Oriental Medicine and Chronic Wound Care: Theory, Practice, and Research

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Abstract
In East Asian countries, oriental medicine (OM) has been used for thousands of years to manage a wide variety of chronic wounds, but in western countries the role of OM in wound care remains to be established. To summarize current practices and available evidence of OM in the management of chronic wounds, a search of Chinese and English databases was conducted and summarized with an emphasis on randomized controlled trials, clinical trials, and meta-analyses of topical and systemic OM treatments. Hundreds of reports were identified, mostly in the Chinese literature, but few randomized controlled clinical studies have been conducted. Available preclinical and clinical evidence suggests there may be a role for OM modalities, especially herbal medicine, in the management of chronic wounds. Before conducting the needed rigorous clinical studies, wound care experts should agree on and help standardize herbal formulations — a unique challenge for the usually individualized OM approach to care. However, the literature suggests uncovering pathways for future research may help patients all over the world benefit from the thousands of years of documented experience managing chronic wounds with OM.

Keywords: review literature, wounds, treatment, oriental medicine, medicinal herbs


Potential Conflicts of Interest: This study was funded by the Student Faculty Interdisciplinary Research Think Tank, Daemen College, Amherst, NY.

Chronic wounds are generally defined as wounds that do not heal in an orderly and timely manner, as compared to acute wounds, which follow a predictable recovery path. All wounds originate from a variety of causes, including trauma, surgery, sickness, or bodily inadequacies (eg, venous insufficiency). Chronic wounds are rarely seen in individuals who are otherwise healthy and are usually complicated by co-morbidities of diabetes mellitus, venous hypertension, alterations in health status, and immune function suppression.

Because of the different ways chronic wounds form, a variety of categories of chronic wounds exist, including venous stasis ulcers, diabetic ulcers, pressure ulcers, and any other wound that fails to heal properly. Acute wounds become chronic when biological and environmental factors combine to create a wound environment that fails to support a natural and timely healing process. Many experts consider a wound chronic when it no longer follows the expected course of events or falls within the range of what is considered a normal healing trajectory. Interruptions within the typical healing process occur more readily as patient age increases and/or health condition declines; chronic wounds fail to respond to treatments appropriately, possess an unhealthy tissue quality, and fail to achieve proper closure, which leaves the wound susceptible to infection.

Chronic wounds may lead to a number of complications. The public health and economic impact of chronic wound care is staggering; global annual cost has been estimated to be upwards of more than $8 billion (US). In the US, chronic wounds affect 5.7 million patients annually. The estimated total direct cost of treating chronic wounds in the US, which includes wound diagnostic and surgical procedures, pharmaceuticals, wound closure devices, and hospital and physician charges, is $20 billion annually; additional indirect costs of chronic wounds are the result of lost work time and impaired quality of life.

In East Asian countries, oriental medicine (OM) has been used for thousands of years for chronic wound care. Herbal therapy, the major branch of OM, is used both internally...
and externally for wound treatment; supplementary therapies may include acupuncture, moxibustion (a heat therapy utilizing mugwort herb burning on the skin), and cupping (a therapy utilizing suction on skin through cups). In western countries, OM remains to be established as an important tool in wound care. For a better understanding of OM in order to improve wound care, the authors reviewed historical perspectives, current practice, and research studies in OM chronic wound management. Challenges and possible pathways for future research on wound healing using herbal medicine also were explored.

Methods

Literature search. Literature searches were conducted in the following databases from their inception through July 2012: China National Knowledge Infrastructure (CNKI), VIP Database for Chinese Technical Periodicals, Chinese Biomedical Literature Database, Wanfang Database, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index to Nursing and Allied Health Literature (CINAHL), and PubMed. The following search terms were used individually or combined in appropriate language forms (Chinese and English): (chronic) wound, skin ulcers, venous stasis, pressure ulcer, diabetic ulcer/wound, diabetic foot ulcer, Chinese Traditional, Chinese Herbal, Oriental Traditional, herb, herbal medicine, acupuncture, cupping, clinical trial, and oriental medicine. The bibliographies of included studies also were searched for additional references.

Results

Randomized, controlled trials (RCTs) and meta-analyses provide the most reliable form of scientific evidence in the efficacy of herbal medicine in wound healing; other research (eg, case studies) also can shed light on clinical interventions in patients with refractory chronic wounds. One hundred, eight (108) clinical trials (including 53 RCTs) on diabetic foot/skin ulcer, 146 clinical trials (including 26 RCTs) on pressure ulcer, and 134 clinical trials (including 17 RCTs) on venous ulcer were identified in Chinese databases. Six articles were identified in English databases; however, only four (two meta-analyses and two RCTs) were reported in English. Based on the authors’ brief assessment of study quality and appropriateness of presentation in the current study, 11 studies were included for discussion of herbal medicine in chronic wound care.

Historical Perspectives: Chronic Wounds and OM

Pathogenesis of chronic wound. Based on OM theories, wounds are considered acute or chronic. Acute wounds often are caused by external factors, including six external pathogenic factors (wind, cold, heat, dampness, dryness, and fire), micro-organism invasion, and trauma. Chronic wounds are often residual symptoms of acute injuries of long-term abnormal emotions, improper diet, and excessive sexual activity. Patients with chronic wounds usually demonstrate physical ramifications of Qi deficiency together with poor blood circulation, disharmony between Qi and blood, and/or emotional abnormalities.

Qi is generally known as the energy source of the human body; propelling blood circulation; when Qi is deficient or lifestyle is deemed improper (eg, sedentary lifestyle with high saturated fatty acid intake), Qi has been or will be excessively consumed, causing poor blood circulation. Meanwhile, Qi shares a close connection with emotions, which means emotion also may contribute to the pathogenesis of chronic wounds. Feng’s Handbook of Secret Medical Records states, “…depression and anger impair liver and spleen…Functions of Qi and blood thus [are compromised], predisposing the human body to ulceration and chronic wounds.” Improper diet also renders the disharmony between and of Qi and blood and fosters chronic wound development. Wang supports that venous ulcers on the leg are caused by abnormal Qi and toxicants from food (lack of Qi will cause improper blood circulation, including blood stasis; toxicants ingested will erode blood vessels). The connection between food and wound healing has been confirmed by modern research studies. A case study has found dietary zinc deficiency to be responsible for compromised immune function and delayed wound healing; vitamin C deficiency is generally known as a factor related to scurvy and poor wound healing. In summary, factors of lifestyle and physical constitution cause disharmony between Qi and blood and poor blood circulation, and thus contribute to the development of chronic wounds.

Treatment of chronic wounds. OM highly values historical experience; management of chronic wounds in OM is heavily based on understanding, experiences, and methods documented in the literature. Qi believes that growth of connective tissue and muscle depends on the function of the spleen and stomach, which supply the human body with
normal Qi and blood; therefore, Qi and blood status are important in the development and management of chronic wounds. Consequently, modern OM wound specialists highly value the use of Qi-enriching herbs such as Huang Qi (Radix Astragali) and blood activation herbs such as Xue Jie (Dragon's Blood). Therapeutic theories and clinical cases are well-documented in various ancient OM publications and modern OM textbooks. OM management principles are similar to those of western medicine — e.g., debridement of devitalized tissue to promote granulation. However, OM methods in wound care differ greatly from conventional therapies. On most occasions, OM practitioners use two management approaches to wound care: internal therapy and external therapy. Internal therapy generally involves ingestion of herbal decoctions. External therapy consists of various applications of herbal plaster or herbal solutions for debridement and promoting granulation tissue growth. Use of herbs in internal therapy is based on a holistic view and yin-yang balance. Herbal formulas for oral administration in wound care usually include Bu Yang Huan Wu Tang, Si Miao Yong An Tang, Tao Hong Si Wu Tang, Sheng Yu Tang, Nei Bu Huang Qi Tang, and Nei Shu Huang Lian Tang. Herbs for topical use often consist of Bingpian (Borneolum syntheticum), Xue Jie (Sanguis draconis/ Dragon's Blood), Ruxiang (frankincense), and Moyao (myrrh), most of which are typically included in externally applied herbal formulas such as Yu Hong Sheng Ji Gao (granulation-promoting Jade Red Paste) and Qu Fu Sheng Ji Gao (paste for granulation formation and debridement). Management principles of debridement, blood activation, and Qi enrichment typically guide the OM management of chronic wounds. The effects of herbal medicine have been tested in clinical trials (see Table 1) and advocated by OM specialists.

Table 1. Summary of clinical trials using herbal management of chronic wounds

<table>
<thead>
<tr>
<th>Herbal products [references]</th>
<th>Route of administration</th>
<th>Indication</th>
<th>Study type</th>
<th>Sample treated (n)</th>
<th>Duration of study</th>
<th>Key findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fu Fang San Huang Gao18</td>
<td>Topical</td>
<td>Venous ulcer</td>
<td>Randomized, controlled trial (RCT)</td>
<td>60</td>
<td>4 weeks</td>
<td>Compared with petrolatum control, herbal medicine group showed higher rate of decrease in wound size and bacterial counts. Treatment group had more exudate at week 1; no difference was found at week 2 and after.</td>
</tr>
<tr>
<td>Yu Yang Ointment19</td>
<td>Topical</td>
<td>Venous ulcer</td>
<td>RCT</td>
<td>46</td>
<td>10 to 20 days</td>
<td>Compared with rhubarb and petrolatum control group, treatment group exhibited significant reduction in wound size, normalized skin color, increased granulation and epithelialization, and decreased bacterial infection ($P &lt;0.05$ for wound reduction)</td>
</tr>
<tr>
<td>Herbal medicine20</td>
<td>Oral</td>
<td>Diabetic Foot ulcer</td>
<td>Meta-analysis</td>
<td>221</td>
<td>21 to 30 days except one study of 8 weeks</td>
<td>Compared with conventional therapy alone, combined oral therapy with conventional care significantly increased healing rate (risk ratio [RR] 0.62 [95% CI, 0.39–0.97]) and decreased diabetic foot ulcer size (RR, 0.81 [95% CI, 0.71–0.92]). Medicine frequently used: Radix Angelicae sinensis, Flos Carthami Tinctorii, Semen Persicae, and/or Radix astragali</td>
</tr>
<tr>
<td>Centella asiatica extract21</td>
<td>Oral</td>
<td>Diabetic wound</td>
<td>RCT</td>
<td>84</td>
<td>21 days</td>
<td>Greater wound volume reduction ($P &lt;0.001$) and less granulation formation ($P &lt;0.001$; the author explained it as better scar formation suppression effects) were found in the herbal treatment group</td>
</tr>
</tbody>
</table>

References:
Clinical trials of the use of herbal medicine in chronic wound care. Among persons with profound philosophical understanding of chronic wounds, OM techniques, especially herbal medicine, have been used for wound care for thousands of years; however, most reports on the therapeutic effectiveness and mechanism of action of herbal preparations are found in Chinese medical literature. More than 300 reports were identified; however, only four studies were published in English. Zhang et al. conducted a randomized, controlled study involving a total of 108 patients—106 treated with external application of an herbal formula and 40 treated with petrolatum. After 4 weeks, a greater decrease in wound size (P < 0.01) and more granulation tissue growth (P < 0.01) was observed in the herbal treatment group.

### Table 1. Summary of clinical trials using herbal management of chronic wounds

<table>
<thead>
<tr>
<th>Herbal Medicine</th>
<th>Type</th>
<th>Condition</th>
<th>Study Design</th>
<th>Studies</th>
<th>Duration</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tangzu Yuyang Ointment</td>
<td>Topical</td>
<td>Diabetic foot ulcer</td>
<td>RCT</td>
<td>28</td>
<td>24 weeks</td>
<td>No significant difference found in healing rate (14/24 versus 19/24) and healing time (96±56 versus 75±53 days, P=0.271) between conventional care and conventional care plus herbal therapy. Significantly better improvement in Wagner’s grade and decrease in ulcer size in treatment than conventional care group alone at week 12 (P =0.017) and week 24 (P=0.036)</td>
</tr>
<tr>
<td>Herbal medicine ointment</td>
<td>Topical</td>
<td>Pressure ulcer</td>
<td>Meta-analysis</td>
<td>893</td>
<td>Mostly 1 week to 3 months</td>
<td>Patients treated with herbal medicine had better outcomes. Quality of studies limits ability provide definitive conclusion</td>
</tr>
<tr>
<td>Qi invigorating and stagnation dispersing herbs</td>
<td>Oral and external</td>
<td>Diabetic skin ulcer</td>
<td>Retrospective case series</td>
<td>38</td>
<td>Unknown; but time to cure was 62±45.3 days</td>
<td>34 patients completely healed; three patients showed decrease in ulcer size &gt; 75%, and one patient showed decrease ulcer size &gt; 25%</td>
</tr>
<tr>
<td>Zedoary Turmeric Oil</td>
<td>Topical</td>
<td>Pressure ulcer</td>
<td>Retrospective case control</td>
<td>29</td>
<td>15 days</td>
<td>Compared with Dragon’s Blood management, Zedoary Turmeric Oil therapy showed significantly better effects in wound size, skin color, granulation tissue size, and exudate amount</td>
</tr>
<tr>
<td>Xiao Fu Sheng Ji San</td>
<td>Topical</td>
<td>Pressure ulcer</td>
<td>RCT</td>
<td>56</td>
<td>18 days</td>
<td>Herbal therapy group demonstrated significantly greater decrease in wound size and greater healing rate (40/56 versus 18/51) and shorter healing time (10.2±1.5 versus 13.4±2.2 days) than petrolatum control group</td>
</tr>
<tr>
<td>Dragon’s Blood</td>
<td>Topical</td>
<td>Pressure ulcer</td>
<td>Systematic review of clinical trials</td>
<td>-</td>
<td>-</td>
<td>Topical use of Xuejie (Dragon’s Blood) could decrease inflammation and promote wound healing</td>
</tr>
<tr>
<td>Sheng Ji Yu Hong Gao</td>
<td>Topical</td>
<td>Chronic wound</td>
<td>Systematic review of clinical trials and basic research studies</td>
<td>-</td>
<td>-</td>
<td>Sheng Ji Yu Hong Gao is widely used in the management of pressure ulcer, chronic venous ulcer, diabetic leg ulcer, burn, and wound status post anorectal surgeries in China. Basic research studies found that Sheng Ji Yu Hong Gao could modulate PGF2, TXB2, and FGF, decrease local pH, improve local microcirculation, and promote the growth of granulation tissues.</td>
</tr>
</tbody>
</table>
another RCT\(^9\) where 46 patients with venous leg ulcers were treated with herbal therapy and 40 were treated with petrolatum, researchers found that topical use of an herbal ointment could effectively reduce wound size, normalize skin color, increase granulation and epithelialization, and decrease bacterial infection after 10 to 20 days of treatment (\(P < 0.05\) for wound size reduction; no other \(P\) values reported).

Chen et al\(^{20}\) conducted a meta-analysis of Chinese herbal medicine studies in the treatment of patients with diabetic foot ulcers. They identified six reports of RCTs involving a total of 221 patients who received oral herbal medicine combined with conventional care. Compared to standard care alone, Chinese herbal medicine significantly increased the number of patients whose ulcers healed (RR 0.62) and decreased the number of patients without any improvement (RR 0.34). Only two of the six studies reported adverse events, which included nausea, epigastric pain, and dry mouth. The results of this meta-analysis were recently confirmed by two RCTs. In one study, 84 patients with chronic wounds were randomized to treatment with herbal therapy (Centella asiatica extract capsules) and 86 received a placebo.\(^{21}\) After 21 days, greater wound volume reduction (\(P < 0.001\)) and less granulation formation (\(P < 0.001\)) were noted in the herbal treatment group; the author explained it as better scar formation and suppression effects. In a multicenter, prospective, randomized, controlled and add-on clinical trial, Li et al\(^{22}\) compared outcomes of diabetic foot ulcer patients receiving standard wound therapy (local debridement of necrotic tissue or callus, offloading, and dressing changes) to standard wound therapy plus Tangzu Yuyang Ointment. The researchers found that patients receiving standard wound therapy plus Tangzu Yuyang Ointment had significantly better improvements in Wagner’s ulcer grade and decrease in ulcer size after 12 (\(P = 0.017\)) and 24 (\(P = 0.036\)) weeks of treatment. In the study, although serious side effects occurred, including five deaths (three in the herbal treatment group and two in the group receiving standard wound care only), and one patient in the herbal treatment group experienced

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**Table 2. Summary of clinical trials and recommendations for use of other OM modalities and clinical indications**

<table>
<thead>
<tr>
<th>OM modality [references]</th>
<th>Indication</th>
<th>Study type</th>
<th>Sample treated</th>
<th>Duration of study</th>
<th>Key findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual acupuncture(^{46})</td>
<td>Ecthyma gangrenosum</td>
<td>Case report</td>
<td>1</td>
<td>Conventional care plus acupuncture once a week for three weeks</td>
<td>The cure of a refractory leg ulcer coincided with the use of acupuncture in the surrounding tissues</td>
</tr>
<tr>
<td>Acupuncture(^{57})</td>
<td>-</td>
<td>NIH Consensus Development Conference Statement</td>
<td>-</td>
<td>-</td>
<td>Acupuncture may be useful as an adjunct treatment or an acceptable alternative or be included in a comprehensive management program for addiction, headache, menstrual cramps, tennis elbow, fibromyalgia, myofascial pain, osteoarthritis, stroke rehabilitation, low back pain, carpal tunnel syndrome, and asthma</td>
</tr>
<tr>
<td>Tui Na (Chinese massage)(^{58})</td>
<td>Musculoskeletal discomfort</td>
<td>Case series</td>
<td>19</td>
<td>Twice per week for 1 month</td>
<td>Massage decreased duration of musculoskeletal ache, pain, or discomfort and increased range of motion in patients with musculoskeletal discomfort</td>
</tr>
<tr>
<td>Tai Chi(^{59})</td>
<td>Knee osteoarthritis</td>
<td>Randomized, controlled trial (RCT)</td>
<td>20</td>
<td>60-minute Tai Chi sessions twice weekly for 12 weeks</td>
<td>Tai Chi was effective in pain reduction and improvements in physical function, self-efficacy, depression, and health-related quality of life for knee osteoarthritis</td>
</tr>
<tr>
<td>Pursed-lips breathing technique(^{60})</td>
<td>Chronic obstructive lung disorders</td>
<td>RCT</td>
<td>32</td>
<td>Use of the technique during exercise</td>
<td>With this respiratory technique, patients walked an average of 37 seconds (16%) longer ((P &lt; 0.01)), and average drop in oxygen saturation was 1.2% less than without the technique</td>
</tr>
</tbody>
</table>
gastrointestinal bleeding (the patient had anaplectic ulcer), the researchers concluded they were not attributable to medication.

In another meta-analysis, researchers assessed the use of herbal medicine ointment in the treatment of pressure ulcers. After combining the data from 10 RCTs (N = 893 patients), Zhang et al concluded that Chinese herbal medicine treatment is effective for pressure ulcers, but most studies are not conclusive. Both Chen et al and Zhang et al reported clinical trials of herbal wound treatment usually have a small sample size and reports often lack sufficient information regarding randomization, group allocation, and blinding.

In a case series study of 38 patients with diabetes mellitus and various skin ulcers, Que et al reported that when using oral herbal treatments based on Qi enrichment and stasis resolution, the rate for complete wound healing was 89.5% with a mean time to healing of 62 ± 45.3 days. In a case-control study involving 29 pressure ulcer patients in each treatment group, Lin et al found that compared with Dragon’s Blood management, Zedoary turmeric oil therapy showed significantly better improvements in wound size, periwound skin color, granulation tissue formation, and amount of exudation in 15 days (P < 0.01 for all variables). Yang et al conducted an RCT to compare herbal therapy versus petrolatum treatment on 107 patients with pressure ulcers (56 in herbal therapy group and 51 in the petrolatum group). A higher proportion of wounds healed in the herbal therapy group (71% compared to 35%) during a shorter period of time (average 10.2 ± 1.5 days versus 13.4 ± 2.2 days) than in the petrolatum control group. In a review article, Wu et al summarized the results of various clinical trials and concluded that topical use of Xue Jie (Dragon’s Blood) could decrease inflammation and promote wound healing. Almost every study suggests that herbal medicine is an effective treatment for wounds, but most studies are not RCTs, have a small sample size, do not report specific inclusion and exclusion criteria or explicit herbal formula interventions, or lack a description of methods used to evaluate therapeutic effectiveness.

Side Effects of Herbal Medicine in Chronic Wound Care

OM practitioners often apply minerals and toxic materials topically for the treatment of refractory wounds, including mercury powder in the formula of Sheng Ji Yu Hong Gao, which OM practitioners and researchers believe is effective in chronic wound treatment. Sheng Dan (a product with high mercury content) is commonly used in OM wound care. Results of an in vivo study have shown Sheng Dan can effectively modulate IL-2R, IL-6, and TNF, which may promote the growth of granulation tissue. Other minerals and toxic substances used in OM wound care include pearl, succinate, borneol, and amber.

Ingestion of these minerals and toxic substances may cause harm to the human body; external applications have not been reported to be toxic, because with proper preparation and external administration these substances may take a long time to accumulate in the body. It has been proposed that with close surveillance and accurate diagnosis and treatment, therapists could greatly minimize potential adverse events related to the use of minerals and toxic substances. The included studies regarding ordinary herbs for the treatment of chronic wounds either demonstrated that no serious side effects were associated with herb use or did not report or monitor for any side effects.

Explanations of OM Mechanisms of Herbal Medicine in Wound Healing

Modern biomedical researchers have been seeking answers to the therapeutic mechanisms of herbal treatments in wound care. In an in vitro wound healing model, Xu et al found that oral administration of herbal medicine (Buyang Huanwu Decoction) could increase the expression of vascular endothelial growth factor (VEGF) and microvessel count. Cao et al reported that mice treated with herbs demonstrated greater growth of new microvessels, fibroblasts, endothelial growth factor (EGF), transforming growth factor-β1 (TGF-β1), and fibronectin in the granulation tissue. These results were partially echoed by a study by Zhang et al in which researchers found TGF-β1 was significantly higher in the granulation tissue of skin ulcers from diabetic rats treated with internal herb administration than in those without treatment. Furthermore, studies also showed that herbal medicine could modulate the synthesis of collagen in wound healing. In a randomized controlled study using rat models with full-thickness black lesions, Li et al found that Type I collagen was higher while Type II collagen was lower in granulation tissues taken from the herbal treatment group than from the normal saline group.

In a diabetic wound in vivo model, Wang et al found that skin ulcers had low levels of substance P and concluded that herbs could possibly promote wound healing by upregulating the expression of substance P. Li et al found that refractory wounds in patients with diabetes had higher expressions of β-catenin, c-myc, and K6 compared with unwounded skin, and topical use of Hongyou Ointment and Shengji Powder could promote wound healing, which the researchers believed...
was due to decreased expressions of β-catenin, c-myc, and K6 (inhibition of the Wnt signaling pathway).

The herbal formula (NF3) of Radix astragali and Radix rhemanniae and the herbal formula of Shengji Gao (granulation growth paste) are of great interest to researchers. Based on results from zebrafish embryos studied in vivo, rat aortic ring assays in vitro, and in vitro culture of human skin fibroblasts NF3 was found effective in activating Wnt and angiogenesis-related pathways, which are directly related to cell proliferation, angiogenesis, extracellular matrix (ECM) formation, and inflammation during the process of wound healing.36,37 Astragaloside IV was found effective in improving the strength of the repaired skin and promoting angiogenesis and collagen synthesis in a rat skin excision model38; whereas, Radixrehmanniaewas reported effective in promoting diabetic foot ulcer healing in rats through the processes of tissue regeneration, angiogenesis, and inflammation control, but not blood glucose control.39

Shengji Gao (granulation growth paste) is another herbal formula commonly used in refractory wound treatment; Yao et al’s40 clinical trial found Shengji Gao increased microvessel density and granulation tissue protein content and increased the healing rate of chronic wounds compared to wounds treated with petrolatum (P <0.05 or P <0.01 for all measurements). Their results were echoed by two in vivo studies.40,41 Using an infected rabbit wound model, Li et al40 found that compared with petrolatum, Shengji Gao induced more protein and higher pH value in wound exudate, as well as a larger reduction in wound size. However, P values were <0.05 for all comparisons. In the other study,41 researchers found Shengji Gao may enhance wound healing through antibacterial activity.

Studies about the use of other single herbs in wound care have been reported. Using an in vivo model, Tang et al42 found that emodin promoted repair of excisional wounds via a complex mechanism involving stimulation of tissue regeneration and regulating the Smads-mediated TGF-beta signaling pathway. In another in vivo study, Gupta et al43 found Rhodiola imbricata application increased DNA, protein, hydroxyproline, and hexosamine contents in comparison to a positive control treated with povidone-iodine ointment, which also was supported by histological changes of an increase in antioxidant and a decrease in lipid peroxide levels in the granulation tissue. In a rat model,44 topical application of Momordica charantia was found to promote wound closure, increase protein content in wound area, and increase collagen fibers within the granulation tissue compared to a nontreated controls, whereas topical use of Ageratum was found in a rat model to cause fewer inflammatory cells, significant greater wound contraction, and fewer fibroblasts than honey and control treatments.45

Other OM Modalities in Chronic Wound Care

Other OM therapeutic modalities used in wound care consist of acupuncture, moxibustion, and cupping; however, no RCTs that could confirm their safety and efficacy have been found in either English or Chinese journals (see Table 2). In the only clinical acupuncture of a one-case study reported in English, Foell46 found that healing of a refractory leg ulcer coincided with the use of acupuncture in the surrounding tissues. Otherwise, results conflict regarding acupuncture in wound healing in animal studies reported in English. Saarto et al47 reported a single acupuncture treatment immediately after surgery in dogs did not appear to have any beneficial effects in surgical wound healing; however, Uema et al48 found electro-acupuncture (EA) was an efficient method to preserve vitality and decrease dorsal skin flap necrosis in Wistar rats, and Lee et al49 found acupuncture accelerated the skin regeneration process following deep second-degree burns in mice. Furthermore, two interesting phenomena exist regarding EA and cupping therapy. In an animal study, Wang et al50 found EA could regulate Th1 and Th2 cytokines at protein and mRNA levels in splenic T cells. This result was echoed by a review article in which Kim et al51 summarized that EA could modulate various immune responses. In clinical studies, electrical stimulation therapy has been reported effective for treating wounds.52,53 In a RCT with spinal cord injury patients treated with either a standard wound care program that included pressure management or the standard program plus high-voltage pulsed current, Houghton et al52 found that pressure management plus electric stimulation therapy significantly decreased wound surface area of pressure ulcers in 16 spinal cord patients, with a percentage of decrease (mean ± SD, 70% ±25% versus 36% ±61%, P = 0.048) in the control group. Similar effects with electric therapy were reported by Ricci et al53 in which stochastic electrical noise applied to hard-to-heal ulcers for 60 consecutive days reduced wound surface area by an average of 82.5% (SD = 25.2%).

Topical negative pressure has been found to be a non-pharmacological tool that can manipulate the wound healing environment using physical forces54,55; cupping, a technique commonly utilized in OM, also creates topical negative pressure effects.56 Therefore, a combination of EA and electric therapy or a combination of cupping with topical negative pressure therapy may affect chronic wound healing.

According to the NIH Consensus Conference on acupuncture (1998) publication, acupuncture has shown positive results in the management of other conditions such as addiction, stroke rehabilitation, headache, menstrual cramps, tennis elbow, fibromyalgia, myofascial pain, osteoarthritis, low back pain, carpal tunnel syndrome, and asthma.57 In patients with these conditions, acupuncture may be useful as an adjunct treatment, an acceptable alternative, or may be included in a comprehensive management program.41

Other OM modalities also have been found effective, such as massage (called Tui Na in OM) for musculoskeletal pains in a case series of 18 patients,58 Tai Chi for osteoarthritis in a RCT with 20 patients,59 and pursed-lip breathing technique (a modified QI Gong technique) for cardiopulmonary
diseases in a RCT with 32 patients treated. Because many chronic wound patients have concomitant conditions such as those mentioned, it is possible that combined management methods including OM may improve the quality of life in patients with chronic wounds.

Discussion

Overview of chronic wound care in OM. Wound management in OM has a history of more than 2,000 years in eastern Asian countries. In most states in the US, acupuncturists utilize therapeutic modalities of OM, and OM school graduate (herbalists and acupuncturists) practitioners provide herbs for wound care.

Based on the results of various clinical trials and basic research studies, herbal formulas and individual herbs seem effective for the treatment of chronic wounds. Other OM treatment modalities, including acupuncture, Tai Chi, and Chi Gong, also may be useful. However, research studies included in the review barely reported any side effects, and to prove the therapeutic effectiveness of OM in chronic wound management, high-quality randomized, double-blinded, controlled trials still are needed to provide definitive scientific evidence to determine the optimal doses, duration, and time of interventions, as well as the basic therapeutic mechanisms.

Challenges for herbal research. Studies involving herbal formulas and single herbs suggest both have efficacy in wound healing however, herbal formulas are generally believed to be more effective than single herbs and thus are more commonly used in OM for wound treatment. OM theory-based wound management highly values a holistic view and pattern recognition (also called syndrome differentiation), a process used by OM practitioners to gather patient signs, symptoms, and other relevant information to generate a theoretical model for the pathophysiological process of the patient’s condition/disease to generate highly individualized treatments and herbal medicine prescriptions. As such, not many patented herbal products are available for wound care. Some internal (eg, Si Miao Yong An Tang) and external herbal formulas (such as Yuhong Gao) are more commonly used than others. Consequently, many over-the-counter (OTC) herbal products for wound care are available on the Chinese market; these OTC herbal products share similar names or herbal ingredients as those listed in the studies in Table 1. Due to metal/mineral and other toxic components or lack of high-level research evidence, those OTC herbal products are only locally/domestically marketed in China.

Specific ingredients. Active ingredients of individual herbs or herbal formulas used in OM are difficult to identify. Although many single herb extracts are currently available, they may not be the active ingredients in the herbal formulas, which is made of several to dozens of individual herbs. Furthermore, herbal extraction is a complex process, and no standardized methods exist for herbal formulas. For these reasons, presenting active ingredients in the herbal formulas used in clinical trials is difficult, although some promising results have been found in isolated OM herb/mineral research. Extracts of some herbs like Radix astragali (Huang Qi) and Radix rehmanniae (Di Huang) showed therapeutic effectiveness in animal studies. Research isolating artemisinin from the herb Artemisia annua showed the former possesses the most rapid action of all current drugs against Plasmodium falciparum malaria, and Shen et al, in a case series of 15 patients with relapsed acute promyelocytic leukemia, found that arsenic trioxide, a toxic substance used in OM, is an effective intervention for acute promyelocytic leukemia.

Because of the previously mentioned difficulties, information regarding the interaction between herbs and western drugs is still scarce. However, based on the experiences of clinicians, the interaction between herbs and western drugs is usually not significant, and reports of severe side effects related to herbal use in wound care are rare.

Commonly used herbal formulas and single herbs in wound care may bridge OM practices with modern biomedical research studies. In addition, because of the possible benefits of OM in wound care, OM practitioners may be widely included in the future healthcare team to provide integrative wound care for patients in the United States and other Western countries.

Recommendations for Future Research

Although OM herbs are commonly used in Eastern Asian countries for wound care, therapeutic mechanisms and biochemical properties of individual herbs and herbal formulas deserve further exploration and investigation. For a better understanding of OM therapy and possible discovery of new powerful herbal products in wound healing, combined research programs between Western and Eastern medicine are needed to test the therapeutic mechanisms and compare OM management to conventional care in wound healing. The following procedures may be adopted (see Table 3).

Herbal formula selection based on biological activity and clinical application. In this stage, conventional medicine wound specialists and OM wound experts would meet to discuss herbal formulas for wound treatment and efficacy assessment criteria. Treatment principles in wound management typically include enriching Qi and activating blood, dredging body meridians, and protecting against inflammation. Potential herbal formulas include topical use Shengji Gao (also known as Shengji Yuhong Gao) and Si Miao Yong An Decotion for oral administration. As for single prospective herbs, in addition to herbs already mentioned such as Radix astragali (Huang Qi) and Radix rehmanniae (Di Huang), herbs that may be prospective research targets include Radix et Rhizoma Notoginseng (San Qi) and Herb houttuyniae (Yu Xing Cao). With input from wound specialists and literature reviews related to particular herbal formulas or individual herbs, specific herbal formulas can be determined for relevant wound types.
Conducting clinical trials with herbal formulas. The variety of herbs used in wound care is based on OM wound specialist expertise. Herbs including minerals and toxicants have specific rules and guidelines in OM theories and state standards in China. Use of herbs including minerals and toxic herbs under these rules and guidelines is generally considered safe, effective, and legal in China. In addition, OM specialists often are well trained and especially aware of possible adverse events related to herbal use. Herbal formulas can be tested under strict surveillance in clinical trials to assess their efficacy in the treatment of certain types of wounds. If the herbal formula is found effective, the following procedures can be performed.

Isolation and purification of active ingredient from herbal formulas and basic research studies of combined ingredients. So far, extracts have been obtained from many herbs, and techniques for herb extraction seem far advanced; therefore, clinical trials of formulas using herbal and herbal formula extracts are possible. Using the results of these trials, preclinical research is needed to evaluate the effects of single herbal/herbal formula extracts and combined ingredients of the herbal formula without minerals and other substances other countries may consider illegal. Based on preclinical study results, clinical studies can be conducted to establish the pharmacological profile, safety, and efficacy of the active ingredient(s) of a specific herbal formula for a certain type of chronic wound.

With these efforts, clinicians and researchers will have definite answers to the following questions: 1) Is a certain herbal therapy effective in chronic wound care? 2) What is the relationship between herb dosage and efficacy, as well as side effects (if any), and what is the optimal herbal dosage? 3) Do herbal extracts have the same effects? 4) What are the therapeutic mechanisms of herbal treatment? 5) What is the best treatment for a chronic wound: herbal therapy, conventional medicine, or combined herbal therapy with conventional care? A collaboration between academic, research, and clinical institutions of conventional medicine and OM will provide opportunities to better understand OM in wound care and allow for integrated research endeavors to validate specific interventions and perhaps to develop new technologies and new herbal products for chronic wound care.

Conclusion

Based on the results of various clinical trials and basic research studies, herbal medicine seems effective in chronic wound management. Side effects related to OM wound management rarely are reported. OM modalities, especially herbal medicine, may be useful adjunct treatments or acceptable alternatives or included in a comprehensive management program of chronic wounds. However, to prove the therapeutic effectiveness of OM in chronic wound management, further research is needed to determine the optimal doses, duration, and time of interventions, as well as increase understanding about the basic therapeutic mechanisms of OM.

References