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Comfrey root extract – indications and patient profiles: findings from an expert round table discussion

Abstract

Treatment of pain in muscles and joints is multifold comprising pharmacological substances and complementary medical treatment modalities. The round table discussion including experts from the medical and pharmaceutical profession focused on identifying patient groups, which can particularly benefit from topical treatment with a herbal medical product with comfrey root extract. In diseases with recurrent pain such as osteoarthritis topical comfrey should be part of an overall treatment concept intending to support mobility and delaying progression of the disease to postpone joint replacement as long as possible. As comfrey root is well tolerated and has no known drug interactions, it is especially well suited for patients with concomitant diseases like elderly patients with osteoarthritis. Moreover, no loss in efficacy is observed even with regular long-term application. Patients with recurrent back pain, who fear adverse events from oral analgesics and want to combine different procedures for pain relief, are more willing to apply a cream on hard-to-reach areas like the back than patients with a single pain episode. In case of acute blunt trauma, topical comfrey root ointment provides local pain relief and may help to accelerate regeneration. Moreover, in contrast to topical diclofenac treatment, comfrey root extract is authorized for paediatric patients above the age of 3years and may be the preferable choice for parents fearing adverse events from oral analgesics.

All experts participating in the discussion agreed that topical treatment with comfrey root extract is at least equally effective as local diclofenac, but with the advantage of providing a good tolerability and combinability with other medications.

Keywords: comfrey root extract, *Symphytum officinale* L., musculoskeletal diseases, osteoarthritis, back pain, blunt injuries, polymedication

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Introduction

The interest on the efficacy and tolerability of herbal medicinal drugs has continuously increased worldwide since 1990 indicated by the growing number of scientific articles in PubMed on this subject.[1] While the importance of phytotherapy is more significant in less developed countries, the public perception of naturopathic treatment and complementary medical practices is also very positive in Europe with still growing interest.[2] The World Health Organization (WHO) has investigated why people choose complementary medicinal treatment options. The reasons are fear of adverse events from synthetic drugs, improved access to health information, shift of values especially regarding perception of health comprising the whole body, and low tolerance of paternalism of the conventional health care system as well as preference of shared decision-making.[3,4]

Comfrey root (Symphyti radix) is derived from *Symphytum officinale* L., which has been used for more than 2000years as medicinal plant.[5,6] Its pharmacological actions and indications are acknowledged by the drug monographs of the DAC (German Pharmaceutical Codex) and the BHP (British Herbal Pharmacopoeia) as well as a monograph published by the European Scientific Cooperative on Phytotherapy (ESCOP) and the European Union herbal monograph on *Symphytum officinale* L., radix published by the European Medicines Agency (EMA).[5,7,8] The main constituent determining the mode of action of comfrey root extract has not been completely elucidated to date[6]. Ingredients of potential relevance for efficacy include mucilage polysaccharides, allantoin, tannins, choline, caffeic acid, and rosmarinic acid.[5,7] Several in-vitro and in-vivo studies as well as pharmacological human studies have demonstrated especially anti-inflammatory and wound healing effects of Symphyti radix.[7]

Comfrey root extract in particular can be used for the topical treatment of pain and swelling in muscles and joints, acute myalgia in the back, strains, contusions, and distortions, as well as epicondylitis, tendovaginitis and periarthritis.[6,7] The discussion during the expert round table especially focused on indications and characteristics of patients, for whom treatment with comfrey root ointment is particularly beneficial.

Osteoarthritis

Complaints in osteoarthritis mainly focus on pain in the afflicted joints either after exercise or at rest[9]. Individual perception of pain influences the choice of treatment in osteoarthritis.[10] However complete analgesia can rarely be achieved in such a chronic condition.[11] Thus patients should be educated (advised) that the primary therapeutic goal is to achieve sufficient pain relief to allow mobilization of the joint.[12,13]

In order to realize this goal guidelines recommend a multimodal treatment approach including general measures as well as medicinal interventions e.g. topical analgesic treatment as first-line therapy.[14,15] Topical comfrey root ointment, which has proven its efficacy for treatment of gonarthritis in a double blind placebo-controlled trial (Table 1), is also part of the German S2k guideline on gonarthrosis.[14]

Oral analgesic treatment as second-line option in osteoarthritis mainly relies on non-steroidal anti-inflammatory drugs (NSAIDs).[14] However, these drugs are associated with particular adverse events and not appropriate for a long-term treatment.[11,17] The experts pointed out that in pharmacies polymedicated patients particularly ask for local applications in order to avoid intake of further tablets and interactions. These patients may be provided with an herbal product like comfrey root ointment without known interactions with other medicinal products.

Patients with osteoarthritis who are open-minded towards phytotherapy, are often characterized by the following: chronically ill with a strong psychological strain, willing to actively support treatment, a long history of medical consultations, and a high educational grade. However, comfrey root extract ointment can also benefit other patients because of its particular advantages, i.e. few adverse events, combinability with any other treatment due to a lack of interactions, and the possibility to purchase the product without prescription in case of acute exacerbations.[5,7,8] Table 2 summarizes the characteristics of patients with osteoarthritis suitable for long-term treatment with comfrey.

Table 1 Clinical trial in patients with chronic gonarthritis

Reference	Study design	Number of patients	Treatment regimen	Primary efficacy parameter	Results
Grube et al.[16]	Double-blind, placebo-controlled	Comfrey cream: 110 Placebo cream: 110	3 times daily for 3weeks	Reduction of total pain score by VAS* as compared to baseline	Comfrey: 55% Placebo: 11% p<0.001

*Visual Analogue Scale

Table 2 Patient characteristics for comfrey treatment in osteoarthritis

Patients and symptoms	a. Mild to moderate pain b. Higher education c. Diagnosed with osteoarthritis d. Established treatment plan
Expectations	a. Due to high level of suffering gradual onset of pain relief is accepted b. Awareness that their chronic disease needs permanent treatment and therefore products with high tolerability should be preferred
Therapeutic goal	a. Improved mobility without guarantee of complete pain relief b. Improved quality of life c. Avoiding or postponing operation d. Decrease of disease progress
Treatment plan	a. Exercise therapy and appropriate regular exercise b. Reduction of overweight c. Analgesia and anti-inflammation with comfrey root extract cream which is well-tolerated and without known interactions with other medications

Back pain

Back pain affects already younger patients, even though a particular age group cannot be defined. Rather than age seasonal peaks are observed, e.g. at the start of outdoor activities in spring. Besides heavy workers people experiencing chronic psychological stress are often affected[18]. Overall musculoskeletal disorders, of which lower back pain is the most frequently diagnosed one, account for the second most reason why physicians put someone on sick leave.[19,20]

The experts agreed that in general working people prefer to administer oral drugs or heat therapy, while application of a cream is more accepted by retired persons or during leisure time when the application form is not an issue. Irrespective of age acceptance of topical treatment is also higher when the complaints occur more frequently. It was also noted by the experts that in case of recurrent pain patients often combine different measures to achieve relief. Combination of procedures is also part of the proposed treatment options of the National Guideline on low back pain, in which comfrey root is considered acceptable for self-management.[21]

Even though comfrey cream has demonstrated its superiority over placebo in a double-blind study (Table 3), its single application rarely is a sufficient measure. However, it certainly has its place in the overall treatment concept, especially in order to reduce the intake of oral analgesics. Table 4 summarizes the characteristics of patients with back pain.

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Table 3 Clinical trial in patients with upper or lower back pain

Reference	Study design	Number of patients	Treatment regimen	Primary efficacy parameter	Results
Giannetti et al. [22]	Double-blind, placebo-controlled	Comfrey cream: 60 Placebo cream: 60	3 times daily for 5days	Reduction of pain sensation on active standardized movement by VAS* as compared to baseline	Comfrey: 95% Placebo: 38% p<0.001

*Visual Analogue Scale

Table 4 Patient characteristics for comfrey treatment in back pain

Patients and symptoms	a. Recurrent mild to moderate non-specific pain b. Prolonged sitting down at work or travel c. Heavy work d. Permanent stress e.g. Job, house work, child-rearing e. Degenerative processes
Expectations	a. Due to high level of suffering gradual onset of pain relief is accepted b. Aware that repeated treatment is needed and therefore product of high tolerability is preferred
Therapeutic goal	a. Reduction of intake of oral analgesics b. Prevention of adverse events c. No interactions with other medications
Treatment plan	a. Exercise therapy b. Combination of measures, e.g. Local heat therapy and massage c. Analgesia with topical comfrey

Blunt injuries

Blunt injuries in the form of strains, sprains, or contusions regularly occur in physically active persons e.g. soccer players. First aid measures comprise rest, cold pack, compression, and elevating the affected limb, but early pharmacological treatment with analgesic and potentially anti-inflammatory effects is equally important in order to support regenerating processes.[23,24]

Apart from analgesia symptoms developing in a later stage such as hematoma are also well suited for the treatment with a herbal drug like comfrey root.[5] Moreover, due to its long-standing safe and effective use there is no need to consider whether anti-inflammation or anti-coagulation etc. is indicated at a particular point during the healing phase.[5,6] There is agreement that in general patients, who experience pain at an injured site, can be easily instructed to treat this particular area instead of using an oral analgesic.[17]

One target group especially suitable for treatment with topical comfrey root is people, who do sports for health reasons. Another important patient group comprises children, for whom some other synthetic medications, e.g. diclofenac, are not approved. Moreover, many parents fear adverse effects and prefer to treat their offspring with natural remedies. In addition, the application of an ointment bandage goes along with special attention to the child, which may further promote the healing process. Elder patients potentially receiving multiple medications, who have experienced a blunt trauma, could also be well provided with a comfrey ointment suspensory bandage. However the experts objected that in paediatricians, the awareness about the efficacy and tolerability of comfrey, which has been proven in two blinded trials – one placebo- and one active-controlled (see Table 5), appears to be low. This is also the case in orthopaedics or accident surgeons examining elder patients after a downfall.

Table 5 Clinical trials in patients with uni-lateral ankle sprain

Reference	Study design	Number of patients	Treatment regimen	Primary efficacy parameter	Results
Koll et al. [25]	Double-blind, placebo-controlled	Comfrey cream: 80 Placebo cream: 63	4 times daily for 8days	Increase in standardized pressure until pain reaction on injured side versus healthy side as compared to baseline	Comfrey: 2.4 kp/cm^2 Placebo: 0.95 kp/cm^2 p<0.0001
Predel et al. [26]	Single-blind, active-controlled	Comfrey cream: 82 Diclofenac gel: 82	4 times daily for 7days	Difference in standard pressure until pain reaction over time (AUC*) between comfrey and diclofenac	AUC with Comfrey +61.08 N/cm^2 x h greater than with Diclofenac (p=0.0046)

*Area-under-the-curve

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There was agreement that the clinical study directly comparing comfrey cream with topical diclofenac for the treatment of sports injuries and demonstrating comparable efficacy provides convincing arguments for patients to choose the less well-known topical alternative comfrey.[26] Table 6 gives an overview of the characteristics of patients with blunt injuries suitable for topical treatment with comfrey.

Table 6 Patient characteristics for comfrey treatment in blunt injuries

Patients and symptoms	a. Mild to moderate pain and swelling b. Children from the age of 3 c. Elderly patients on multiple medications
Expectations	a. Avoiding synthetic drugs in children b. Avoiding drug interactions in elderly patients c. Early analgesic and anti-inflammatory treatment to promote regeneration
Therapeutic goal	a. Reducing pain and swelling b. Prevention of adverse events c. No interactions with other medications d. Treatment at least as effective as topical diclofenac
Treatment plan	a. RICE = rest, ice, compression, and elevation b. Bandage with comfrey cream

Polymedication

Medical error reporting systems have been developed to learn from defects: By analyzing multiple medical error cases, we can find patterns and even identify the mechanism describing how an error occurs.[27] Due to the demographic change occurring in Western countries the elder population, which often suffers from various pain syndromes, is continuously growing. Therefore pharmacists are frequently confronted with patients who have been prescribed numerous drugs by several physicians. In addition, pharmacists are more and more entrusted with the task to monitor medication plans of their customers. For example, oral analgesics like NSAIDs have a high risk of adverse events and interactions, e.g.[11]

a. With inhibitors of the renin-angiotensin system potentially leading to a loss of antihypertensive effect
b. By triggering a cardiovascular event in patients with cardiovascular disease
c. Acute gastrointestinal bleeding in patients with latent gastritis.

The knowledge and sensitivity about drug interactions is also increasing in the public awareness. There is general agreement among the experts that in case of multiple medications predictive factors for the use of a naturopathic medicine such as gender or level of graduation become negligible, since synthetic painkillers should be rejected for safety reasons. Therefore a product like comfrey cream, for which so far no interactions have been identified despite many years of pharmacovigilance, would be a rather safe treatment option. Table 7 summarizes the characteristics of patients with multiple medications, who could be appropriately treated with comfrey root extract cream.

Table 7 Patient characteristics for comfrey treatment in patients receiving polymedication

Patients and symptoms	a. Mild to moderate pain e.g. Osteoarthritis, back pain, contusions b. Elderly especially in nursing homes c. Patients with chronic diseases like i. Diabetes mellitus ii. Hypertension iii. Mental illness iv. Cancer v. Impaired renal or hepatic function vi. Gastritis
Expectations	a. Avoiding drug interactions b. Avoiding additional oral medication c. Avoiding systemic effects for localized symptoms
Therapeutic goal	a. Reduction of pain b. Prevention of adverse events

Conclusion

Comfrey root extract has demonstrated its non-inferiority in a large well-designed study in patients with ankle distortions, in which it was compared to topical diclofenac.[26] That goes along with a significant upgrade of the herbal medicinal product, which is still commonly perceived as being less effective, and provides comfrey with a more appropriate status. Overall the distinction between conventional synthetic and traditional naturopathic medicinal products is arbitrary and does not allow a rational approach to treatment alternatives.

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Conflicts of interests

Authors declare that there is no conflict of interest.

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