CASE STUDY

Novel Wound Healing Powder Formulation for the Treatment of Venous Leg Ulcers

Angela V. Ghatnekar, PhD^{a,b}, Tuan Elstrom, BS^a, Gautam S. Ghatnekar, PhD^c,
Teresa Kelechi, PhD^{d,*}

^aRegranion, LLC, Charleston, SC 29412, USA

^bDepartment of Medicine, Division of Rheumatology, Medical University of South Carolina, Charleston, SC 29425, USA

^cDepartment of Comparative Medicine, Medical University of South Carolina, Charleston, SC 29425, USA; and

^dCollege of Nursing, Medical University of South Carolina, Charleston, SC 29425, USA

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Abstract Chronic venous disorders are common in the Western world. The current treatment of venous leg ulcers is unsatisfactory despite the availability of well-documented standards of care. Patients today are interested in alternative approaches to modern medicine. We have developed a wound-healing powder containing natural ingredients with absorptive, aromatic, antiseptic, and anti-inflammatory synergistic properties. This report describes 3 cases that were successfully treated with the powder, demonstrating the potential of herbal remedies in the clinical treatment of venous leg ulcers.

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Nonhealing wounds, particularly those of venous origin, are perplexing and challenging to manage, even by the most experienced clinician. One must consider the complex pathogenesis when establishing a treatment plan. Current trends in research are aimed at immune function,¹ the role of genes,² and the presence of chronic inflammation and infection.³ Given the increasing incidences of drug-resistant organisms and wound bioburden, the topical use of antibiotics has become a central, if not a controversial, issue in wound management. Thus, there is a reason to search for alternatives such as herbal remedies to speed up the healing of wounds and also reduce the potential for infection. Herbal therapy is an increasingly popular treatment for

wound care because numerous herbs and their extracts have the potential to serve as antimicrobial and antifungal agents.⁴

Herbal remedies are the basis of various traditional medicine systems around the world and date back thousands of years. Chinese and Indian (Unani and Ayurveda) medicinal systems, as well as the Amazonian ethnomedicine system, rely primarily on herbs for health preservation and healing. Herbal medicines have been described in traditional texts, and there is a growing body of scientific literature on the use of plants for wound healing.^{5–9} There are emerging data to support the effectiveness of herbal extracts in treating small to medium wounds, skin abrasions, excoriations, and skin infections.^{10,11} However, there is a paucity of evidence that demonstrates clinical efficacy and cost effectiveness, especially for healing chronic wounds such as venous leg ulcers (VLUs). The financial burden of venous ulcer disease on the health care system is significant. Over \$3 billion is spent annually on leg ulcer care,^{12,13} which adds a tremendous burden to the US health care system.

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* Corresponding author.

E-mail address: kelechtj@musc.edu

In our case reports, we describe the use of MittiHeal, an herbal wound powder that was applied to VLU in 3 patients at risk of developing infection. Plant extracts having antiseptic, granulation-stimulating, anti-inflammatory activities, as well as odor reduction and absorption qualities, were used to develop the powder. MittiHeal is a homeopathic and natural powder extract formulation composed of a mixture of active and inactive ingredients that include *Calendula officinalis* L (SI 0.1% vol/wt) plus *Arnica montana* L (SI 0.01% vol/wt) and inactive ingredients *Mentha arvensis* (mint, 90% wt/wt) plus *Santalum album* (sandalwood, SI 10% wt/wt; Figure 1). The powder formulation was prepared in accordance with the *Homeopathic Pharmacopoeia of the United States* and manufactured under good manufacturing practice conditions, as defined by the US Food and Drug Administration under Section 501(B) of the 1938 Food, Drug, and Cosmetic Act (21USC351). The ingredients of MittiHeal were chosen because they are not only time tested but also based on scientific evidence of antiseptic, anti-inflammatory, absorptive, aromatic, and synergistic properties. Specifically, the *Mentha* component absorbs excessive wound secretions, thereby preventing the wound environment from serving as a bacterial growth medium; the *Arnica* mother tincture component is a well-known and studied anti-inflammatory agent, whereas the sandalwood powder is cooling and aromatic. Combined with *Calendula Arnica* mother tincture is known for its anti-inflammatory and lymphocyte activation properties. These components, in a powder form, work synergistically, each contributing known characteristics, to absorb wound exudate, control malodor, provide a protective barrier against microbial colonization, and promote natural autolytic debridement, as well as increase wound healing.¹⁴⁻¹⁸

Case Reports

Three individuals with VLUs volunteered to participate. They resided in a senior housing complex, were ambulatory (one used a walker), were informed that these data would be submitted for publication, and provided verbal consent. Approval was received from the housing complex's administration. The housing complex's nurse provided the wound care. Physician approval was sought prior to inclusion. The volunteers were assessed by 1 of the investigators, who is a certified wound care nurse (CWCN), for clinical signs of infection and potential for wound healing, including an ankle-brachial index. The volunteers had ankle-brachial indexes between 0.8 and 1.3 mm Hg, considered to be adequate for healing and acceptable for the use of high compression, a standard of care for wound healing.¹⁹ This information accompanied the volunteers, who received medical clearance from their physicians and verified that the wounds were not infected. The treatment protocol consisted of daily cleansing of the ulcer with sterile saline, application of the powder, and use of a short-stretch compression bandage or compression

Figure 1 MittiHeal: Natural Wound Care Powder Mixture.

stocking to manage edema. Each volunteer was instructed after the initial treatment to self-administer the treatment protocol and to come back for follow-up visits to the housing complex's nurse once or twice each week.

Case 1

A 68-year-old woman had fallen over her walker 3 weeks earlier, which resulted in 4 full-thickness ulcers on the medial aspect of the right leg that were composed of at least 90% granulation tissue. The sizes (as measured width by length) of each ulcer, from medial to lateral, were 2.4×2.1 cm, 1.5×1.3 cm, 1.2×1.2 cm, and 1.2×1.1 cm. All wounds were superficial, with an approximate depth of 0.1 cm. She had experienced a left-sided stroke 8 months earlier and had been diagnosed with chronic venous disorders about 9 years ago, after frequent bouts of lower extremity swelling. She had been obese for most of her adult life, having lost about 60 pounds (27 kg) after the CVA. Comorbid conditions were hypertension, elevated cholesterol, and osteoarthritis. She was taking metoprolol, pravastatin, and diclofenac to manage these conditions.

After twice weekly wound treatments with a hydrocolloid dressing, the peri-ulcer skin became red and severely pruritic, with significant maceration (Figure 2). There was no change in the size of the ulcers over the 3-week treatment period. She wore a compression stocking during this time. There was moderate drainage without odor. As shown in Figure 2, there was significant erythema consistent with venous eczema or cellulitis, a clinical concern raised by the CWCN. However, cellulitis, a localized skin infection, was ruled out by the volunteer's physician on the basis of the skin's appearance (skin temperature not elevated, only localized redness) and lack of elevated inflammatory markers (white blood cells, C-reactive protein). The leg circumference measured 35.6 cm over the midcalf region.

The hydrocolloid dressing was discontinued as it was unable to adequately absorb the drainage. The new ulcer treatment protocol consisted of cleaning with sterile saline, application of the MittiHeal powder, and continued

Figure 2 Case 1. Patient During Initial Visit. Erythema of Peri-ulcer Skin With Severe Pruritus.

compression. The volunteer reported she had great difficulty donning the compression stockings, so she was educated in applying a short-stretch compression wrap instead. She reported her pain as 7 (on a scale from 0 to 10, with 10 being the most severe). After 8 days of treatment (visit 2), the peri-ulcer maceration and redness had decreased significantly, as shown in [Figure 3](#). The itchiness completely subsided; the pain score was 2 during wound care and 0 at all other times. The ulcers were reduced in size by 50%. A considerable amount of epithelial tissue was observed, and by day 12 ([Figure 4](#)), all 4 ulcers had healed. The skin was almost normal in color, and the volunteer reported no itchiness. The pain score was 0 at the end of the treatment. The leg circumference had decreased to 33.2 cm.

Case 2

An 80-year-old woman with a long-standing history of chronic venous disorders, diabetes, hypertension, and atrial

Figure 3 Case 1. Day 8. Decrease of Redness and Re-epithelialization.

Figure 4 Case 1. Day 12. Significant Re-epithelialization, No Erythema, Ulcer Healed.

fibrillation developed multiple lower extremity ulcers on both legs. She was taking exenatide (Byetta), metformin, lisinopril, coumadin, and aldactazide. There was also a prescription bottle with ramipril, but she denied taking it. She had varicose veins and severe venous eczema bilaterally, with complaints of leg heaviness, burning, and itchiness. The right leg midcalf circumference was 36.8 cm when the patient was first seen, after having the open wounds for approximately 6 weeks. She wore compression stockings but had not used them for the past 2 weeks because she could not put them on. Her daughter, who usually assisted her, was away. She cleaned the ulcers with warm

Figure 5 Case 2. Patient During Initial Visit. Ulcers With Increased Exudate.

Figure 6 Case 2. Day 4. Reduced Erythema, Swelling, Exudate, and Increased Granulation.

Figure 7 Case 2. Day 8. Reduction of Ulcer Size by 50%.

water, dabbed them with white vinegar, and rubbed on antibiotic ointment. Petrolatum was applied to the entire leg, and the ulcers were dressed with nonabsorbent, nonstick bandages. Although neither a health care provider nor wound care specialist had ordered this treatment, the volunteer insisted that this treatment had healed the ulcers in the past.

The volunteer sought assistance when the full-thickness ulcers increased in size and developed increased exudate (Figure 5). She also reported that the pain increased and was 4 on a scale of 0 to 10. The proximal ulcer to the right lower extremity measured 2.1 cm wide $\times$ 2.5 cm long, and the distal ulcer measured 3.2 cm wide $\times$ 3.3 cm long. The ulcers were covered with about 50% necrotic debris with moderate exudate. There was significant erythema and pitting edema. The volunteer also had chronic heart failure that contributed to lower extremity edema. She admitted to intermittently taking aldactazide, prescribed for the edema, and her “heart” pill, although it was not listed on the medication list. She was instructed to discontinue the ulcer care she had been doing and begin daily MittiHeal applications to the 2 right anterior leg ulcers. She refused to stop the treatment on the left leg because those ulcers were “not bothering her.”

After day 4 (visit 2), the ulcers were drier, with decreased erythema and swelling (Figure 6). The patient stated that she had applied MittiHeal but that it didn’t stick because the ulcers were “crusted” over, a typical finding

noted with use of the powder during the ulcer healing process. The powder sticks to the wound, forming a hard, crustlike covering. There was increased granulation tissue, a new finding, observed after the nurse thoroughly cleansed the wound and removed the “crust.” The edema was also reduced, and the volunteer reported the pain to be minimal, at 1 on the scale of 0 to 10. The volunteer reported that secondary to the decreased edema, she was able to commence wearing her compression stockings, with the assistance of a friend, after day 2 and continued to wear them throughout treatment.

By day 8 (visit 3), the ulcers were reduced in size by half (Figure 7), and the patient reported all painful symptoms had subsided as the ulcers continued to reduce in size (Figure 8). After 20 days (visit 4), both ulcers were closed and completely epithelialized (Figure 9). The redness had completely subsided, and the small visible scars were flush with the skin. The leg circumference had decreased to 32 cm. Pain was 0 on the scale from 0 to 10. The ulcers on the left leg were still open but were smaller, approximately 1 cm. The volunteer continued to refuse left leg ulcer treatment with the powder.

Case 3

A 76-year-old man with a history of a venous thromboembolism of the left leg, with subsequent edema and VLUs,

Figure 8 Case 2. Day 12. Further reduction in size.

Figure 9 Case 2. Day 20. Ulcer Closed and Complete Re-epithelialization.

developed several new ulcers on the anterior and lateral aspect of the left leg. He had a history of prostate cancer, chronic obstructive pulmonary disease, (COPD), and hypertension. He was taking prednisone, albuterol, ipratropium, and guaifenesin for chronic obstructive pulmonary disease and had several pill bottles in his apartment for hypertension, including hydrochlorothiazide, enalapril, and amlodipine. He said he took the “water pill” most of the time but the others made him feel bad; thus the nurse was unsure which of these medications the patient was taking for hypertension. The housing complex nurse reported that he was nonadherent to taking his medications. He had undergone radiation therapy for cancer about 6 years ago. He refused to wear compression stockings to manage the edema as part of the prevention plan of care. As a result, he developed chronic edema from the venous thromboembolism and had experienced approximately 15 VLUs over the course of 10 years. He reported that most of the previous ulcers took about 5 to 7 months to heal. The “typical” treatment for these ulcers, according to the volunteer, was his remedy of hydrogen peroxide. However, he had received treatment in a wound care clinic during the past 3 years on the insistence of his primary care provider. He

Figure 10 Case 3. Patient During Initial Visit. Ulcer Covered With Thin Necrotic Debris.

Figure 11 Case 3. Day 8. 100% Clean Wound Bed, 25% Granulation Tissue, and 75% Epithelial Tissue.

Figure 12 Case 3. Day 12. Some Residual MittiHeal Noted on Wound Bed.

could not report the type of dressing used but did say they “bound up my leg with all kinds of things.” The housing complex nurse reported the last treatment was with a silver hydrofiber and short-stretch bandages.

The volunteer sought assistance from the nurse after about 7 days of unsuccessful self-care in which he cleaned the ulcers with hydrogen peroxide and covered them with damp gauze dressings. During the first visit (**Figure 10**), the full-thickness ulcer most proximal to the knee (A) measured 4.0 cm wide $\times$ 3.0 cm long and was 75% covered with thin necrotic debris. A slight odor was noted. The smaller full-thickness distal ulcer (1) was 1.5 cm wide $\times$ 1.5 cm long and 100% free of necrotic debris. Moderate exudate and extensive peri-ulcer maceration was noted around ulcer (A). The circumference of the widest part of the calf over the proximal ulcer was 42.6 cm. The pain score was 5 on a scale from 0 to 10. Both ulcers were treated with MittiHeal applied daily after the patient cleaned them with sterile saline. After the powder was applied, the patient would dress the ulcers with nonadherent thin absorbent foam dressing, and the entire lower leg was wrapped in a short-stretch compression bandage. During visit 2, after 8 days of treatment (**Figure 11**), the proximal ulcer had a 100% clean wound bed with about 90% granulation tissue. No odor was noted. The smaller distal ulcer was 0.5 cm wide $\times$ by 0.8 cm long. The periulcer skin was intact without maceration. The patient reported the pain to be 1 on the

scale from 0 to 10. On day 12 of treatment, the periulcer skin was much less erythematous, and epithelialization was noted (**Figure 12**). After 16 days of treatment (**Figure 13**), wound contracture was observed. The size of the larger ulcer decreased to 3.0 cm wide $\times$ 2.0 cm long. There was minimal drainage and no odor. The leg circumference over the ulcer was reduced to 37.2 cm through use of the short-stretch wrapping. The volunteer reported that the throbbing and burning sensations were resolved. The last time we saw the volunteer was at 20 days of treatment (**Figure 14**). The wound had continued to contract and was 2.5 cm wide $\times$ 1.5 cm long. The smaller ulcer was completely healed. The pain score was 0 on the scale from 0 to 10. The volunteer then went on vacation at day 21 and was lost to follow-up.

Discussion

In all 3 cases, healing outcomes were achieved after application of MittiHeal. There were no adverse effects or complications. The powder, in combination with the use of compression stockings or wraps, was found to reduce wound pain and accelerate the healing of slow-to-heal wounds. The powder uniquely absorbed excessive wound exudate, formed a “crust” that prevented overdrying, sealed the wound from bacteria, helped maintain moisture balance

Figure 13 Case 3. Day 16. Wound Contracting and Covered With Epithelial Tissue.

Figure 14 Case 3. Day 20. Significant Contraction of Ulcer. Complete Healing of Smaller Distal Ulcer. The Patient Was Feeling Much Better and Went on Vacation After Day 20.

in the wound bed, and also reduced the lingering of malodor. It is possible that the powder may have suppressed localized infection. While compression, particularly multilayer systems, is widely accepted as the cornerstone of therapy for VLUs, it is difficult to ascertain the contributive effect of compression on wound healing with just 3 cases using a multilayer system, and this issue will be the focus of a future study. The volunteers were able to apply MittiHeal to their wounds on a daily basis, thus demonstrating its potential of an easy and effective self-treatment for VLUs.

The housing complex nurse reported that she was surprised to find that the powder's absorbency properties surpassed those of many other types of dressings, such as foam and alginates, and found it was a safeguard against maceration. She also reported the volunteers told her they were pleased with the "numbing" effect on the ulcers.

When treated with the current standard of care alone (the use of compression, leg elevation, physical activity), about 50% of VLUs remain unhealed at 6 months, and up to 60% recur within 4 years.²⁰ Unfortunately, approximately 600,000 new cases of VLUs occur each year in the United States.²¹ Venous leg ulcers are associated with substantial morbidity, decrements in quality of life, and economic burden.²² Thus new methods to augment the standard of care are needed.

A wide variety of advanced healing methods, including skin grafts, biologic agents, hyperbaric oxygen therapy, negative pressure therapy, and bioengineered skin

substitutes, are available. These methods have shown marginal utility, are generally expensive and cumbersome, and have demonstrated limited efficacy.²³ For example, a treatment with a bioengineered skin substitute is reimbursed at approximately \$1500, requires low-temperature refrigeration, and has a very short shelf life. In practice, the product requires the rapid identification of a nonhealing wound in a good wound care setting, specific patient selection criteria, and expert physician knowledge of the proper use of the product and may require multiple applications to achieve healing.²⁴

We also recognize that these leg ulcers might have healed with the use of moist wound healing principles and compression, with good oversight of dressing changes provided by the CWCN. Further studies are needed to enhance our understanding of the underlying mechanisms responsible for the results obtained with MittiHeal. However, our results are consistent with findings from the emerging scientific literature on the wound healing properties of the ingredients contained in the powder. Although demonstrated with a small number of patients, the results in this case report suggest the potential for optimizing and implementing a multifunctional approach to treatment of difficult-to-heal wounds that uses a synergistic formulation of multiple plant extracts with documented effects.

The main active ingredient in MittiHeal, *C. officinalis* L, commonly known as marigold, has been used topically

since ancient times, as well as recently in Europe and the United States to heal wounds. Consistent with wound healing findings from a plethora of earlier studies,²⁵⁻²⁹ a 3-week trial of 21 randomized patients with 33 VLUs treated with an ointment containing marigold found that compared with 13 control patients with 22 VLUs receiving saline solution dressings, wound healing was statistically significantly accelerated in the marigold group. A decrease in total surface area of 41.71% vs 14.52% ($P < 0.05$) suggests a positive effect on venous ulcer epithelialization.^{14,24} Saponins, micronutrients, flavonoids, and polysaccharides, the constituents identified in *Calendula* species, may be responsible for the anti-inflammatory, antioxidant, antiseptic, and wound healing effects of the plant.

Arnica species, another active ingredient in MittiHeal, are plants belonging to the Compositae family. *Arnica* species are a popular homeopathic treatment for acne, bruises, sprains, muscle ache, trauma pain, and absorption of edema.¹⁵ They are also one of the most studied plants for their anti-inflammatory properties.³⁰⁻³⁴ Active compounds have been identified in their leaves, flowers, and roots. These compounds include alcohols, tannins, flavonoids, and sesquiterpene lactones, specifically helenalin. Helenalin exhibits an action similar to that of corticosteroids by inhibiting elastase and hyaluronase (involved in proteoglycan degradation at the capillary endothelium) and thus prevents vascular leakage.³⁴ Although helenalin's use is widespread, its efficacy remains inconclusive, with effectiveness demonstrated depending on a variety of different medical situations.^{30,35}

An inactive ingredient, *Mentha arvensis*, is a perennial herb, and oil extracted from its leaves yields an aromatic and antiseptic powder.^{16,36} Similarly, the essential oil of *M piperensis* contains the analgesic component of menthol.¹⁷ Sandalwood is another inactive ingredient of MittiHeal. The essential oil obtained from sandalwood is widely used as an antidepressant, an anti-inflammatory, an antifungal, an antiviral, and an astringent.^{18,37} It is also cooling and aromatic.³⁸

Conclusion

The preliminary signals of healing described in this case report support the use of topical herbal treatments for VLUs and their potential antimicrobial and healing effects in practice. In a larger future prospective clinical trial of MittiHeal, we hypothesize that we will achieve similar findings, with an additional aim that will include a reduction in pain.

A major existing challenge faced in the field of wound care is treating chronic hard-to-heal wounds. The longer a wound remains open, the greater the risk for infection, leading to severe complications. Several medicinal plants are known for their antibacterial properties and might hold the key to future approaches to prevention of wound infection. However, 2 key issues are the tremendous out-

of-pocket costs of most of the conventional approaches and the significant burden to the patient in terms of ease of use of some of the devices and techniques, such as compression stockings, etc. MittiHeal offers an inexpensive (< \$5 per application) yet effective combination of plant-based ingredients that can be applied directly on the wound. MittiHeal's wound healing properties and its potential for reducing pain and preventing infection make it an attractive therapy for patients who are dissatisfied with conventional approaches. The powder offers a wound healing option, especially to those with VLUs who seek an economical and natural alternative. Unfortunately, the general healing prognosis for a patient with VLUs is usually poor, especially in the absence of compression. The presented cases provide initial evidence to suggest that this herbal treatment for VLUs is promising for patients who experience delayed healing and recurrent ulcerations. Prospective trials of safety and effectiveness of this herbal treatment compared with the standard of care are needed to confirm the results reported here.

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