

Analgesic and Anti-Inflammatory Potential of *Nardostachys jatamansi* and *Pongamia Pinnata*: Phytochemical and Pharmacological Perspectives

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Abstract

The pain and inflammation are complex biological processes that are linked to many acute and chronic disorders. While effective, these conventional treatments also have side effects like gastrointestinal irritation, renal toxicity, and dependence, creating a need for safer alternative treatments. The natural diversity of phytochemicals and multi-target activity of medicinal plants has made them a hotspot for future research in the development of new anti-inflammatory and analgesic compounds. In this review, two important medicinal plants, *Nardostachys jatamansi* and *Pongamia pinnata*, were discussed, along with their phytochemical composition and the pharmacological mechanisms involved in pain and inflammation management.

Nardostachys jatamansi is abundant in sesquiterpenes, lignans, and phenolic compounds, which are known for their neuroprotective, anti-inflammatory, and antioxidant effects through regulation of cytokines such as TNF- α and IL-6, as well as the NF- κ B signaling pathway. *Pongamia pinnata* contains bioactive furanoflavonoids, chalcones and phenolics like karanjin and pongamol with potent COX and LOX inhibitory activity, thereby lowering the inflammatory responses mediated by prostaglandins. Experimental and in silico studies also highlight their antinociceptive actions, mediated both centrally and peripherally, including interactions with opioid receptors, inhibition of nitric oxide, and modulation of ion channels.

Multiple phytoconstituents act synergistically in both plants, yielding a wide range of therapeutic activities that make them promising candidates for the development of plant-based formulations of analgesics and anti-inflammatory drugs. This review also highlights recent pharmacological insights, mechanisms of action, and future perspectives such as clinical validation and nanoformulation approaches to improve the bioavailability and therapeutic efficacy.

Keywords: *Nardostachys jatamansi*, *Pongamia pinnata*, analgesic activity, anti-inflammatory, phytochemicals, COX inhibition, NF- κ B, herbal medicine.

Introduction

Traditional use of these plants worldwide has sparked new research into their potential as natural sources for chronic pain and systemically inflammatory diseases, including *Nardostachys jatamansi* as a source of natural anti-inflammatory steroids and *Pongamia pinnata* as a source of natural analgesics. The antinociceptive and anti-inflammatory activity of *Pongamia pinnata* is mediated through the modulation of several inflammatory pathways like COX-2 and NF κ B, which are highly appreciable and interesting when compared to *Nardostachys jatamansi* with its potent neuroprotective and sedative effects due to various sesquiterpenes and essential oils (Dudhatra et al., 2026; Srinivasan et al., 2003; Chakraborty et al., 2026). In mice, both hydro-ethanolic and chloroform extracts of *P. pinnata* seeds have been shown to effectively reduce acetic acid-

induced writhing and carrageenan-induced paw edema (Rahman et al., 2025). On the other hand, the rhizomes of *N. jatamansi* act synergistically due to the presence of lignans and phenolic compounds, which have been reported to modulate neurotransmitter signaling and inhibit cytokine-mediated inflammatory responses (S & Antony, 2026).

Herbal and Traditional Remedies

A perennial herb, *Nardostachys jatamansi* is native to the Himalayas, and has long been used in Ayurvedic and Tibetan medicine for its calming effects on the nervous system and anti-inflammatory properties (Chakraborty et al., 2026). The pharmacological profile is attributed to the complex chemical matrix that includes sesquiterpenes, coumarins and flavonoids that together help in the neuroprotective and anti-inflammatory actions (Kumari & Arora, 2026; S & Antony, 2026). *Pongamia pinnata* stem bark is also known to exhibit high safety in both acute and chronic anti-inflammatory activity models, with significant anti-inflammatory and analgesic activity even at high dose levels, without gastric lesions or systemic toxicity (Sagar et al., 2010). Additionally, the use of these botanical agents in polyherbal formulations has been increasing, providing a comprehensive approach to pain management, as the secondary metabolites of these plants exhibit various synergistic interactions (Ghadigaonkar et al., 2024). Specifically, it has been observed that the efficacy of *P. pinnata* against bradykinin- and PGE₁-induced inflammation suggests that it could be beneficial in modulating the eicosanoid pathways involved (Singh & Pandey, 1996) while the phenolics present in *N. jatamansi* confer additional antioxidant defence (Kumari & Arora, 2026).

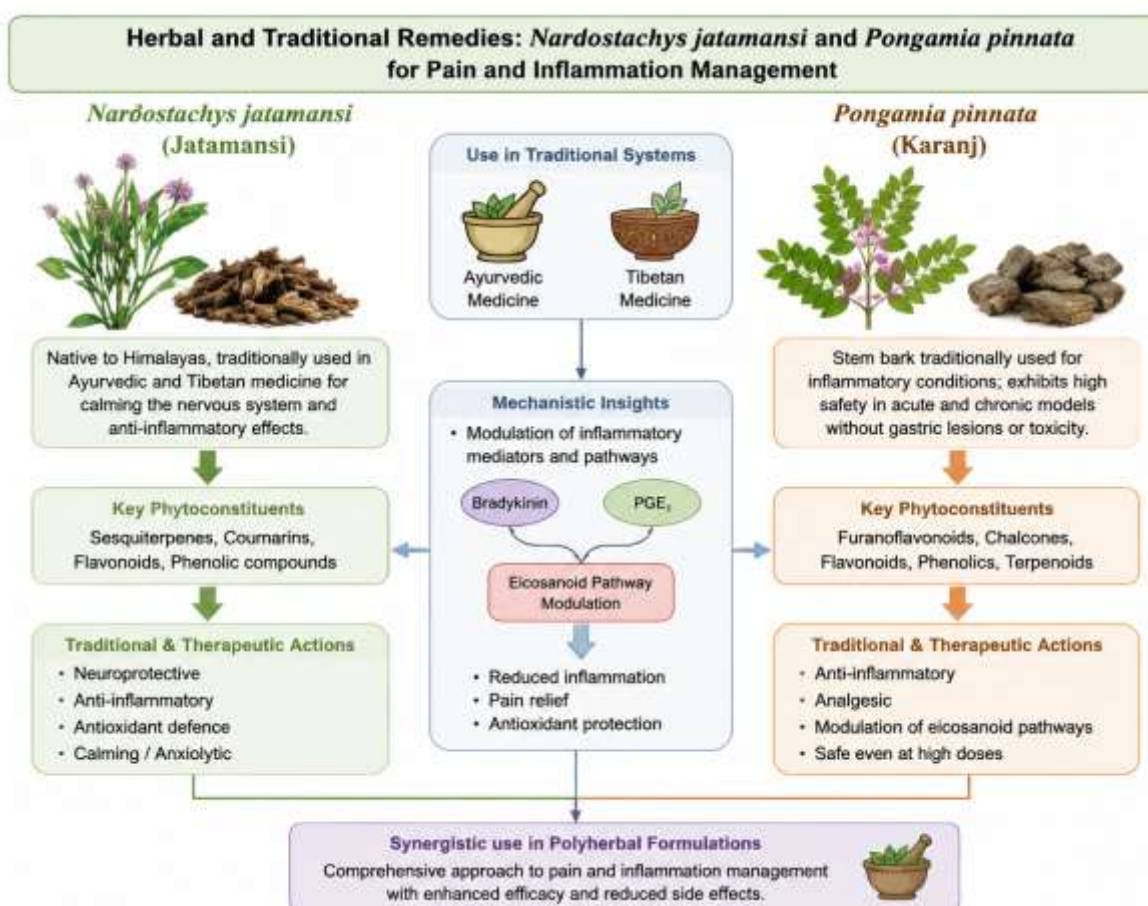


Figure 1: Herbal and Traditional Therapeutic Profile of *Nardostachys jatamansi* and *Pongamia pinnata* in Pain and Inflammation Management

Nardostachys jatamansi and *Pongamia pinnata* are medicinal plants traditionally used to treat pain and inflammation. The bioactive constituents, such as sesquiterpenes, coumarins, and flavonoids, found in *N. jatamansi* support its traditional uses in Ayurvedic and Tibetan medicines for calming the nervous system and anti-inflammatory effects. *P. pinnata* stem bark is effective and safe for anti-inflammatory and analgesic purposes, even at high doses, without causing toxicity. Both plants are increasingly used in polyherbal

formulations, where their secondary metabolites play a synergistic role. In particular, the pathways involving bradykinin and PGE1 (eicosanoid pathways) are regulated by *P. pinnata*, and *N. jatamansi* provides additional antioxidant protection.

Nardostachys jatamansi characteristics

The rhizomes and roots are rich in a variety of chemical constituents, such as the sedative sesquiterpene valeranone and compounds including spirojatamol, nardostachysin, and jatamols A and B (Rao et al., 2012, p. 26). Furthermore, recent phytochemical studies have resulted in the identification of new sesquiterpenoids, including kanshone L, M and N that have been shown to have potent anti-neuroinflammatory properties in inhibiting nitric oxide production in microglial cells (Yoon et al., 2018). Moreover, its main constituents, including valeranone and nardosinone, are known to be potent inhibitors of inflammatory cytokines such as IL-1 β , IL-6, and tumor necrosis factor alpha, which can deactivate the p38 mitogen-activated protein kinases (Ovais et al., 2018: p. 288). Along with these molecular effects, *N. jatamansi* has also been shown to be a multi-use herb due to its complex secondary metabolites which balance out the emotional and neurological systems and also help in reducing systemic oxidative stress (Rode, 2026a, 2026b).

Pongamia pinnata characteristics

This leguminous tree has a rich source of antioxidants and neuroprotective agents like furanoflavonoids and chalcones such as karanjin and pongamol, which are seen as significant therapeutic properties (Devidas et al., 2023, p. 1260166; Suganitha et al., 2024, p. 877). These bioactive components play a crucial role in regulating the cyclooxygenase-2 (COX-2) pathway, which is essential for prostaglandin production associated with nociceptive signaling (Takeda & Sashide, 2025). Moreover, evidence from the experimental studies indicated that the furanoflavonoids have multimodal analgesic activity by reducing secretion of peripheral inflammatory mediators (Sharma & Sonia, 2024, p.723). Other than these main functions, the polyphenolic composition of *P. pinnata* containing flavonoids and volatile oils highlights its traditional applications in the management of various pathologies, such as rheumatism, inflammatory skin infections (Jain, 2024). These various phytochemicals also help suppress lipid peroxidation, thereby protecting the cell membrane from oxidation in an inflammatory environment (Kumari et al., 2025).

Phytochemical Composition Analysis

Mainly, *Nardostachys jatamansi* has an abundance of sesquiterpenes such as valeranone and nardosinone, complex lignans, and fatty-acid glycosides which have neurotrophic factor expression modulating activities (Jadge, 2025). Furthermore, certain sesquiterpenoids from the rhizomes have been found to inhibit the production of pro-inflammatory cytokines like TNF- α and IL-12, and pro-inflammatory mediators such as nitric oxide and PGE2 in lipopolysaccharide-stimulated microglial cells (D. Kim et al., 2020, p. 2; K.-W. Kim et al., 2021). In contrast, *Pongamia pinnata* contains high levels of compounds such as furanoflavonoids and prenylated chalcones that regulate NF- κ B activation downstream of the activation pathway and thereby inhibit downstream inflammatory markers (Aggarwal et al., 2011, p. 1617; Shal et al., 2018, p. 554). Further, quantitative analysis using GC-MS has confirmed the presence of appreciable amounts of bioactive components in the ethanolic extract of these seeds, such as karanji, thereby underscoring the therapeutic potential of the plant.

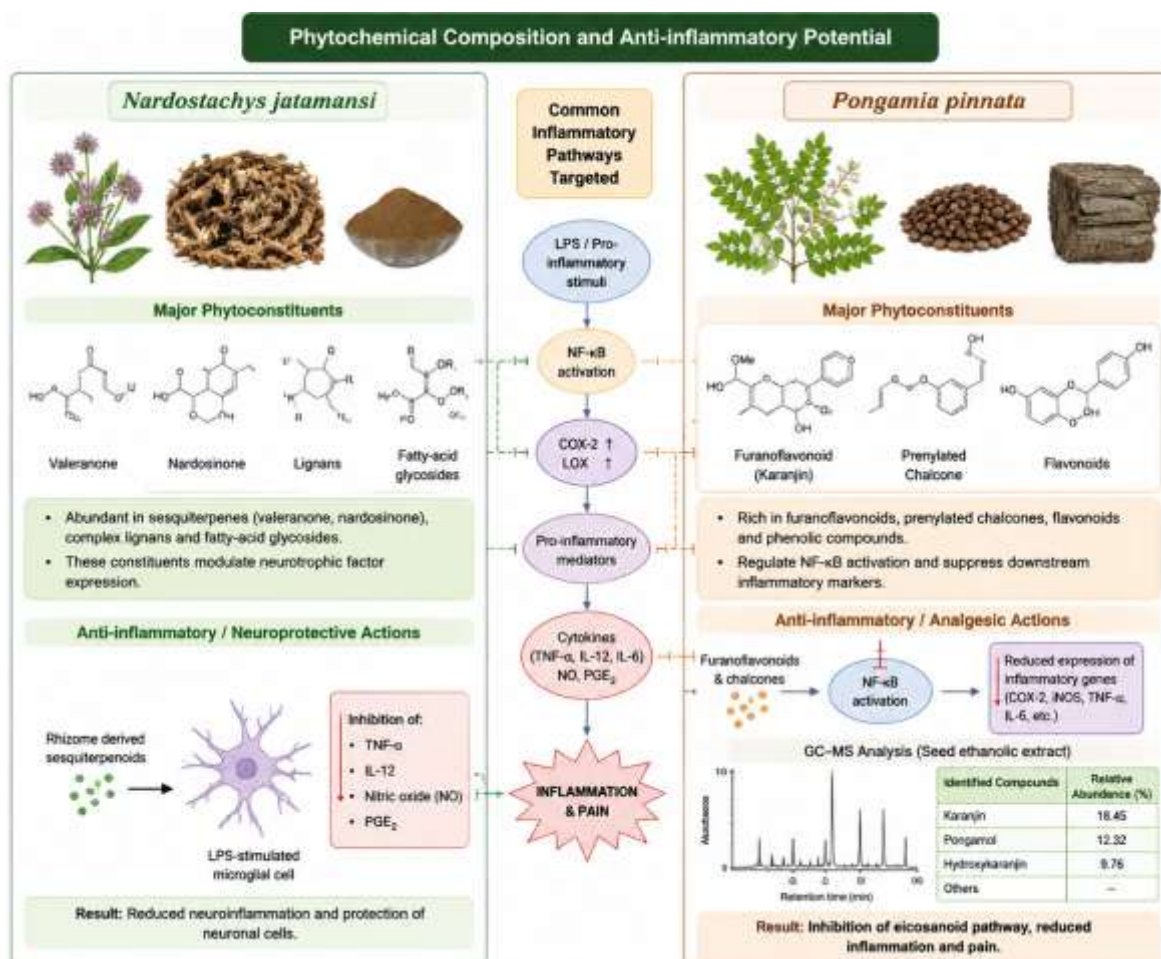


Figure 2: Phytochemical Composition and Anti-inflammatory Mechanisms of *Nardostachys jatamansi* and *Pongamia pinnata*

Nardostachys jatamansi contains important bioactive compounds such as sesquiterpenes (valeranone, nardosinone), lignans, and fatty acid glycosides, which contribute to its neuroprotective and anti-inflammatory effects by reducing pro-inflammatory mediators such as TNF- α , IL-12, nitric oxide, and PGE₂. In contrast, *Pongamia pinnata* is rich in furanoflavonoids (karanjin), chalcones, flavonoids, and phenolics, which act primarily by inhibiting the NF- κ B pathway and suppressing COX-2 and LOX enzymes, thereby reducing inflammatory responses. GC-MS analysis further confirms the presence of multiple bioactive constituents, supporting the strong pharmacological potential of both plants in pain and inflammation management.

Major bioactive compounds

P. pinnata contains significant amounts of flavonoids, alkaloids and saponins, among which obovatachalcone and glabrachalcone are notable chalcone derivatives (Fugare et al., 2021, p. 209; Thakur et al., 2021, p. 16). In addition to phenolic acids, these compounds have been found to play key roles in the plant's anti-inflammatory properties by inhibiting protein denaturation, a process essential for the plant's defense against inflammation-related diseases (Bairagi et al., 2023, p. 8; Jain et al., 2025). Additionally, studies show that the aqueous extracts of the stem bark retain this therapeutic effect in both subacute and chronic inflammation models and do so without being ulcerogenic, a well-known downside of conventional non-steroidal anti-inflammatory drugs (Nimesh et al., 2021, p. 197).

Secondary metabolite profiles

Polyphenols and flavonoids are characteristic of the metabolic fingerprint of *Nardostachys jatamansi*, which has been found to have a remarkable ability to scavenge free radicals and prevent oxidative damage to cellular biomolecules (Razack et al., 2015). Recent computational studies have also shed light on these mechanisms and the stability of complexes formed between active markers, such as spirojatamol, and critical gene targets, such as PS1, further underscoring the plant's involvement in the neuroprotective pathways (Shah et al., 2025). Meanwhile, the latest phytochemical study of the roots of *Pongamia pinnata* has revealed that a wide range of

flavanones and flavanols exhibit significant nitric oxide (NO)- production inhibitory activity in lipopolysaccharide (LPS)-stimulated microglial cells (Wen et al., 2018). The wide variety of these constituents, especially chalcone derivatives, have also been identified as precursors for the synthesis of biologically active heterocycles, thus further augmenting their therapeutic potential (Mathaiyan et al., 2018, p. 283). In addition, these secondary metabolites interact synergistically with key signaling pathways such as MAPK and PI3K/Akt, and this interaction helps achieve strong downregulation of pro-inflammatory gene expression (Chukwuma et al., 2024, p. 8).

Pharmacological Analgesic Mechanisms

The anti-nociceptive effect of these medicinal plants is mainly due to the inhibition of cyclooxygenase and 5-lipoxygenase (5-LOX) pathways thus preventing the formation of pro-nociceptive prostaglandins and leukotrienes (Rudrapal et al., 2023, p. 8658). This broad-spectrum inhibitory effect targets the inducible isoform of COX, which is induced by inflammatory stimuli, and lipoxygenase enzymes that contribute to persistent pain signaling (Ballo et al., 2023, p. 35; Nguyen et al., 2020, p. 15970). Moreover, these plants have antinociceptive effects by interacting with the mu-opioid receptor complex and inhibiting nitric oxide synthase activity, thereby disrupting the transduction of painful stimuli at both peripheral and central sites (Manjeera et al., 2025; Sultana et al., 2022, p. 911281). Moreover, the isolated compounds have been shown to be potent inhibitors of the COX-1 and COX-2 receptors during docking studies which explains their less gastrointestinal toxicity than the conventional synthetic analgesics.

Central antinociceptive activity

The activation of opioid receptors through the action of bioactive components act as a mechanism to inhibit neurotransmitter release and thus reduce pain perception through modulation of the complexes of ligands with an inhibitor protein. This action is similar to that of traditional therapeutic opioids that are extensively distributed in the central and peripheral nervous systems to modulate important effects in the areas of pain and sedation (Rauf et al., 2024, p. 52). Likewise, the inhibition of Toll-like receptor signaling pathways prevents downstream transcription factors, such as NF- κ B, from becoming activated, thereby limiting the production of pro-inflammatory cytokines in response to chronic noxious stimuli (Mahnashi et al., 2024, p. 1366696). Besides these, the modulation of voltage-gated ion channels by alkaloids and terpenoids extracted from plants also contributes to the stabilization of neuronal membranes, thereby increasing the threshold for pain. In addition to these pathways, the modulation of voltage-gated ion channels by alkaloids and terpenoids in plants also stabilizes neuronal membranes, thereby raising the threshold for pain sensation (Aly et al., 2025; Mehta et al., 2026). In addition, peripheral and central antinociceptive modulation is often cited as an important pharmacological mechanism by which these herbal extracts mediate their effects (Yousofvand & Moloodi, 2022).

Peripheral pain inhibition

The peripheral analgesic effect is mainly mediated by the inhibition of prostaglandins and leukotrienes which play an important role in the transduction of the nociceptive signals from the location of tissue injury (Aleebrahim-Dehkordy et al., 2017, p. 303). These phytoconstituents help to decrease the effects of these inflammatory mediators, making the nociceptors less sensitive to release and blocking the transmission of painful signals generated by local tissue damage (Barrera et al., 2024: 19). Furthermore, these compounds have a powerful pharmacological effect on reducing pain in periphery by reducing the secretion of peripheral pain causing molecules like interleukins and tumor necrosis factor, which lend a strong pharmacological basis in the treatment of inflammatory related nociception (Wang et al., 2018, p. 447). These botanical agents have also recently been shown to be important for regulating the activity of ion channels, such as TRPV1, to avoid the chronic sensitization that occurs in neuropathic pain states (Liu et al., 2025, p. 1656500).

Anti-inflammatory Biological Activities

Their anti-inflammatory effects involve the suppression of key molecular pathways, including the NF- κ B transcription factor and the ERK/MAPK signaling cascade, which control the production of important pro-

inflammatory cytokines, such as TNF, IL-12, and IL-23 (Verma et al., 2026). These phytochemical constituents effectively inhibit the production of interleukins such as interleukin-6 and tumor necrosis factor-alpha, thereby helping to minimize the body's inflammatory response (Emeje et al., 2024, p. 5). Additionally, the phytochemicals are structurally diverse and can offer potent protection against multiple pro-inflammatory mediators, providing a multi-targeted approach to chronic inflammatory disorders (E. et al., 2007, p. 2868).

Cytokine modulation pathways

In addition, the simultaneous reduction in TNF- α levels has been shown to reduce anxiodepressive symptoms frequently experienced with chronic nociceptive pain (Khan et al., 2021, p. 174095; Thouaye & Yalçın, 2023, p. 108557). In addition to being an inhibitor of cytokines, these secondary metabolites also help immobilize leukocytes which decreases recruitment of inflammatory cells that are responsible for the maintenance of neuropathic allodynia (Akbar, 2019 p. 108). Moreover, inhibiting ROS production would diminish the activation of intracellular inflammatory mediators that follow, thereby breaking the circle of oxidative stress-induced ROS production and subsequent activation of these mediators (Zouhri et al., 2023, p. 22891).

Enzymatic inhibition studies

One of the main areas where the expression of the inflammatory enzymes remains a point of consideration for assessing the potency of these botanicals in modulating inflammatory enzyme expression is the inhibition of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) (Manouze et al., 2017, p. 608; Qin et al., 2019, p. 360). In addition to these enzymatic targets, certain alkaloids can inhibit voltage-dependent sodium channels, thereby reducing spontaneous activation and hyperexcitability in dorsal root ganglion neurons (Santos et al., 2022, p. 1001289). Furthermore, it was found that these lipid-based prostaglandins are downregulated, and this has therapeutic benefit in chronic pain management due to arthritis, as these prostaglandins are unable to convert arachidonic acid into pro-inflammatory intermediate products (Viljoen et al., 2012, p. 2104). Furthermore, the synergistic effect of different phenolic compounds and secondary metabolites help to maintain the cellular redox state, which is one of the characteristics of chronic autoimmune diseases, and this interaction helps to prevent the damage caused by reactive oxygen species in chronic autoimmune diseases (Nazar et al., 2023; Sandrah, 2025; p. 119).

Clinical Therapeutic Perspectives

The shift from efficacy in preclinical studies to clinical trials demonstrates the increasing importance of traditional herbalism as a first or second choice treatment for chronic inflammatory conditions such as rheumatoid and osteoarthritis. Phytotherapeutic treatments have an advantageous safety profile compared to synthetic opioids, and with continued demand for extended pain management methods, these are promising treatments (Petitjean et al., 2022, p. 945450). The incorporation of these traditional treatments into clinical practice, based on scientific evidence, could be a potential alternative to traditional approaches to treating illnesses, as these medicines may have fewer side effects and be more affordable than conventional medicines (Patel2, 2026). In addition, the multifaceted therapeutic potential of *Nardostachys jatamansi* and *Pongamia pinnata* supports the overall pharmacological goal of managing joint pathology through pathways such as immune function modulation and cartilage preservation (Patel2, 2026).

Current medical applications

Today, medicinal plants like *Nardostachys jatamansi* and *Pongamia pinnata* are being effectively used in polyherbal formulations to control both acute and chronic synovitis and arthritis through different pathways of inflammation (Kaur et al, 2024: p 1706). These extracts are continually being validated not only to preserve important indigenous knowledge but also to identify bioactive compounds with chondroprotective and analgesic properties (Choudhary et al., 2015, p. 170; Deshpande et al., 2025). These plants have proven to affect various parameters, including the expression of markers like MMPs and PGE2, which play an important role in the pathophysiology of chronic arthritic conditions, and have the potential to improve the symptoms associated with such conditions, including joint tenderness, swelling, and cartilage degradation (Azevêdo et al., 2000).

Future research directions

Future studies should focus on conducting in-depth human clinical trials to translate current in vitro and animal model studies into standardized, safe therapeutic interventions (Dragoş et al., 2017). In addition, understanding the molecular mechanisms that underlie the interactions between these plants will be crucial to overcoming the current lack of evidence in humans and make these extracts a viable evidence-based alternative for the treatment of chronic joint disorders (Bhattacharya et al., 2020, p. 5; Melinte et al., 2021, p. 64). The bioavailability and targeted tissue accumulation of these phytochemicals can be further improved by using an advanced nanocarrier-based delivery system, which can overcome the pharmacokinetic limitations of conventional herbal preparations (Madan et al., 2022, p. 994). Moreover, the gastrointestinal absorption and systemic metabolism of herbs remain important issues to resolve for the successful clinical translation of herbal therapies, and thorough pharmacokinetic research is crucial to address current concerns (Mobasheri, 2012, p. 613).

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