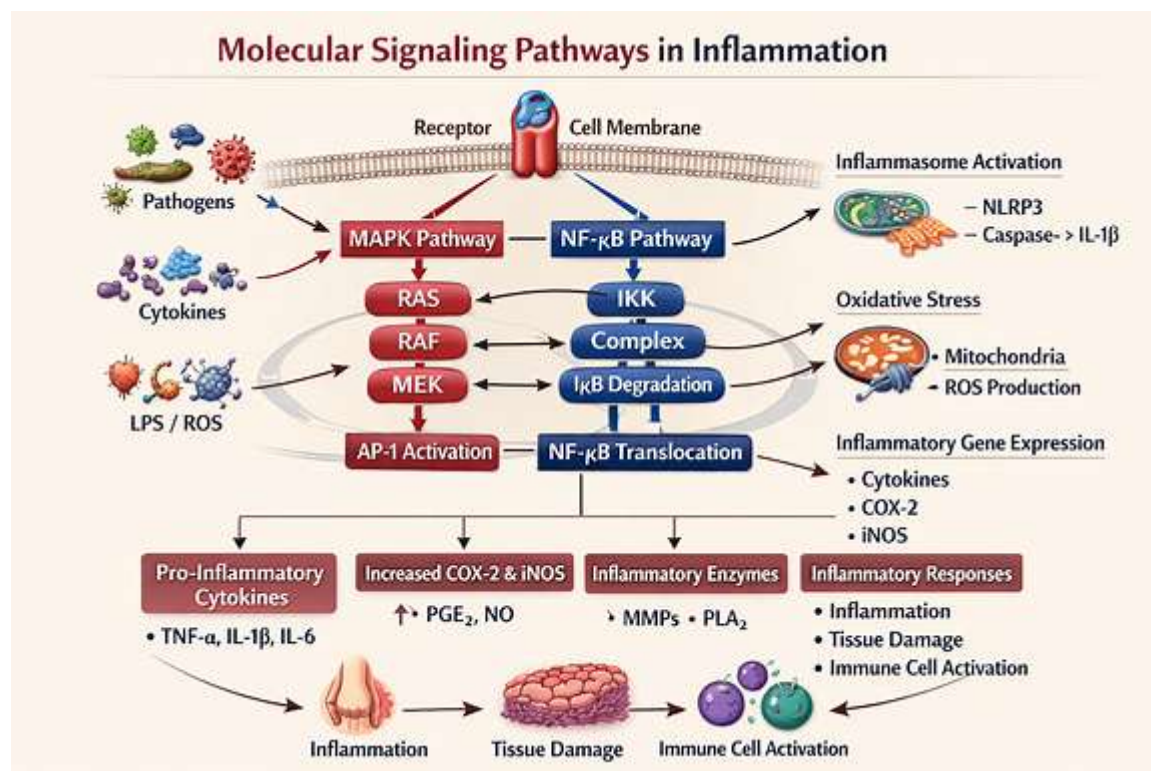


Figure 1: Molecular Signaling Pathways and Biochemical Mechanisms Involved in Inflammation

This figure illustrates key molecular signaling pathways involved in inflammation, including NF-κB, MAPK, JAK-STAT, and arachidonic acid pathways (COX and LOX). These pathways regulate the production of pro-inflammatory mediators, including cytokines, prostaglandins, and nitric oxide, thereby leading to tissue inflammation and pain.

Prostaglandin Synthesis Pathways

Cyclooxygenase enzymes play a major role in the synthesis of prostaglandins which are the mediators of pain and inflammatory signaling, the process of which is largely controlled by the catalytic activity of cyclooxygenase enzymes (Attiq et al., 2018, p. 976). There are two main variants of these enzymes, namely COX-1 and COX-2, of which the latter is a key enzyme for inflammatory conditions as it plays a crucial role in the formation of mediators during inflammation (Dixit et al., 2025). Selectively inhibiting the inducible isoform, COX-2, is the main therapeutic target to reduce gastrointestinal toxicity of the non-selective NSAIDs (Sasi, 2025, p. 1657) in order to maintain physiological homeostasis and maintain gastric mucosal integrity.

Cytokine Signaling Regulation

The NF-κB signaling pathway is the mechanism that upregulates pro-inflammatory cytokines like tumor necrosis factor α (TNF-α) and interleukin 1 (IL-1), which natural products modulate (Ferrer et al., 2018, p. 3234). In particular, bioactive components can inhibit phosphorylation of the mitogen-activated protein (MAP) kinases, which in turn helps to block the downstream transcription and secretion of cytokines (Hirsa et al., 2025, p. 102; Sadgrove & Jones, 2019, p. 2487). Also, these phytoconstituents have immunomodulatory properties, by inducing anti-inflammatory cytokines that actively inhibit the pro-inflammatory signaling pathway, such as IL-10 (Viljoen et al., 2012, p. 2104). These phytochemicals can also play a role as immunomodulatory molecules by altering the generation of ROS and nitric oxide (NO) from inflammatory cells (E et al., 2007 p. 2876).

Phytochemical Constituents Overview

This section classifies the major groups of plant derived compounds (such as polyphenols, terpenoids and alkaloids) which are the backbone of the inflammatory pathway modifiers. (Chen, 2011) Polyphenolic compounds, in particular, exhibit strong radical-scavenging activity and possess COX and LOX enzyme inhibitory activity, thereby reducing oxidative stress that may aggravate tissue degradation (Bhowmik et al. al 2023, p. 2). Furthermore, alkaloids and terpenoids are responsible for these therapeutic effects by interacting with intracellular molecules, including signaling molecules and transcription factors such as nuclear factor erythroid 2-related factor 2 (Nrf2), which regulates the cellular response to oxidative injury (Mahnashi et al., 2024, p. 1366696). Notably, the dual inhibitory activity against cyclooxygenase and lipoxygenase enzymes overcomes the limitations of conventional therapies, which cannot inhibit both arms of the arachidonic acid cascade (Mukhopadhyay et al., 2023; Rudrapal et al., 2023, p. 8658).

Alkaloids and Flavonoids

Alkaloids are capable of inducing various therapeutic effects via different mechanisms such as inhibition of the inducible nitric oxide synthase and immune cell infiltration in tissues of the joints and gastrointestinal tract (Kaushik, 2025). Similarly, flavonoids are strong antioxidants that also modulate transcription factors to reduce the synthesis of pro-inflammatory cytokines and restore homeostatic balance in damaged tissues (Goyal, 2026; Sandrah, 2025). For example, tetrandine has been reported to be clinically effective against both the COX and lipoxygenase pathways and is thus a good inhibitor of complex rheumatic diseases (Beg et al., 2011, p. 122). Apart from these basic components, saponins are known to be important modulators that specifically target fibroblast-like synoviocytes to stop joint deterioration and erosion of cartilage (Santiago et al., 2021, p. 2). This dual action of multiple molecular pathways by these secondary metabolites (glycosides and tannins) offers a multifaceted approach to managing systemic inflammation (Tushar et al., 2026; Yuandani et al., 2024).

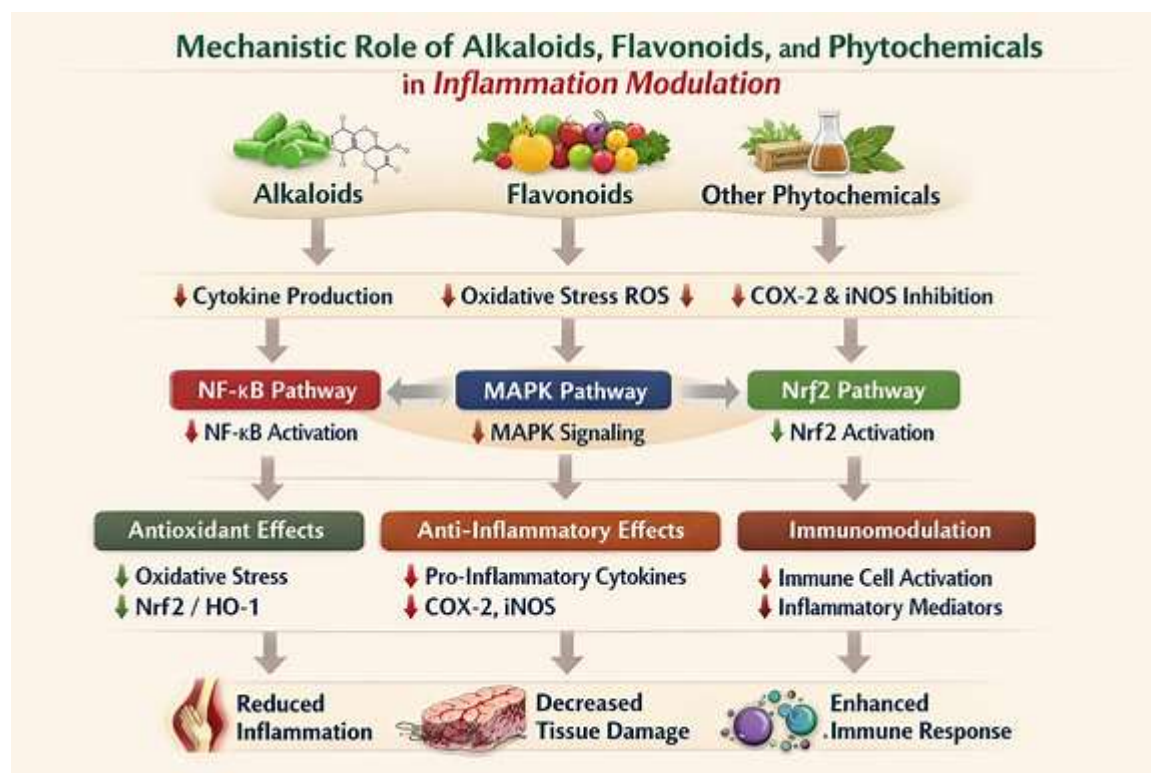


Figure 2: Mechanistic Role of Alkaloids, Flavonoids, and Other Phytochemicals in Modulating Inflammatory Pathways

This figure illustrates the roles of major phytochemicals, including alkaloids, flavonoids, saponins, glycosides, and tannins, in regulating inflammation. These compounds exert anti-inflammatory effects by inhibiting enzymes such as COX and LOX, suppressing cytokine production, reducing oxidative stress, and modulating immune cell activity, thereby helping control pain and inflammation.

Terpenoids and Phenolics

The anti-inflammatory properties of terpenoids, including sesquiterpenes and triterpenoids, were found to be effective in regulating signaling in immune cells and suppressing the expression of pro-inflammatory genes, as reported by Bhatia et al. (2025) and Khairy et al. (2023, p. 9540). These compounds block the NF- κ B nuclear translocation and inhibit the downstream expression of adhesion molecules which help to limit the recruitment of leukocytes to an injured site (Shitole, 2025). These are complemented by the activity of the phenolic compounds, which act as scavengers of free radicals, thus minimizing the propagation of chronic inflammatory damage caused by excess free radicals (Kataki, 2025; Shitole, 2025). In particular, their several phenolic rings have hydrogen-donating or electron-donating properties that directly reduce oxidative stress-induced gene expression (Chukwuma et al., 2024, p. 8).

Clinical Efficacy Evidence

Clinical observations increasingly favor the use of these plant extracts for therapeutic purposes, suggesting that they have therapeutic efficacy comparable to conventional pharmaceuticals with an improved safety profile (Wang et al., 2024, p. 9). The ability to target multiple signaling pathways, including the downregulation of pro-inflammatory cytokines and the inhibition of synovial hyperplasia, makes these natural alternatives promising for treating chronic diseases such as RA (Bala & Gupta, 2026; Kaur et al., 2024, p. 1706). These interventions have been shown to have a beneficial effect on proliferation and migration of fibroblast-like synoviocytes and block osteoclast differentiation (Liu et al., 2022), which helps to reduce joint damage and loss of function (Palanikumar et al., 2025).

Analgesic Properties Evaluation

Phytochemical modulation of pain: This involves examining the effects of phytochemicals on peripheral and central nociceptive pathways and their ability to increase pain thresholds across different models of inflammatory hyperalgesia (Makkar et al., 2020). These compounds often act on transient receptor potential channels and opioid receptors, thereby efficiently dampening primary afferent neuronal sensitization during the inflammatory process. Additionally, new preclinical evidence suggests that these plant extracts can modulate ion channel expression, potentially dampening the transmission of nociceptive signals and easing the chronic pain associated with joint degeneration. (Kciuk et al., 2024; Patel2, 2026)

Table 1: Comparative Review of Phytochemical Analgesic Mechanisms in Pain Modulation

Study / Author	Plant / Phytochemicals	Model Used	Mechanism of Action	Key Findings
Makkar et al., 2020	Various medicinal plant extracts (flavonoids, alkaloids)	Inflammatory hyperalgesia models	Modulation of peripheral and central nociceptive pathways	Increased pain threshold via inhibition of nociceptor activation
Kciuk et al., 2024	Plant-derived bioactive compounds	Neuropathic and inflammatory pain models	Regulation of ion channels and TRP receptors	Reduced transmission of pain signals and neuronal sensitization

Study / Author	Plant / Phytochemicals	Model Used	Mechanism of Action	Key Findings
Patel2, 2026	Herbal medicinal plant extracts	In vivo analgesic models	Interaction with opioid receptors and TRP channels	Significant reduction in chronic pain and improved analgesic response
Current review (conceptual synthesis)	Flavonoids, alkaloids, terpenoids	Peripheral & central pain pathways	COX/LOX inhibition, ion channel modulation, opioid pathway interaction	Multi-target analgesic effects with reduced hyperalgesia

Anti-Inflammatory Activity Assessments

Botanical extracts are evaluated using standardized assays to quantify inhibition of pro-inflammatory mediators, providing empirical evidence of their effects on systemic inflammatory responses (Recio et al., 2012). For instance, in vitro models have been employed to assess the ability of these compounds to downregulate pro-inflammatory immunochemokines and to induce apoptosis in pathological cell lines via mitochondrial signaling pathways, with particular interest in the latter (Long et al., 2023, p. 1024121). Moreover, many validations frequently involve in vivo protocols to support ethnobotanical claims, demonstrating that these herbal remedies can effectively treat extra-articular manifestations and inhibit disease progression. The studies use a comprehensive multidimensional approach that includes in silico molecular docking to identify therapeutic targets, followed by in vivo studies with long-term functional recovery and safety profile monitoring (Gandhi et al., 2022; Samy et al., 2024).

The Safety And/Or Toxicity Profiles of The Products are Provided

The study on the safety of the above-mentioned botanical agents highlights the need to establish dosage limits and assess dosage-drug interactions to reduce systemic toxicity (Choudhary et al., 2015, p. 148). To avoid adverse effects while retaining therapeutic efficacy, a rigorous pharmacokinetic evaluation and well-structured animal study are necessary to determine the dosing regimen(s) (Shi et al., 2020, p. 561972). While this potential exists, many phytopharmaceuticals have faced hurdles in the transition from discovery to clinical use because active ingredients tend to have poor bioavailability, and advanced delivery systems are often needed to achieve clinically relevant plasma concentrations (Mobasheri, 2012, p. 604). To overcome these drawbacks, formulation scientists are developing innovative strategies to improve pharmacokinetic stability and potency, such as nano-based delivery systems and standardized botanical extracts (Yadav et al., 2026).

Future Research Directions

Future investigations should focus on the development of a clinical prioritisation of botanicals based on a standardized clinical hierarchy where rapid-onset analgesic activity is related to objective measures of protection of structural cartilage (Gil-Kulik et al., 2026). In addition, the lack of human clinical studies to confirm these agents as pharmacological alternatives for treating autoimmune diseases is a key problem that needs to be addressed, as it is essential to bridge the current gap and validate them as potential treatments for the human population (Melinte et al., 2021, p. 64; PARCHAMI et al., 2023, p. 41). Furthermore, the incorporation of novel methods such as systems pharmacology, chinmedomics and biolabelled research patterns will be crucial to gain a deeper understanding of the mechanisms of action and to understand the chemical basis of these herbal therapies (Li & Zhang, 2020, p. 89).

The school holds a vision of establishing a standard and ensuring quality control

For this reason, it is crucial to establish analytical requirements for raw material procurement and manufacturing processes to meet regulatory requirements and ensure consistent therapeutic efficacy of phytomedicinal products (Lei et al., 2025, p. 1662141; Tyagi et al., 2026). Furthermore, intense research of possible contamination from pesticide and metal residues is crucial to ensure the safety of consumers and compliance with regulations (Zhang et al., 2022, p. 118). Establishing partnerships between regulatory agencies and botanical facilities is essential for implementing a comprehensive quality assurance process that accounts for environmental variability and cultivation methods (Madan et al., 2022, p. 1032). Moreover, the use of advanced metabolomic and bioinformatic analyses can help precisely identify bioactive components, ensuring uniformity of plant-based drugs and optimizing their therapeutic standardization (Vieira et al., 2024, p. 446).

Translational Clinical Applications

Further studies should bridge the gap between preclinical and clinical research, moving from case reports to the demonstration of therapeutic effectiveness, and should be conducted using a randomized clinical trial design (Mobasheri, 2013, p. 371; Noviana et al., 2022, p. 853038). In particular, high-power trials across multiple centers with good patient selection criteria should be conducted to validate active phytochemicals as standalone anti-arthritic agents or as effective complementary agents in combination therapy (Bhattacharya et al., 2020, p. 5; Toumi & Mazor, 2019, p. 81). Further, systematic studies are urgently needed to understand the exact nature of bio-effects, dose–effect relationship and safety profiles of these compounds in order to maximize their clinical utility and pave the way towards the development of standardized 'green pharmaceuticals' (Aloke et al., 2022; Fang et al., 2024, p. 46). Based on this, further clinical research is needed to specifically examine the immunomodulatory effects of these herbal compounds using serological markers such as rheumatoid factor or anti-cyclic citrullinated peptide antibody to obtain measurable evidence of their immunomodulatory effects (Wang et al., 2022, p. 978582).

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