Botanical Briefs: Comfrey (*Symphytum officinale*)

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Practice Points

- Comfrey is a traditional herb with great efficacy in the treatment of pain, inflammation, and swelling, and may be included as a rational phytotherapy in a physician's standard treatment protocol.
- Although comfrey shows undoubted effectiveness, this plant should be used with caution, especially when taken orally, as the toxic effects from its pyrrolizidine alkaloids are not clear.

Commonly known as comfrey, *Symphytum officinale* (family Boraginaceae) has a long traditional use as a poultice to promote wound healing and reduce joint inflammation.[1] Comfrey is an evergreen perennial plant with large hairy leaves, narrowing ends, and small yellowish to red-violet flowers (Figure). Comfrey is native to the United Kingdom but can be found throughout Europe, North America, and Asia, mainly in damp places and particularly near rivers and streams.[2]

Clinical Uses

Comfrey roots and leaves have been used in herbal medicine for more than 2000 years and are administered both internally and externally for treatment of several diseases.[3] In folk medicine, *S officinale* traditionally is applied externally (eg, cataplasm) to treat broken bones, tendon damage, inflammatory joint disorders, painful muscular distortions, hematomas, open wounds, and infected skin lesions.[2-4] Comfrey also can be ingested in the form of herbal teas and capsules to treat ulcerations and other digestive disorders (eg, diarrhea), dysmenorrhea, bronchitis, rheumatoid arthritis, and a variety of allergies.[1,2,5,6] The plant also can be decocted for use as a gargle to treat oral and pharyngeal conditions. The ethanolic comfrey root extract has been extensively used in European indigenous medicine for the treatment of various ailments.

Although the therapeutic effects of comfrey are widely recognized, oral consumption of this plant warrants particular caution, as it potentially can be toxic. Because it contains many essential nutrients (ie, proteins, antioxidants, and vitamins [particularly vitamin B_{12}]), some ethnic groups include comfrey in their daily diet,[3] added to fresh salads, fried

Leaves of the comfrey plant *(Symphytum officinale).*

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with other greens, and mixed with meat or old bread to make meatballs.[7,8] However, this consumption of comfrey is not safe.

Comfrey has been cited as a demulcent herb that can be used to treat lichen planus, a chronic immune-mediated mucocutaneous disease,[9] but there have not been any reports of the clinical efficacy of comfrey in the treatment of immune-mediated skin disorders. On the other hand, the pharmacologic effects and clinical efficacy of topical comfrey preparations are supported by several studies that evaluated its effects in the treatment of pain, inflammatory conditions, and cutaneous wounds. In these trials, *S officinale* proved efficacious as an anti-inflammatory and analgesic wound healer and promoter of granulation.[10-13]

Phytochemical analyses have isolated several compounds, including allantoin, choline, triterpenoids, saponins, rosmarinic acid (RA) derivatives, tannins, and essential oils, that may be partly responsible for the pharmacologic properties of comfrey due to their known biologic activities.[14,15] Rosmarinic acid may be responsible for the anti-inflammatory properties of comfrey, though its wound-healing action is attributed to allantoin. Other components such as saponins possess antibacterial and antiedematogenic properties, and choline causes vasodilation.[2]

Rosmarinic acid has demonstrated astringent, antioxidant, anti-inflammatory, antimutagen, antibacterial, and antiviral properties.[16] Huang et al[17] reported that RA inhibited cyclooxygenase 2 expression in macrophages in culture. Because cyclooxygenase 2 is a crucial inflammatory enzyme, its inhibition suggests anti-inflammatory activity. Rosmarinic acid also reduced the development of atopic dermatitis–like lesions in mice by suppressing the production of IFN-γ and IL-4 by activated T cells.[18] Moreover, allergic inflammatory conditions such as allergic rhinitis and allergic rhinoconjunctivitis seem to be attenuated with RA treatment by the reduction of IgE and histamine levels, cytokine expression, and cell infiltration.[19]

Allantoin, which also seems to contribute to the biologic activities of comfrey, occurs naturally in several plant species and in animal species as a uric acid catabolite.[2] According to the US Food and Drug Administration, allantoin acts as a skin conditioner and protection agent and has been used in a variety of skin care products (eg, cosmetics).[20] Beyond its emollient and soothing properties, allantoin also is a wound-healing agent. Topical preparations containing allantoin were shown to reduce neoangiogenesis in hypertrophic scars and keloids and promote clinical improvement of skin wounds.[21,22] Araújo et al[23] demonstrated that allantoin improved the wound-healing process in rats by stimulating fibroblastic proliferation and extracellular matrix synthesis, contributing to faster and better reestablishment of normal skin. The modulation of the wound-healing process seemed to be partly due to regulation of the inflammatory response.[23] This anti-inflammatory activity also was observed in 2010[24] in ovalbumin-induced lung inflammation in a murine allergic model. Allantoin reduced IgE levels and cytokine production (eg, IL-4 and IL-5) and alleviated airway inflammatory cell infiltration. Allantoin also acts as a free radical scavenger, directly protecting DNA from the damage induced by oxidative stress,[25] which is intimately related to the inflammatory process. Because reactive oxygen species are known to contribute to several skin disorders (eg, skin carcinogenesis), free radical scavengers are of great interest in dermatology.

Despite its medicinal properties, comfrey also is known to be poisonous. *Symphytum officinale* contains at least 9 pyrrolizidine alkaloids (PAs), which have been known to be toxic with ingestion since 1920.[2,26] These components are distributed throughout the entire plant, but the highest concentrations occur in the roots.[14] After comfrey is consumed, the PAs are transformed to pyrroles, which exert their toxic effects by binding and reacting with cellular macromolecules.[3] In humans, the primary manifestation of comfrey ingestion is hepatotoxicity, specifically the veno-occlusive disease caused by the PAs. The toxic effects of comfrey also can cause mutagenesis, carcinogenesis, and pulmonary hypertension; however, the influence of individual susceptibility or doses on these toxic effects is not well elucidated.[2,27] Although there is no evidence of toxicity when comfrey is topically applied, studies are needed to further evaluate the safety of this practice. Because the mutagenic potential of *S officinale* has been demonstrated, comfrey extract potentially contains carcinogens that could damage cells when in contact with the skin.

Distribution

Comfrey was once one of the most popular herbal teas in the world, but its popularity has declined with the knowledge of its dangers.[27] In some countries, the use of comfrey is controlled; for instance, its distribution has been restricted in Canada, and in Germany its use is limited to external products. In the United States, the US Food and Drug Administration has requested the removal of products containing comfrey since 2001.[28] In the United Kingdom, comfrey was included on a list of herbs under consideration for restriction to prescription only.[3] Today, it is

known that daily intake of comfrey is restricted to an equivalent of 100 μg of PAs, which can be irrelevant when the extract is prepared from the aerial parts of the plant, as a lesser concentration of PAs is found in the leaves.[14] Although the carcinogenic activity of comfrey is described by several authors, the antineoplastic effects such as inhibition of cell proliferation and modulation of atypical phenotype have been demonstrated; however, this pharmacologic effect must be further explored.[29]

Comment

Comfrey seems to be a promising strategy for treating various skin problems based on its traditional use in ethnopharmacology as well as the biologic effects of its compounds; however, preclinical and clinical trials still need to be developed to increase knowledge of the effectiveness and safety of the topical application of comfrey.

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