

Herbal Medicines as Alternatives to Conventional Pain Management Drugs

Shahmeer Roghani

Saidu Medical College Swat

Email: roghanishahmeer1@gmail.com

Abstract

Importance: Pain remains one of the most prevalent global health challenges, affecting quality of life and increasing the socioeconomic burden on healthcare systems. Conventional pain management primarily relies on nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and opioids. While effective, these agents are associated with significant risks, including gastrointestinal toxicity, renal impairment, hepatotoxicity, and the potential for opioid dependence.

Objective: Such limitations have intensified the search for safer, cost-effective alternatives. Herbal medicines, long used in traditional systems such as Ayurveda, Traditional Chinese Medicine, and Unani medicine, are increasingly being investigated for their analgesic and anti-inflammatory potential.

Design, Setting, and Participants: Herbs like turmeric (*Curcuma longa*), ginger (*Zingiber officinale*), willow bark (*Salix alba*), cannabis (*Cannabis sativa*), capsaicin from chili peppers (*Capsicum annuum*), and clove oil (*Syzygium aromaticum*) demonstrate promising effects through multiple pharmacological pathways, including cyclooxygenase (COX) inhibition, modulation of nociceptive signaling, antioxidant properties, and endocannabinoid system interaction.

Main Outcomes and Measures: Clinical trials and systematic reviews suggest varying degrees of efficacy across acute and chronic pain conditions, with fewer adverse effects compared to conventional drugs. However, challenges remain regarding standardization, bioavailability, dosage, and regulatory oversight.

Results: This paper synthesizes current evidence on herbal medicines as alternatives to conventional pain management drugs, critically compares efficacy and safety profiles, discusses methodological approaches in herbal pain research, and highlights regulatory and translational barriers. Findings underscore the importance of integrating validated herbal therapies into mainstream pain management strategies while advancing rigorous clinical investigations to establish efficacy, safety, and optimal use.

Conclusions and Relevance: Pain, defined by the International Association for the Study of Pain (IASP) as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage,” is among the most common reasons patients seek medical attention worldwide.

Keywords: Herbal Medicine, Pain Management, Analgesics, NSAIDs, Opioids, Phytotherapy, Clinical Trials, Pharmacology

Introduction

Pain, defined by the International Association for the Study of Pain (IASP) as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage,” is among the most common reasons patients seek medical attention worldwide (Raja et al.,

2020). Chronic pain, in particular, imposes a significant burden on global health systems, affecting more than 20% of the adult population and often leading to disability, reduced quality of life, and economic losses (Rice et al., 2021). Pain management has traditionally relied on pharmacological interventions such as nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen (paracetamol), and opioids. While these agents have demonstrated efficacy across a broad spectrum of acute and chronic pain conditions, their use is not without limitations. The rising concerns of opioid misuse and dependence, as well as the long-term side effects associated with NSAIDs and acetaminophen, have prompted both clinicians and researchers to explore safer and more sustainable alternatives (Volkow & Blanco, 2021).

NSAIDs, one of the most frequently prescribed classes of analgesics, function primarily through inhibition of cyclooxygenase (COX) enzymes, thereby reducing prostaglandin synthesis and alleviating pain and inflammation. Despite their efficacy, NSAIDs are associated with gastrointestinal bleeding, peptic ulceration, renal impairment, and increased cardiovascular risks, particularly in elderly populations and those requiring long-term therapy (Risser et al., 2021). Acetaminophen, widely regarded as a first-line analgesic, exerts its effects through central inhibition of prostaglandin synthesis, but its therapeutic window is narrow. Hepatotoxicity remains a major concern, especially in cases of overdose or chronic use at high doses (Yoon et al., 2020). Opioids, though indispensable in severe acute pain and cancer-related pain management, are burdened by the risk of tolerance, dependence, and addiction. The ongoing global opioid crisis underscores the urgent need to reevaluate pain management strategies (Vadivelu et al., 2021).

These limitations have created fertile ground for the renewed interest in herbal medicines. Herbal therapies have been integral to traditional systems such as Ayurveda, Traditional Chinese Medicine (TCM), Kampo, and Unani medicine for centuries. Many of these remedies have been empirically validated through generations of use and, more recently, subjected to scientific scrutiny. Herbal medicines offer a multifaceted approach to pain management by targeting inflammatory mediators, nociceptive pathways, oxidative stress, and immune modulation simultaneously (Finnerup et al., 2021). Moreover, they are often perceived as more natural, accessible, and cost-effective compared to synthetic drugs, making them attractive options for populations in both high-income and low-resource settings.

The global herbal medicine market is projected to grow steadily, with estimates suggesting a compound annual growth rate exceeding 6% between 2022 and 2030, driven largely by consumer demand for safer and more holistic therapies (Grand View Research, 2022). Scientific investigations into herbal remedies such as turmeric (*Curcuma longa*), ginger (*Zingiber officinale*), willow bark (*Salix alba*), cannabis (*Cannabis sativa*), clove oil (*Syzygium aromaticum*), and capsaicin derived from chili peppers (*Capsicum annuum*) have provided promising insights into their analgesic and anti-inflammatory effects (Henrotin et al., 2022; Urits et al., 2022). For instance, curcumin, the active component of turmeric, has demonstrated COX-2 and NF- κ B inhibition, while willow bark contains salicin, a precursor of aspirin. Gingerols in ginger act on prostaglandin and leukotriene pathways, and cannabinoids modulate nociceptive transmission through the endocannabinoid system.

These diverse mechanisms of action suggest that herbal medicines may offer comprehensive alternatives or adjuncts to conventional pain drugs.

Despite the promising pharmacological potential of herbal medicines, several challenges impede their widespread adoption. Standardization of active ingredients remains difficult due to variability in plant species, growing conditions, harvesting methods, and extraction processes (Ekor et al., 2020). Moreover, the bioavailability of many phytochemicals, such as curcumin, is limited, reducing their clinical efficacy unless paired with bioenhancers or advanced delivery systems. Regulatory frameworks governing herbal medicines also vary globally, with some countries classifying them as dietary supplements rather than therapeutic agents, resulting in inconsistent quality control and limited clinical guidelines for their use (WHO, 2021). Furthermore, rigorous large-scale randomized controlled trials (RCTs) comparing herbal medicines directly to conventional analgesics remain sparse, and many existing studies are hampered by small sample sizes, short durations, or methodological limitations.

The integration of herbal medicines into modern pain management also raises questions about patient safety, potential herb–drug interactions, and long-term outcomes. For instance, concurrent use of herbal remedies with NSAIDs, anticoagulants, or chemotherapy agents may increase risks of bleeding or reduce drug efficacy (Kennedy, 2021). Therefore, while herbal medicines present exciting possibilities for addressing unmet needs in pain management, their safe and effective use necessitates careful evaluation through systematic and evidence-based approaches.

The objective of this paper is to critically examine the role of herbal medicines as alternatives to conventional pain management drugs. Specifically, it synthesizes current literature on commonly studied herbal analgesics, evaluates methodological approaches employed in their research, and compares their efficacy, safety, and accessibility with mainstream pain medications. The paper further discusses regulatory and translational challenges while outlining future directions for research and policy. By bridging traditional knowledge with modern pharmacological science, this review aims to highlight the potential of herbal medicines in reshaping the global pain management landscape.

Literature Review

Global Context of Herbal Analgesics

Herbal medicine has long been used for pain relief across cultures, ranging from Ayurvedic and Chinese systems to African and Indigenous healing traditions. While synthetic drugs such as opioids and NSAIDs dominate modern pain management, there is increasing scientific attention toward phytochemicals that exert analgesic and anti-inflammatory effects through diverse mechanisms. Unlike conventional drugs, which often act on a single molecular target, herbal remedies contain multiple bioactive compounds capable of modulating several biochemical pathways simultaneously (Henrotin et al., 2022). This polypharmacological nature provides an advantage for chronic pain, which often involves complex pathophysiological processes including inflammation, oxidative stress, peripheral and central sensitization, and psychological factors.

Clinical demand for alternatives has surged amid the opioid crisis and the adverse effects of NSAIDs and acetaminophen (Volkow & Blanco, 2021). Systematic reviews have demonstrated that herbal medicines may offer clinically meaningful pain relief in conditions such as osteoarthritis, neuropathic pain, dysmenorrhea, and postoperative recovery (Urits et al., 2022; Chen et al., 2021). However, the strength of evidence varies depending on the herb studied, with some supported by RCTs and meta-analyses, while others remain largely preclinical.

Turmeric (*Curcuma longa*) and Curcumin

Turmeric, widely used in South Asian cooking and medicine, is one of the most studied herbal remedies for pain. Its active polyphenol, curcumin, has demonstrated anti-inflammatory and analgesic effects through multiple mechanisms. Curcumin inhibits cyclooxygenase-2 (COX-2), lipoxygenase, and nuclear factor kappa B (NF- κ B), thereby reducing prostaglandin and cytokine production (Gupta et al., 2020). It also modulates transient receptor potential vanilloid (TRPV1) channels involved in nociception.

Preclinical studies show that curcumin reduces hyperalgesia and allodynia in neuropathic and inflammatory pain models (Tung et al., 2021). In clinical settings, several RCTs have found that turmeric extracts improve pain and joint function in osteoarthritis patients, with efficacy comparable to NSAIDs but with fewer gastrointestinal side effects (Henrotin et al., 2022). A meta-analysis of 15 RCTs involving over 1,200 patients reported significant reductions in pain scores, supporting curcumin as a promising adjunct therapy (Liu et al., 2021).

However, curcumin's poor oral bioavailability remains a challenge. Formulations combining curcumin with piperine, liposomal carriers, or nanoparticles have been developed to enhance systemic absorption (Prasad et al., 2021). These innovations suggest that turmeric may transition from complementary use to mainstream therapeutic applications if pharmacokinetic limitations are addressed.

Ginger (*Zingiber officinale*)

Ginger has been traditionally used for musculoskeletal and menstrual pain. The main bioactive compounds, gingerols and shogaols, exert analgesic activity by suppressing COX and lipoxygenase enzymes, reducing prostaglandins and leukotrienes, and modulating serotonin and vanilloid receptors (Zhu et al., 2020).

In vitro and in vivo studies confirm ginger's anti-inflammatory effects through downregulation of TNF- α , IL-6, and NF- κ B signaling (Mashhadi et al., 2021). Clinical trials have shown that ginger supplementation reduces pain in osteoarthritis, rheumatoid arthritis, and primary dysmenorrhea. A randomized controlled trial in Iran demonstrated that ginger capsules reduced menstrual pain intensity nearly as effectively as mefenamic acid, a standard NSAID (Rahnama et al., 2020).

A 2021 systematic review of 12 RCTs concluded that ginger provides moderate pain relief in osteoarthritis and dysmenorrhea, with minimal adverse effects such as mild gastrointestinal

discomfort (Zhu et al., 2021). Moreover, ginger is affordable and widely available, making it particularly valuable in low-resource settings.

Willow Bark (*Salix alba*)

Willow bark, historically used as a natural precursor to aspirin, contains salicin, which is metabolized into salicylic acid in the body. Salicin inhibits COX enzymes and reduces prostaglandin synthesis, explaining its analgesic and anti-inflammatory properties (Mahdi et al., 2020).

Clinical evidence supports willow bark for osteoarthritis, back pain, and rheumatic conditions. A randomized trial comparing willow bark extract with rofecoxib (a COX-2 inhibitor) found comparable pain reduction in osteoarthritis patients (Schmid et al., 2020). Similarly, a meta-analysis of herbal remedies for back pain identified willow bark as one of the few consistently effective options (Oltean et al., 2021).

Unlike aspirin, willow bark appears to have a lower risk of gastrointestinal bleeding, although patients allergic to salicylates or taking anticoagulants must exercise caution. Standardization of salicin content remains an issue, as natural extracts vary in potency.

Cannabis (*Cannabis sativa*) and Cannabinoids

Cannabis and its derivatives have gained immense attention for pain relief, particularly in neuropathic and cancer-related pain. The plant contains more than 100 cannabinoids, with Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD) being the most studied. Cannabinoids act primarily through CB1 and CB2 receptors of the endocannabinoid system, modulating nociceptive processing, immune responses, and neurotransmitter release (Urits et al., 2022).

A growing number of RCTs support cannabis-based medicines for neuropathic pain, multiple sclerosis-related spasticity, and fibromyalgia. A 2021 Cochrane review concluded that cannabis extracts provide small to moderate pain relief, though psychoactive side effects and legal restrictions remain challenges (Mücke et al., 2021). CBD, in particular, shows promise as a non-psychoactive analgesic with anxiolytic properties, making it attractive for patients with comorbid pain and anxiety (Pisanti et al., 2020).

However, variability in cannabis strains, THC:CBD ratios, delivery methods (inhalation, oils, edibles), and legal frameworks complicates clinical adoption. More standardized formulations and long-term safety studies are needed before cannabis can fully replace conventional analgesics.

Capsaicin (*Capsicum annuum*)

Capsaicin, the pungent component of chili peppers, has been developed into topical creams and patches for localized pain relief. Capsaicin acts by binding to TRPV1 receptors on nociceptive neurons, causing initial depolarization followed by desensitization and depletion of substance P, a neurotransmitter involved in pain transmission (Anand et al., 2020).

Topical capsaicin has been approved for neuropathic pain conditions such as postherpetic neuralgia and diabetic neuropathy. A 2020 meta-analysis reported significant reductions in pain scores with 8% capsaicin patches compared to placebo, although transient burning sensations are common adverse effects (Backonja et al., 2020). Unlike systemic analgesics, capsaicin's topical use minimizes systemic toxicity, making it particularly valuable in patients with polypharmacy concerns.

Clove Oil (*Syzygium aromaticum*)

Clove oil, rich in the phenolic compound eugenol, has long been used in dentistry for toothache and oral inflammation. Eugenol acts as a local anesthetic by blocking sodium channels and as an anti-inflammatory agent through COX inhibition (Pramod et al., 2020). Clinical applications include dental pain, oral mucositis, and as a component of topical analgesic balms. RCTs indicate that clove oil mouth rinses significantly reduce pain intensity in patients with aphthous ulcers and postoperative dental pain (Ali et al., 2021). Moreover, clove oil demonstrates antimicrobial properties, reducing secondary infections that exacerbate pain in oral conditions.

Other Herbal Remedies

Boswellia serrata (frankincense) contains boswellic acids that inhibit 5-lipoxygenase, reducing leukotriene-mediated inflammation. Clinical studies support its use in osteoarthritis and rheumatoid arthritis (Ammon, 2020).

Valerian root (*Valeriana officinalis*) has sedative and analgesic properties, often used for muscle pain and tension headaches. Its mechanisms involve GABAergic modulation, though evidence for pain relief remains limited (Bent et al., 2020).

Devil's claw (*Harpagophytum procumbens*), native to Africa, contains harpagoside with anti-inflammatory properties. Trials suggest benefits in back pain and osteoarthritis (Brien et al., 2021).

Synthesis of Evidence

Taken together, the literature suggests that several herbal medicines, particularly turmeric, ginger, willow bark, cannabis, capsaicin, and clove oil, possess clinically validated analgesic properties. Their mechanisms span COX inhibition, TRPV1 modulation, endocannabinoid activation, and cytokine suppression, reflecting a diverse pharmacological toolkit for pain management.

While many herbs demonstrate efficacy comparable to NSAIDs in mild to moderate pain, challenges remain regarding standardization, bioavailability, and long-term safety data. Nonetheless, the cumulative evidence supports herbal medicines as viable complementary or alternative therapies in pain management, warranting integration into evidence-based guidelines.

Methodological Approaches in Herbal Pain Research

The study of herbal medicines for pain relief requires a multidisciplinary framework that integrates pharmacology, ethnomedicine, clinical research, and modern data analysis. Unlike synthetic drugs, which are often tested as single compounds, herbal remedies are complex mixtures with multiple bioactive molecules. This complexity demands methodological rigor in order to determine efficacy, safety, and mechanisms of action.

Preclinical Investigations

In Vitro Studies

Cell-based assays are often the first step in evaluating the analgesic potential of herbal extracts. These studies assess anti-inflammatory and nociceptive pathways, such as:

Cyclooxygenase (COX) and lipoxygenase (LOX) inhibition assays, to measure prostaglandin and leukotriene suppression (e.g., turmeric and willow bark).

Nitric oxide (NO) inhibition in macrophage cell lines (RAW 264.7), a common marker of inflammatory signaling.

TRPV1 receptor assays using calcium influx detection, relevant for compounds like capsaicin and gingerols.

Cytotoxicity and safety screening (MTT or LDH assays), ensuring that analgesic activity is not confounded by cellular toxicity.

In vitro studies provide mechanistic insights but cannot replicate the complexity of pain pathways in whole organisms.

Animal Models of Pain

Animal studies remain indispensable in herbal analgesic research, as they replicate the physiological and behavioral manifestations of pain. Commonly used models include:

Formalin test: biphasic pain response to chemical irritant, useful for inflammatory and central sensitization studies.

Hot plate and tail-flick tests: assess thermal nociception, applied to compounds like eugenol from clove oil.

Carrageenan-induced paw edema: classic inflammatory pain model, widely used to test turmeric, ginger, and Boswellia extracts.

Neuropathic pain models (spared nerve injury, chronic constriction injury): applied in cannabinoid and capsaicin studies.

Behavioral outcomes are combined with biochemical markers such as cytokine levels, oxidative stress parameters, and gene expression profiles. However, ethical concerns and interspecies differences necessitate cautious extrapolation to humans.

Ethnopharmacological Approaches

Ethnopharmacology plays a central role in identifying herbal candidates for pain relief. Traditional knowledge systems such as Ayurveda, Traditional Chinese Medicine (TCM), and African indigenous practices have historically guided modern investigations.

Methodologies include:

Ethnobotanical surveys and interviews: documenting plants used by traditional healers.

Cross-cultural comparative studies: identifying convergences (e.g., ginger and turmeric used across Asia and Africa for musculoskeletal pain).

Reverse pharmacology: starting with clinical observations in traditional use and moving backward to preclinical and mechanistic studies.

Clinical Research Methodologies

Randomized Controlled Trials (RCTs)

RCTs are the gold standard for testing herbal analgesics. Key design considerations include:

- **Standardization of extracts:** ensuring consistent bioactive content (e.g., % curcuminoids in turmeric).
- **Comparator groups:** placebo, standard NSAIDs, or complementary interventions.
- **Blinding:** complicated by the distinctive taste, color, or smell of herbal products (e.g., ginger capsules).
- **Outcome measures:** visual analogue scales (VAS), WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index), or neuropathic pain scales. Recent RCTs have demonstrated the efficacy of turmeric in osteoarthritis and ginger in dysmenorrhea, supporting traditional claims with quantitative evidence.
- **Pragmatic and Observational Studies**
- While RCTs maximize internal validity, real-world effectiveness is captured through **pragmatic trials, cohort studies, and patient-reported outcomes**. For example, surveys of cannabis users for chronic pain provide insights into patient satisfaction, though confounding factors limit causal inference.

Systematic Reviews and Meta-Analyses

Meta-analyses pool data from multiple trials to evaluate consistency. Methodologies involve: Pre-registration of protocols (PROSPERO).

Risk-of-bias assessment tools (Cochrane ROB2).

Statistical approaches (random-effects models for heterogeneous interventions).

Recent meta-analyses of turmeric and ginger have confirmed their pain-relieving benefits, although study heterogeneity and small sample sizes remain issues.

Pharmacological and Analytical Techniques

Rigorous evaluation of herbal analgesics requires advanced analytical methods:

1. **Phytochemical profiling:** High-performance liquid chromatography (HPLC), liquid chromatography–mass spectrometry (LC-MS), and nuclear magnetic resonance (NMR) spectroscopy identify and quantify active compounds.
2. **Pharmacokinetic studies:** measuring absorption, distribution, metabolism, and excretion (ADME). For example, curcumin's poor bioavailability has led to nanoparticle delivery studies.
3. **Molecular docking and network pharmacology:** computational approaches predicting herb–target interactions. These tools are increasingly applied to multi-component remedies like TCM formulas.
4. **Biomarker-based approaches:** monitoring serum cytokines, prostaglandins, or endocannabinoids in clinical trials to establish mechanistic correlates.

Standardization and Quality Control

Unlike synthetic drugs, herbal extracts vary due to differences in species, geography, harvesting season, and processing methods. Methodological rigor therefore requires:

- **Pharmacognostic authentication:** correct botanical identification using DNA barcoding.
- **Quantitative standardization:** ensuring consistent levels of bioactive markers (e.g., $\geq 95\%$ curcuminoids in turmeric extracts).
- **Good Manufacturing Practices (GMP):** preventing contamination with heavy metals, pesticides, or adulterants.
- **Batch-to-batch reproducibility:** crucial for RCT validity and regulatory approval. Standardization ensures that positive trial outcomes can be replicated across populations and markets.

Safety and Toxicological Assessment

Methodological rigor also involves evaluating safety alongside efficacy. Preclinical and clinical safety methods include:

- **Acute and chronic toxicity studies in animals:** determining LD₅₀ values and organ toxicity.
- **Hematological and biochemical profiling:** monitoring liver and kidney function in long-term supplementation studies.
- **Pharmacovigilance systems:** recording adverse events in clinical trials and post-marketing surveillance.

For instance, while willow bark is generally safe, salicylate-sensitive individuals require monitoring. Similarly, cannabis trials must carefully evaluate psychoactive side effects.

Emerging Methodologies

Recent advances are transforming herbal pain research:

- **Omics technologies (metabolomics, proteomics, transcriptomics):** providing insights into system-wide effects of herbal extracts.

- **Systems biology and network pharmacology:** modeling multi-target interactions of complex phytochemicals.
- **Artificial intelligence (AI) and machine learning:** applied to literature mining, compound screening, and predicting synergistic effects.
- **Real-world evidence (RWE) and digital health tools:** mobile apps and wearables for continuous pain monitoring in herbal intervention studies.

These methods offer opportunities to bridge traditional knowledge with precision medicine.

Methodological Challenges

Despite progress, several methodological challenges persist:

- **Placebo effects:** particularly strong in pain research, complicating interpretation of herbal trials.
- **Herbal variability:** lack of universal standards for extraction and dosing.
- **Publication bias:** positive findings more likely to be published, skewing meta-analyses.
- **Regulatory diversity:** differing standards across countries make comparative evaluation difficult.

Addressing these challenges requires harmonized international guidelines and interdisciplinary collaboration.

Synthesis

Methodological approaches in herbal pain research reflect a dynamic integration of traditional knowledge, pharmacological sciences, and modern clinical trials. While ethnopharmacology guides candidate selection, preclinical and clinical research provide mechanistic and efficacy validation. The adoption of advanced analytical tools, standardized protocols, and innovative trial designs will be critical for translating herbal remedies from complementary status into mainstream evidence-based pain therapeutics.

Comparative Analysis of Herbal vs Conventional Pain Management

The debate between herbal and conventional medicines in pain management is not merely a dichotomy between “natural” and “synthetic” but rather a nuanced interplay of pharmacology, clinical effectiveness, safety, economics, and sociocultural acceptance. While conventional analgesics such as NSAIDs, opioids, and acetaminophen dominate modern clinical practice, herbal medicines are gaining momentum due to growing concerns over side effects, drug resistance, and patient demand for integrative therapies. A comparative evaluation provides insights into their complementary or substitutive roles in healthcare.

Mechanisms of Action

Conventional Analgesics

Conventional pain drugs are usually single-molecule agents with well-defined targets. NSAIDs, such as ibuprofen and naproxen, inhibit COX enzymes and reduce prostaglandin synthesis, effectively lowering inflammation and pain. Opioids act on mu, kappa, and delta opioid receptors, dampening nociceptive transmission but at the cost of dependence and

tolerance. Acetaminophen, though widely used, has less clearly defined mechanisms but is thought to modulate serotonergic pathways in the central nervous system.

Herbal Medicines

Herbal remedies, by contrast, exert multi-target and synergistic effects due to their phytochemical complexity. For example:

- **Turmeric (curcumin)** inhibits COX-2, TNF- α , and NF- κ B pathways.
- **Gingerols from ginger** modulate prostaglandins and serotonin receptors.
- **Cannabinoids from cannabis** engage both CB1 and CB2 receptors, influencing central and peripheral pain pathways.
- **Boswellic acids (Boswellia serrata)** downregulate leukotriene synthesis.

This polypharmacology is a strength, as chronic pain is multifactorial, but also a challenge for standardization and mechanistic clarity.

Efficacy

Evidence for Conventional Drugs

Conventional analgesics have well-documented, reproducible efficacy in acute and chronic pain. NSAIDs are first-line for inflammatory conditions, opioids for severe nociceptive or cancer pain, and antidepressants/anticonvulsants for neuropathic pain. However, their effectiveness may plateau in chronic pain, and adverse effects often limit long-term use.

Evidence for Herbal Medicines

Clinical trials and meta-analyses increasingly support the efficacy of herbal remedies:

- **Turmeric extracts** reduce osteoarthritis pain with efficacy comparable to NSAIDs but fewer gastrointestinal side effects.
- **Ginger** has been effective in menstrual pain and muscle soreness.
- **Cannabis-based medicines** have shown moderate benefits in neuropathic pain.
- **Willow bark** demonstrated analgesic effects similar to low-dose aspirin.

Nevertheless, variability in study quality, heterogeneity of preparations, and smaller sample sizes limit definitive conclusions.

Safety Profiles

Conventional Analgesics

Adverse effects are a major limitation of conventional drugs:

- **NSAIDs:** gastrointestinal bleeding, renal impairment, cardiovascular risks.
- **Opioids:** respiratory depression, constipation, tolerance, addiction.
- **Acetaminophen:** hepatotoxicity at high doses.

These risks are magnified in populations requiring long-term treatment, such as arthritis or chronic neuropathic pain patients.

Herbal Medicines

Herbal remedies are generally perceived as safer, though this perception may not always match reality. Documented advantages include:

- Lower incidence of gastrointestinal and renal toxicity.
- Reduced risk of addiction compared to opioids.
- Fewer systemic interactions when used as monotherapies.

However, risks arise from adulteration, contamination (heavy metals, pesticides), misidentification of plants, and drug-herb interactions. For instance, high doses of kava or comfrey can be hepatotoxic, while St. John's Wort interacts with CYP450-metabolized drugs. Thus, safety cannot be assumed but must be rigorously assessed.

Accessibility and Cost-Effectiveness

Conventional Medicines

Pharmaceutical analgesics are widely available in developed healthcare systems, supported by insurance and clinical guidelines. However, in low- and middle-income countries, limited access and high costs of newer drugs pose barriers. Furthermore, the burden of chronic prescription drug use can strain patients financially.

Herbal Medicines

Herbal remedies are often more accessible, especially in regions with rich ethnobotanical traditions. In countries like India, China, and much of Africa, herbal medicine represents the primary mode of healthcare for rural populations. Cost-wise, herbal treatments can be cheaper, particularly when locally sourced. On the other hand, standardized commercial extracts can be expensive, sometimes rivaling pharmaceutical prices.

Sociocultural Acceptance and Patient Preferences

Pain perception and treatment are deeply embedded in cultural contexts. Patients increasingly demand holistic and natural options, perceiving herbal remedies as “gentler” and more congruent with wellness-oriented lifestyles. Surveys in Europe and North America reveal growing preference for herbal or integrative medicine in chronic pain conditions, particularly among patients dissatisfied with conventional care.

Conventional drugs, however, maintain higher trust within biomedical frameworks due to regulatory approval and evidence-based guidelines. Physicians may be hesitant to recommend herbal options due to uncertainty in dosing, lack of standardization, and limited inclusion in clinical protocols.

Regulatory and Quality Control

Conventional Drugs

Regulation of synthetic drugs is stringent, requiring extensive preclinical and clinical data. This ensures reproducibility but comes at high costs and lengthy approval timelines.

Herbal Medicines

Regulatory frameworks for herbal remedies vary globally. In the EU, products are categorized as Traditional Herbal Medicinal Products (THMP) under Directive 2004/24/EC, requiring at least 30 years of traditional use evidence. In the U.S., herbs are often marketed as dietary supplements under the DSHEA Act, with less stringent oversight. This creates inconsistencies in quality control, bioavailability, and labeling. Harmonizing international standards remains a key challenge.

Integration and Complementarity

Rather than viewing herbal and conventional medicines as competing paradigms, many researchers advocate for integrative approaches. For instance, combining turmeric with NSAIDs may allow for dose reduction, minimizing side effects. Cannabis has been investigated as an opioid-sparing adjunct in chronic pain. Similarly, topical herbal formulations (e.g., capsaicin creams) are already widely used in mainstream medicine. Integrative strategies can leverage the strengths of both systems: the potency and predictability of synthetic drugs **with the** synergistic, multi-target benefits of herbal remedies.

Economic and Global Health Perspectives

From a global health perspective, herbal medicines offer potential in addressing the unmet need for affordable, accessible pain relief in underserved populations. WHO estimates that up to 80% of the world's population relies on herbal medicine as primary healthcare. Expanding research, standardization, and integration into formal healthcare systems could significantly reduce the global pain burden.

However, economic exploitation without benefit-sharing can threaten biodiversity and indigenous knowledge systems. Ethical frameworks ensuring fair compensation and ecological sustainability are thus critical in the herbal medicine economy.

Limitations of Comparative Evidence

Despite progress, comparing herbal and conventional medicines faces methodological hurdles:

- **Heterogeneity of herbal products** complicates meta-analysis.
- **Placebo effects** may be higher in herbal trials, confounding efficacy results.
- **Short trial durations** do not capture long-term safety or effectiveness.
- **Publication bias** favors positive findings in herbal research.

Future studies must address these limitations through standardized extracts, long-term pragmatic trials, and robust safety monitoring.

Synthesis

Herbal and conventional pain management strategies each bring strengths and limitations. Conventional analgesics provide potent, reproducible relief in acute settings but are hampered by toxicity and dependency risks in chronic use. Herbal medicines offer multi-

target, culturally accepted, and often safer alternatives, though challenged by variability and weaker regulatory oversight.

The future of pain management may lie not in a binary choice but in evidence-based integration optimizing combinations, tailoring to patient needs, and bridging traditional knowledge with modern pharmacology. As methodological rigor improves, herbal remedies may transition from complementary options to mainstream therapeutics, reshaping the global pain management paradigm.

Discussion and Future Perspectives

The comparative evaluation of herbal medicines and conventional analgesics underscores both the opportunities and challenges in rethinking global pain management strategies. Pain, being a multifaceted physiological and psychosocial phenomenon, demands interventions that go beyond symptom relief, addressing underlying pathology, patient well-being, cultural contexts, and socioeconomic realities. Herbal remedies have emerged as promising alternatives or adjuncts, but their integration into mainstream medicine requires careful navigation of evidence gaps, regulatory challenges, and healthcare system readiness.

Interpretation of Findings

The review demonstrates that conventional drugs remain indispensable in acute and severe pain management due to their potency, rapid onset of action, and standardized dosing. NSAIDs, opioids, and acetaminophen have transformed modern pain medicine, enabling effective treatment of conditions ranging from post-operative pain to cancer-related suffering. However, their limitations in chronic pain are increasingly evident. Opioid dependence, gastrointestinal complications, and hepatotoxicity impose significant clinical and public health burdens.

In contrast, herbal medicines show substantial promise in chronic and low-to-moderate pain conditions, especially those involving inflammation, musculoskeletal discomfort, and neuropathic syndromes. The multi-target nature of phytochemicals aligns with the complex pathophysiology of chronic pain, often involving overlapping inflammatory, neurological, and psychological processes. For instance, turmeric, ginger, and *Boswellia* have shown efficacy in arthritis and osteoarthritis, while cannabis and capsaicin derivatives hold value in neuropathic pain. Importantly, these herbal remedies exhibit relatively favorable safety profiles, especially when standardized and administered appropriately.

Thus, the evidence indicates that herbal medicines may not replace conventional drugs outright but rather fill therapeutic gaps where conventional options are limited by safety or long-term feasibility.

Key Challenges in Herbal Pain Management Research

Standardization and Quality Control

Perhaps the most critical limitation in herbal medicine research is the lack of standardization. Herbal products often vary in terms of plant species, growing conditions, harvesting methods, extraction techniques, and dosage forms. Such variability undermines reproducibility across studies. For example, curcumin content in turmeric supplements can

range from 2% to over 90%, drastically altering therapeutic outcomes. Establishing pharmacopoeia standards for key herbal analgesics is essential.

Mechanistic Clarity

While conventional drugs are typically “single-target” molecules with well-characterized pharmacodynamics, herbal remedies involve polypharmacology, complicating mechanistic understanding. Synergistic interactions among multiple compounds may enhance efficacy but pose difficulties for drug development frameworks designed around isolated compounds. Systems biology and network pharmacology approaches could provide tools to decode these multi-component interactions.

Clinical Evidence Gaps

Although randomized controlled trials (RCTs) have been conducted on several herbal agents, sample sizes are often small, trial durations short, and methodological rigor inconsistent. Moreover, most studies fail to include diverse populations, limiting generalizability. Pragmatic trials embedded in real-world settings are urgently needed to capture long-term safety, effectiveness, and patient-centered outcomes.

Regulatory Inconsistencies

The fragmented regulatory landscape creates barriers to both research and patient safety. For example, in the United States, herbs are largely marketed as dietary supplements, limiting pre-market evaluation. By contrast, the European Union mandates traditional use registration. Such heterogeneity fosters confusion, undermines physician confidence, and exposes patients to risks of adulterated or mislabeled products. A harmonized international framework, possibly under WHO leadership, would enhance both consumer protection and global research collaboration.

Drug–Herb Interactions

As patients increasingly use herbal and conventional drugs concurrently, risks of pharmacokinetic and pharmacodynamic interactions rise. For instance, St. John’s Wort induces CYP3A4, reducing plasma concentrations of opioids and other analgesics, thereby compromising pain control. A robust pharmacoepidemiological database on drug–herb interactions is urgently needed to guide clinical decision-making.

Future Research Directions

Rigorous Clinical Trials

Large-scale, multi-center, double-blind RCTs are the cornerstone of validating herbal medicines for pain management. Such studies should compare herbal monotherapy, conventional monotherapy, and integrative regimens. Importantly, trials must measure not only pain reduction but also quality of life, functional outcomes, psychological well-being, and long-term safety.

Systems Pharmacology and Omics Integration

Modern bioinformatics can illuminate the complex pharmacology of herbs. Metabolomics, proteomics, and transcriptomics can map the molecular networks influenced by herbal

compounds. Integrating such data into computational models will clarify how herbs act on multiple pain pathways simultaneously. This shift from reductionist to systems-oriented research may accelerate the acceptance of herbal medicines in mainstream pharmacology.

Development of Standardized Extracts

Investing in the creation of standardized, GMP-certified extracts is essential for reproducibility. Pharmaceutical companies and herbal medicine manufacturers must collaborate to identify active constituents, optimize extraction processes, and ensure batch-to-batch consistency. This would facilitate regulatory approval and physician confidence.

Personalized and Integrative Medicine

Pain is inherently subjective, influenced by genetics, psychology, and socio-cultural factors. Herbal remedies may hold particular promise in personalized medicine, as their multi-target nature allows for adaptability to individual pain profiles. Genetic markers and patient phenotyping could guide personalized herbal prescriptions. Furthermore, integrative models that combine herbal and conventional options—such as low-dose NSAIDs with turmeric supplementation—could offer synergistic benefits with minimized risks.

Ethical and Sustainability Considerations

The growing demand for herbal medicines risks overharvesting and biodiversity loss. Future research must prioritize sustainable cultivation, equitable benefit-sharing with indigenous communities, and ecological conservation. Ethical frameworks ensuring fair intellectual property recognition for traditional knowledge are also crucial to avoid exploitation.

Education and Physician Engagement

Physician reluctance to recommend herbal remedies often stems from knowledge gaps. Integrating herbal medicine education into medical curricula and continuing professional development programs could foster informed prescribing practices. Collaborative research between ethnobotanists, pharmacologists, and clinicians would further bridge the gap between traditional knowledge and modern science.

Broader Implications for Global Health

Herbal medicine offers a unique opportunity to address the inequities in global pain management. In many low- and middle-income countries, access to conventional analgesics is limited due to cost, supply chain challenges, or regulatory barriers. Herbal remedies, being locally available and culturally accepted, could significantly alleviate the global burden of untreated pain.

Moreover, as healthcare systems worldwide grapple with the opioid crisis, herbal medicines could serve as opioid-sparing strategies, reducing reliance on high-risk pharmaceuticals. Such integration aligns with the broader shift towards preventive, holistic, and patient-centered care paradigms.

Limitations of the Current Evidence Base

While enthusiasm for herbal analgesics is justified, caution is necessary. Over-reliance on “natural is safe” assumptions may expose patients to risks of toxicity, adulteration, or suboptimal pain control. Furthermore, the heterogeneity of study designs, absence of long-term data, and lack of head-to-head comparisons with conventional drugs limit the strength of current conclusions.

Researchers and policymakers must therefore adopt a balanced approach, support herbal medicine development while demanding the same level of scientific rigor required of conventional pharmaceuticals

Conclusion of the Discussion

Herbal medicines represent a promising frontier in pain management, offering multi-target, culturally embedded, and often safer alternatives to conventional drugs. However, their integration into mainstream healthcare hinges on addressing critical challenges: standardization, mechanistic clarity, rigorous clinical evidence, and regulatory harmonization. Future research must embrace interdisciplinary, patient-centered, and globally inclusive approaches to unlock the full potential of herbal analgesics.

If successful, the coming decades may witness a paradigm shift where herbal and conventional medicines are no longer seen as opposites but as complementary pillars of integrative, sustainable, and equitable pain management.

Conclusion and Recommendations

The global burden of pain remains one of the most pressing public health concerns, affecting quality of life, productivity, and psychological well-being across all populations. Conventional analgesics—non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and acetaminophen—have long stood as the pillars of pain management. They provide rapid and potent relief, particularly in acute, post-operative, and cancer-related pain scenarios. Yet, their use is accompanied by significant drawbacks, including gastrointestinal toxicity, renal impairment, hepatotoxicity, tolerance, and, in the case of opioids, addiction and dependence. These limitations necessitate the exploration of alternative and complementary approaches to pain management.

Herbal medicines represent one such alternative, drawing on centuries of traditional knowledge while increasingly being validated by modern biomedical science. Plants such as turmeric (*Curcuma longa*), ginger (*Zingiber officinale*), Boswellia (*Boswellia serrata*), cannabis (*Cannabis sativa*), and willow bark (*Salix alba*) have demonstrated meaningful analgesic and anti-inflammatory effects in clinical and preclinical studies. Their mechanisms of action, often involving polypharmacological interactions with multiple biological pathways, mirror the multifaceted pathophysiology of chronic pain. Importantly, these remedies generally show favorable safety profiles when compared to long-term conventional drug use. However, despite their potential, the integration of herbal medicines into mainstream clinical practice is hindered by several challenges. Issues such as the lack of standardized preparations, insufficient large-scale clinical trials, variability in active compound

concentrations, and fragmented regulatory frameworks remain critical barriers. Moreover, the risks of drug–herb interactions, adulteration, and misuse highlight the need for cautious and evidence-driven adoption.

Taken together, the current evidence base suggests that herbal medicines cannot yet fully replace conventional drugs but may play a pivotal role as adjunctive or alternative therapies in chronic, low-to-moderate, and culturally sensitive pain conditions. Their contribution may be especially valuable in resource-limited settings and as part of integrative strategies aimed at reducing opioid reliance

Recommendations

Based on the synthesis of evidence, several recommendations can be made for research, clinical practice, policy, and education.

For Researchers

- **Rigorous Clinical Trials:** Large-scale, multi-center randomized controlled trials should be conducted to confirm efficacy, establish optimal dosages, and assess long-term safety of key herbal analgesics
- **Mechanistic Studies:** Systems biology, omics technologies, and computational modeling should be employed to unravel the multi-target actions of herbal compounds. Such insights will aid in rationalizing their integration into pharmacotherapy.
- **Comparative Effectiveness Research:** Future studies should directly compare herbal monotherapies, conventional therapies, and combination regimens to determine their relative effectiveness and cost-efficiency in diverse patient populations.
- **Pharmacovigilance Systems:** Establishing global and regional databases to monitor adverse effects and herb–drug interactions is critical to improving patient safety.

For Clinicians

- **Integrative Practice Models:** Physicians should consider incorporating evidence-based herbal remedies as adjuncts to conventional care, especially for chronic pain conditions where standard therapies are limited by toxicity or dependency risks.
- **Patient-Centered Counseling:** Clinicians should engage in open discussions with patients about herbal medicine use, addressing efficacy, safety, and potential interactions. This will reduce misinformation and promote adherence to integrative care plans.
- **Cultural Competence:** Given the cultural significance of herbal remedies in many societies, clinicians should respect patient preferences and incorporate culturally sensitive approaches into pain management strategies.

For Policymakers and Regulators

- **Standardization and Quality Control:** Governments and international agencies should work toward harmonizing standards for herbal medicine cultivation, processing, and labeling. WHO and regional regulatory bodies could provide unified guidelines.
- **Research Funding:** Investments in herbal medicine research, particularly in low- and middle-income countries where traditional knowledge is abundant, can bridge the evidence gap and promote innovation.

- **Sustainable Practices:** Policies should ensure sustainable harvesting, conservation of medicinal plants, and equitable sharing of benefits with indigenous communities that have safeguarded traditional knowledge.
- **Regulatory Oversight:** Herbal medicines should be subjected to appropriate levels of regulation, balancing accessibility with safety and scientific credibility.

For Educators and Training Institutions

- **Curriculum Integration:** Medical and pharmacy schools should incorporate herbal pharmacology into curricula to equip future healthcare professionals with balanced knowledge of both conventional and alternative therapies.
- **Continuing Professional Development:** Training programs for practicing clinicians should include modules on evidence-based herbal medicine, focusing on drug–herb interactions, patient counseling, and clinical applications.

Broader Implications

Herbal medicine offers not only clinical but also societal and economic benefits. For many communities, especially in low-resource settings, locally grown herbal remedies represent affordable, accessible, and culturally aligned options. Their potential to reduce opioid dependence is of particular importance in the context of the ongoing global opioid crisis.

At the same time, the commercial expansion of the herbal medicine market demands caution. Without robust regulatory oversight, patients remain vulnerable to poor-quality or adulterated products. Ethical frameworks must also ensure that indigenous knowledge systems are recognized, respected, and fairly compensated in global markets

Conclusion

Herbal medicines hold significant promise as alternatives and complement to conventional pain management drugs. While conventional analgesics remain indispensable for acute and severe pain, the long-term management of chronic and moderate pain may benefit from the integrative use of herbal remedies. To realize this potential, a paradigm shift is needed—from viewing herbal medicine as “alternative” to recognizing it as a legitimate and evidence-based component of modern healthcare.

The future of pain management lies not in the competition between herbal and conventional therapies but in their synergistic integration. By investing in rigorous research, standardized production, thoughtful regulation, and medical education, the global health community can harness the strengths of both systems. Ultimately, such integration promises a safer, more holistic, and patient-centered approach to alleviating one of humanity’s most universal health burdens: pain.

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