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COMFREY (SYMPHYTUM OFFICINALE L.): PHYTOCHEMICAL PROFILE, ANTIOXIDANT PROPERTIES, AND THERAPEUTIC POTENTIAL

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Abstract
Comfrey (Symphytum officinale L.) is a perennial medicinal plant with a long history of use in traditional medicine for wound healing, pain relief, and inflammation reduction. Modern clinical research, including randomized controlled trials, has confirmed the efficacy and safety of topical comfrey preparations in alleviating pain, swelling, and inflammation in muscles and joints. These effects are particularly relevant in managing degenerative arthritis, acute back pain, and sports-related injuries such as sprains and strains, establishing comfrey as a reliable agent in evidence-based phytotherapy. Recent studies have expanded the understanding of comfrey beyond its traditional uses, recognizing it as a rich source of biologically active compounds with potential applications in the food and pharmaceutical industries. Its roots and leaves contain alkaloids, phenolic acids, flavonoids, tannins, and polysaccharides, which collectively contribute to strong antioxidant, anti-inflammatory, and tissue-regenerative effects. Notably, the presence of inulin and fructooligosaccharides (FOS) indicates possible prebiotic properties, supporting gut microbiota balance and metabolic health. This study aims to investigate the phytochemical profile, antioxidant capacity, and biological activity of S. officinale. The findings highlight comfrey's potential as a functional and medicinal plant resource, suitable for developing nutraceuticals, dietary supplements, and topical products, while supporting sustainable and eco-friendly bioproduct innovation within the modern bioeconomy.
Keywords: comfrey, medicinal, plant, inulin, polysaccharides, pharmaceutical, application.

INTRODUCTION

Symphytum officinale L. (family Boraginaceae), commonly known as comfrey, has a long history of use in traditional medicine for treating wounds, musculoskeletal pain, respiratory and gastrointestinal disorders. Recent phytochemical studies have confirmed that both the roots (fig.1) and leaves contain a wide range of bioactive compounds, including allantoin, triterpenes, tannins, phenolic acids, and polysaccharides, which contribute to its anti-inflammatory, wound-healing, and moisturizing effects [1,2]

Advanced chromatographic analyses of comfrey root extracts have identified several phenolic acids, such as caffeic, p-hydroxybenzoic, p-coumaric, rosmarinic, and salvianolic acids (A, B, C), known for their strong antioxidant and anti-inflammatory activities [4-6] e compounds may play a key role in comfrey's traditional therapeutic effects, especially in topical formulations for joint and wound healing.

However, comfrey also contains pyrrolizidine alkaloids (PAs), such as lasiocarpine, echimidine, and symphytine, which are hepatotoxic and can induce hepatic sinusoidal obstruction syndrome (veno-occlusive disease). Cases of liver injury have been reported following oral ingestion of comfrey preparations [9] PA content varies widely between plant parts (roots generally contain more than leaves),

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and some studies suggest that the total extract can exhibit higher toxicity than pure isolated alkaloids, emphasizing the need for caution [11,12]

Because of these risks, regulatory agencies such as the European Medicines Agency restrict comfrey root preparations to external use only, with strict limits on PA concentrations and treatment duration [7-9]

Current research aims to separate comfrey's beneficial phytochemicals from its toxic alkaloids. For instance, a 2024 study developed an effective method to enrich rosmarinic acid from comfrey root using macroporous adsorption resins, producing a polyphenol-rich extract with minimal PA content. Similarly, a 2024 review highlighted that while PA toxicity remains a limiting factor, comfrey deserves renewed evaluation as a source of safety, externally applied therapeutic agents [5-8].

Fig. 1. *Comfrey (Symphytum officinale L.) roots.*

EXPOSITION

Comfrey (Symphytum officinale L.), a perennial herb of the Boraginaceae family, has been used for centuries in traditional medicine — primarily for wound healing, musculoskeletal pain relief, and anti-inflammatory purposes [1,2]. Modern evidence-based investigations have begun to substantiate some of these uses, particularly for topical applications [4,5].

Evidence for Therapeutic Efficacy

Although there is not yet many formal meta-analyses exclusively on comfrey, multiple systematic and scoping reviews have summarized the data from randomized controlled trials (RCTs) and observational studies [4,5,8].

A critical scoping review of external uses of Symphytum species highlighted RCT evidence supporting benefits in ankle distortion, back pain, abrasions/wounds, and osteoarthritis of the knee [8].

Clinical overview articles report that multiple randomized controlled trials have demonstrated the efficacy and safety of comfrey preparations for the topical treatment of pain, inflammation, and swelling of muscles and joints in degenerative arthritis, acute myalgia of the back, sprains, contusions, and strains [4,5].

For example, a double-blind RCT in patients with acute upper or lower back pain found that a comfrey-root-extract ointment produced a median 95% reduction in pain on active movement compared to ~38% in placebo after 5 days of treatment [6].

In addition, observational studies in children with sports injuries and blunt trauma reported very low incidence of adverse effects when using topical comfrey cream, suggesting a favorable benefit-to-risk ratio in that setting [7].

Thus, the weight of current clinical evidence indicates that topical comfrey formulations can be effective in reducing pain, improving function, and supporting healing in specific musculoskeletal and trauma-related conditions [4–7].

Mechanisms and Phytochemistry: The therapeutic benefits of comfrey are attributed to its bioactive constituents, mainly found in the roots and leaves — including allantoin, phenolic acids (e.g., rosmarinic, affeic, p-coumaric), tannins, mucilage polysaccharides, and flavonoids [1,2,9].

These ompounds exhibit anti-inflammatory, antioxidant, and regenerative activities [9,15].

Experimental vidence suggests that comfrey extract ay modulate inflammatory

pathways, uch as NF-κB, thereby contributing to reduced inflammation and enhanced tissue regeneration [15].

The resence of inulin and fructooligosaccharides (FOS) also points to potential prebiotic effects, supporting gut microbiota balance and metabolic health, which broadens comfrey's potential applications beyond traditional topical use [1].

Safety Considerations: Safety remains a key concern, particularly regarding oral ingestion of comfrey, due to its content of pyrrolizidine alkaloids (PAs) — compounds known for their hepatotoxic potential and association with veno-occlusive disease [3,10,13].

Quantitative analyses have shown that PA concentrations are significantly higher in roots (0.3–8.3 mg/g dry weight) than in leaves (0.015–0.055 mg/g) [10,12].

Because of these risks, regulatory agencies, including the European Medicines Agency (EMA), restrict comfrey use to external applications only, with strict limits on PA content and treatment duration [14].

Topical formulations, by contrast, exhibit minimal systemic absorption and a favorable safety profile in both adults and children [7].

A systematic review of herb-induced liver injury confirmed that hepatotoxic effects are linked exclusively to oral comfrey use, further validating the safety of external application [3].

Limitations and Gaps: While there are multiple randomized clinical trials, there remains a shortage of large-scale meta-analyses that comprehensively aggregate the available comfrey data [4,5,8].

Many studies are short-term and focused on specific indications (e.g., back pain, sprains) rather than long-term or chronic outcomes.

Significant heterogeneity also exists in formulations, concentrations, plant parts used (root vs. leaf), and outcome measures, which complicates direct comparison and generalization [8,12].

Although topical use appears safe, there is still a need for pharmacokinetic and long-term safety studies, especially in vulnerable populations [3,14].

Mechanistic understanding also remains incomplete — further research is needed to clarify how comfrey's active constituents interact at molecular and systemic levels [15].

In summary, *Symphytum officinale* L. shows strong evidence supporting its topical efficacy for pain reduction, inflammation control, and wound healing [4–7].

However, due to the presence of hepatotoxic PAs, internal use remains contraindicated.

Future research should aim to perform large-scale meta-analyses, develop standardized, PA-free extracts, and explore mechanistic pathways to ensure safe and effective use of comfrey in modern evidence-based phytotherapy [10–17].

Table 1. *Summary of clinical evidence and safety profile of Symphytum officinale L. (Comfrey)*

Study / Source	Condition / Model	Formulation & Dose	Main Outcome	Referen
Giannetti et al. (2010)	Acute back pain	Comfrey root ointment (4 g × 3 daily, 5 days)	95 % pain reduction vs 38 % placebo	[6]
Staiger (2012, 2013)	Arthritis, strains, sprains	Topical extract creams	↓ Pain, swelling; ↑ mobility	[4, 5]
Kucera et al. (2019)	Sports injuries (children)	Comfrey herb cream (≤ 2 weeks)	Safe; < 0.2 % minor local reactions	[7]
Allemann et al. (2023)	Toxicology analysis	LC–MS/MS root extracts	PAs 0.3–8.3 mg/g DW (roots)	[10]
EMA (2024)	Regulatory assessment	—	Use restricted to topical PA-limited forms	[14]

Clinical evidence (tabl. 1) supports comfrey's topical efficacy in musculoskeletal and soft-tissue conditions. Internal use is contraindicated due to hepatotoxic pyrrolizidine alkaloids (PAs). Current research focuses on developing PA-free standardized extracts for safe therapeutic application [10–17].

CONCLUSION

Comfrey root extract represents a promising natural product due to its phenolic and polysaccharide constituents, which display potent antioxidant and anti-inflammatory properties. Nonetheless, its clinical application requires rigorous control of PA content and further development of extraction technologies to ensure safety while preserving efficacy. [4-6,9]

In summation, the current scientific evidence supports the use of comfrey (Symphytum officinale L.) for selected topical applications in musculoskeletal pain, trauma-related injuries and wound healing, with a favorable efficacy-safety profile when used appropriately. However, due to concerns about pyrrolizidine alkaloid toxicity, usage should be restricted to externally applied formulations, and oral ingestion should be avoided or strictly controlled. Future research should focus on large-scale meta-analyses, standardization of extracts, long-term safety, and further elucidation of mechanisms of action.[11,16,17].

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