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Herbal Treatment For Dermatologic Disorders

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Abstract

Systems of herbal use developed regionally in Europe, the Middle East, Africa, India, China, Japan, Australia, and the Americas. Two well-known systems still in use are the Ayurvedic herbs in India and herb combinations developed as part of traditional Chinese medicine (TCM) in China . In Europe and the United States, use of herbs declined as purified extracts and synthetic chemical drugs became available. In recent years, there has been a resurgence of the use of herbs due to the following reasons: the sideeffects of chemical drugs became apparent, there was a call to return to nature, natural remedies became a part of the green revolution, and there was a return to organic produce. Herbal remedies, including those for skin disorders, are currently gaining popularity among patients and to a lesser degree among physicians. In Asia, especially in China and India, herbal treatments that have been used for centuries are now being studied scientifically. In Germany, the regulatory authority Commission E oversees herbal preparations and their recommended uses . Currently, the United States does not regulate herbal products except as dietary supplements.

INTRODUCTION

Herbal therapy for skin disorders has been used for thousands of years. Even our biologically close relatives, the great apes, use herbal self- medication . Specific herbs and their uses developed regionally, based on locally available plants and through trade in ethnobotanical remedies.

There is no standardization of active ingredients, purity, or concentration. There are also no regulations governing which herbs can be marketed for specific indications.

Included in this review of herbal medications are those medications that show scientific evidence for clinical efficacy, as well as the more common herbs found to be useful in the treatment of dermatologic disorders.

Information regarding the safety of each herb is also included in this article to better enable physicians to decide which herbal therapies they may want to use in practice. Common drug interactions and the side effects of herbal medicines that may be seen in the dermatologic setting are also included in this discussion.

1. BACKGROUND AND CONTEXT

In India, records of Ayurvedic medicine date back to about 3000 BC. The system of Ayurvedic medicine combines physiological and holistic principles. It is based on the concept that the human body consists of five energy elements that also make up the universe: (1) earth, (2) water, (3) fire, (4) air, and (5) space. The interactions of these five elements give rise to the three *doshas* (forces), seven *dhatu*s (tissues), and three *malas* (wasteproducts). All diseases are attributed to an imbalance among the three *doshas*. Diagnosis is made by an elaborate system of examining the physical findings, pulse, and urine, as well as by an eightfold detailed examination to evaluate both the physical and mental aspects of the condition. The treatment is then tailored to suit an individual based on the findings.

Records of TCM date back to about 4000 years. Similar to Ayurvedic medicine, TCM also is aimed at treating the whole person. It is based on the complementary forces *yin* and *yang*. In healthy individuals, *yin* and *yang* are in balance, and illness occurs when there is inequality between the forces.

The Chinese also recognize five elements: (1) earth, (2) water, (3) fire, (4) air, and (5) metal, each related to specific organs. In addition, they recognize a flow of energy, called *chi* or *qi*, through the body in 14 major meridians. The Chinese evaluate the exchange between the environment and the body, such as food, drink, and air into the body and waste leaving the body. Special attention is given to the physical examination of the tongue, iris, and pulses of the individual to determine the cause of the imbalance and then to determine the appropriate individual treatment.

Treatment is usually a mixture of herbs, massage, and acupuncture. An entire textbook on dermatology in TCM is available.

In Western medicine, herbal therapy began as folk medicine. In the United States, it began in the colonial days, when homemade botanicals were used by women at home. Native American use of botanical treatments also greatly influenced the use of herbal therapy in the United States. Iroquois medical botanicals in the northeastern United States became well known to the colonists. In the nineteenth century, these Old World European and Native American traditions were expanded and used by a group of physicians known as the

-eclectics. As herbal medicine continued to develop in the United States, it was further influenced by European and Chinese practices.

Herbal therapy has increased in popularity in the past two decades among patients seeking alternative treatments to conventional Western allopathic medicine. The number of visits to alternative medicine practitioners in the United States has grown rapidly and in 1997 it was estimated to be 629 million, surpassing the number of visits to all primary care physicians (1).

Approximately US\$27 billion was spent on these alternative therapies in

1997, of which US\$3.24 billion was spent on herbal therapy (1). It has been estimated that about 50% of the population uses some form of alternative medicine. Many patients choose not to tell this information to their physicians. The group most likely to use unconventional treatment modalities according to a previous survey consisted of nonblack, college-educated individuals between the ages of 25 and 49 years, having an annual income greater than US\$35,000 (1). Most patients seek alternatives because conventional therapy has failed to help them sufficiently or because they feel there are fewer side effects with the natural products. The recent increase in the use of alternative medicine has led to more research regarding alternatives and requires education of physicians on the subject to enable them to better inform and care for their patients. In the United States, herbal remedies continue to be sold as dietary supplements, with no standards of potency and efficacy required currently. The Dietary Supplement Health and Education Act of 1994 did set purity standards for some commonly used herbs. In Germany, a regulatory authority known as Commission E extensively reviewed common European botanicals. In all, Commission E evaluated the quality of evidence for the clinical efficacy, safety, and uses of 300 herbal preparations. In Germany, this information has led to standardization of herbal treatments. A number of herbal therapies have stood the test of time for their efficacy in treating dermatologic conditions, with a few having significant scientific evidence of usefulness.

HERBAL TREATMENTS FOR DERMATOLOGIC DISORDERS

Most common dermatologic disorders have beneficial herbal treatments available. The disorders are listed in below.

1.1 ACNE

Fruit acids, such as citric, gluconic, gluconolactone, glycolic, malic, and tartaric acids, used topically have demonstrated some effectiveness in treating acne because of their exfoliative properties. In one study, gluconolactone was found to be as effective in clearing inflamed and noninflamed acne lesions as 5% benzoyl peroxide and more effective than placebo. Irritation is the main adverse effect of fruit acids, especially in higher concentrations. When contained in the fruit, they are Class 1.

Tannins have natural astringent properties and are used topically to treat acne. Witch hazel (*Hamamelis virginiana*) bark extract is commonly used as a household remedy by making a decoction from 5 to 10 g of herb in 1 cup (0.24 L) of water. Witch hazel is considered very safe to use topically and is Class 1. Similar astringents can be made from white oak tree bark or the English walnut tree bark. These preparations should be strained before use and can be used two or three times a day. Commercially available preparations are not astringent, as the tannins are lost in the distillation process.

Tea tree oil is an essential oil extracted from the leaves of *Melaleuca alternifolia*, a small tree indigenous to Australia. It contains approximately 100 compounds, mainly plant terpenes and their corresponding alcohols. A study of 124 patients compared 5% tea tree oil in a water-based gel with 5% benzoyl peroxide. Although the tea tree oil did not act as rapidly as benzoyl peroxide, it did show statistical improvement in the number of acne lesions at the end of 3 months, and there was a significantly lower incidence of adverse effects such as dryness, irritation, itching, and burning with tea tree oil (44%) than with benzoyl peroxide (79%). There have been occasional reports of allergic contact dermatitis and of poisoning if taken internally.

However, it is the degradation products of monoterpenes in the tea tree oil that actually appear to be the sensitizing agents. Hence, topical treatment is considered very safe.

Oral administration of vitex (*Vitex agnus-castus*) is effective in treating premenstrual acne. The whole-fruit extract has an amphoteric hormone-regulating effect that is thought to act on follicle-stimulating hormone and luteinizing hormone levels in the pituitary to increase progesterone levels and reduce estrogen levels. It is included in Classes 2b, 2c, and 2d, and may counteract the effectiveness of oral contraceptives. The German Commission E monographs recommend a dose of 40 mg/day. The main adverse effects reported are gastrointestinal tract distress and occurrence of rashes. It should not be taken by pregnant or nursing women.

Bitter herbs that stimulate digestive function, including acid secretion, may improve acne. Commission E also approved topical bitter-sweet nightshade (*Solanum dulcamara*) and orally administered brewer's yeast (*Saccharomyces cerevisiae*, 118) for the treatment of acne because of their antimicrobial effects. Topical duckweed (*Lemna minor*) is used in China to treat acne. Herbal mixtures are also used in China both internally and externally to treat acne.

1.2 ALOPECIA

Essential oils have been studied in a randomized, controlled, double-blind study of 86 patients with alopecia areata. A mixture of essential oils including thyme, rosemary, lavender, and cedarwood in carrier oils with grape seed and jojoba (a liquid wax) was massaged into the scalp daily.

The control group massaged only the carrier oils into the scalp. Success was evaluated on the basis of sequential photographs, by both a six-point scale and a computerized analysis of areas of alopecia. The treatment group had a statistically significant improvement over the control group (44% vs. 15%). There were no reported adverse effects.

A double-blind study that lasted 6 months and in which 396 patients participated evaluated the topical use of a Chinese herbal formula, Dabao (manufactured by Engelbert & Vialle, Venlo, Netherlands), for the treatment of androgenic alopecia. The ingredients of Dabao include 50% ethanol, 42% water, and 8% Chinese herbal extracts, including saffron flowers, mulberry leaves, stemona root, fruits of the pepper plant, sesame leaves, skin of the Szechuan pepper fruit, ginger root, Chinese angelica root, bark of the pseudolarix, and fruit of the

hawthorn plant. The ingredients of the placebo included 50% ethanol, 48% water, and 2% odorizing and coloring agents consisting of cherry laurel water, cinnamon water, licorice syrup, sugar syrup, and a solution of burned sugar. In both groups, there was an increase in nonvellus hairs. Although the Dabao group was statistically superior to the placebo group in number of nonvellus hairs, the cosmetic improvement in both groups was minimal. There were no reported adverse effects. Other TCM herbal mixtures have also been used for alopecia areata

1.3 BACTERIAL AND FUNGAL INFECTIONS OF SKIN

Garlic (*Allium sativum*) contains ajoene, which has been demonstrated to exhibit antifungal activity. In a study of 34 patients treated topically with 0.4% ajoene cream once a day for tinea pedis, 79% noted clearing within 7 days and the remainder reported clearing within 14 days. In a 3-month follow-up, all participants remained free of fungus. Contact dermatitis has occasionally been reported with frequent topical exposure. Oral administration should be avoided while breast-feeding as this is regarded as a Class 2c herb. Prolonged bleeding may occur when garlic is taken orally.

Tea tree oil (see for a description of tea tree oil) is applied topically for treatment of bacterial and fungal infections. Tea tree oil has shown in vitro activity against a wide variety of microorganisms, including *Propionibacterium acnes*, *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans*, *Trichophyton mentagrophytes*, and *Trichophyton rubrum*. Tea tree oil 10% cream was compared in a randomized, double-blind trial of 104 patients with 1% tolnaftate cream and placebo cream. Although symptomatic relief was comparable in tea tree oil and tolnaftate groups, there was significantly greater mycologic cure in the tolnaftate group (85%) than the tea tree oil group (30%). Cure rates between the tea tree oil and placebo groups were not statistically different. Another randomized, double-blind study of 117 patients compared a solution of 100% tea tree oil with 1% clotrimazole solution in the treatment of onychomycosis. The two groups showed comparable results after 6 months of treatment in terms of mycologic cure (11% for clotrimazole and 18% for tea tree oil), clinical assessment, and subjective rating of appearance and symptoms (61% for clotrimazole and 60% for tea tree oil). Tea tree oil may thus have a role in at least the symptomatic treatment of tinea pedis, onychomycosis, and other superficial wounds. However, it should not be used on burns because of its cytolytic effect on epithelial cells and fibroblasts.

Thyme oil from thyme (*Thymus vulgaris*) has been used topically as an antibacterial and an anticandidal agent, and is Class 1. The traditional Korean antifungal herb *Galla rhois* was found to have a methanol extract active against *Candida albicans* (Seong 2007). The TCM herbal mixtures for treating bacterial and fungal infections of the skin are extensively discussed by Xu (2004).

DERMATITIS

Arnica is derived from the dried flowers of *Arnica montana* or other arnica species. Although oral administration can cause severe health hazards even in small amounts, preparations for external use are very safe and effective. Arnica has been used for centuries as an anti-inflammatory drug to rub into sore muscles and joints, bruises, insect bites, boils, inflamed gums, acne eruptions, and hemorrhoids. It is also an ingredient found in many seborrheic dermatitis and psoriasis preparations. It is approved by Commission E for topical treatment of skin inflammation. When used as a compress, 1 tablespoon (tbsp; 15 mL) of tincture is mixed with 0.5 L of water; if used as an infusion, 2 g of dried arnica is mixed with 100 mL of water. Cream or ointment preparations should contain a maximum of 15% arnica oil or 20–25% tincture. The active ingredients of arnica are the sesquiterpene lactones such as helanalin, 11 α ,13-dihydrohelenalin, chamissonolid, and their ester derivatives. These components reduce inflammation by inhibiting the transcription factor nuclear factor κ B (NF- κ B). The factor NF- κ B controls the transcription of many genes, including cytokines such as interleukin (IL)-1, IL-2, IL-6, IL-8, and tumor necrosis factor α , as well as adhesion molecules such as intercellular adhesion molecule 1, vascular cellular adhesion molecule 1, and endothelial leukocyte adhesion molecule 1. It also inhibits many genes responsible for antigen presentation and activation of cyclooxygenase 2. There are reports of contact dermatitis caused by arnica. There are also several reports of irritation when arnica is used at stronger concentrations or for longer periods than are recommended. It is not recommended for use on open wounds or broken skin, and is included in Class 2d. It is important to buy arnica from a reputable source, because it is a protected species in some countries and other plants are substituted fraudulently.

German chamomile (*Matricaria recutita*), a member of the daisy family, has been used for centuries, both internally and externally, for treating many conditions, especially gastrointestinal tract symptoms, oral or skin inflammation, as well as dermatitis. A tea is made by using 2–3 teaspoons (tsp; 10–15 mL) of dried flowers per cup of water and is taken internally or used as a compress. Topical preparations with cream or ointment bases are also used and researched in Germany (Bisset and Wichtl 2001). Studies have demonstrated that topical chamomile is comparable with 0.25% hydrocortisone and shows improvement in sodium lauryl sulfate–induced contact dermatitis). A small double-blind trial found that chamomile significantly decreased the surface area of wounds and, in animal studies, healing time was found to be reduced with chamomile. Chamomile also shows in vitro antimicrobial activities (). The main adverse effect reported is allergic contact dermatitis. Chamomile is considered safe to use topically and orally, and is included in Class 1 (). The anti-inflammatory, wound-healing, and antimicrobial effects of German chamomile are attributed to an essential blue oil that contains sesquiterpene alcohol, α -bisabolol, chamazulene, and flavinoids. These substances showed anti-inflammatory and antispasmodic properties in animal studies, due in part to the inhibition of cyclooxygenase and lipoxygenase in vitro. The flavinoids also act by inhibiting histamine release from antigen-stimulated human basophilic polymorphonuclear leukocytes (). The substance α -isabolol also demonstrated promotion of granulation tissue in wound healing (). Bittersweet nightshade (*S. dulcamara*) and brewer's yeast (*S. cerevisiae*) are thought to have similar anti-inflammatory and antibacterial effects.

Herbal medicine derived from TCM for the treatment of atopic dermatitis has been reported effective by British studies. In TCM, the body is treated as a whole and the aim of therapy is to restore harmony to the functions of the body (). A mixture of various herbs is individually formulated for a patient (), making it difficult to undertake randomized, controlled trials. Two randomized, placebo-controlled crossover trials were performed in England to study the effects of standardized oral herbal TCM in the treatment of atopic dermatitis cases for which traditional Western therapy had failed. The investigators were aided by a Chinese physician who created a standardized mixture of 10 herbs useful for treating atopic dermatitis characterized by erythema, lichenification, and plaques of dermatitis in the absence of active exudation or clinical infection. The 10 herbs used were *Potentilla Chinensis*, Class 1; *Tribulus terrestris*; *Rehmannia glutinosa*, Class 2d; *Lophatherum gracile*; *Clematis armandii*, Class 1; *Ledebouriella saseloides*, Class 1; *Dictamnus dasycarpus*; *Paeonia lactiflora*, Class

1; *Schizonepeta tenuifolia*; and *Glycyrrhizia glabra*, Class 1 (Sheehan and Atherton 1992; McGuffin et al. 1997). These herbs were placed in sachets and boiled to make a decoction that was orally administered daily as a tea. The placebo consisted of a decoction made from several herbs with similar smells and tastes that have no known efficacy in the treatment of atopic dermatitis. The first study with 37 children demonstrated a median decrease in erythema score of 51.0% in the treatment group compared with only a 6.1% improvement in the placebo group. The percentage surface involvement also decreased by 63.1% and 6.2% for the herb-treated and placebo groups, respectively. In this initial study, no serious adverse effects were found. These 37 children were offered continued treatment with the TCM herbal mixture and were then followed up for 1 year (Sheehan and Atherton 1994). Eighteen children completed the year of treatment and showed 90% reduction in eczema activity scores. The children who withdrew from the study did so because of lack of further response to treatment, unpalatability of the tea, or difficulty in preparation of the treatment. By the end of 1 year, seven patients were able to discontinue therapy without relapse. Asymptomatic elevation of aspartate aminotransferase level was noted in two patients, the levels returning to normal after discontinuing treatment. No serious adverse effects were observed. The design was similar in the other study that involved 31 adult patients with atopic dermatitis (Sheehan et al. 1992). The decrease in erythema and surface damage was statistically superior in the herb-treated group compared with the placebo group. There was also subjective improvement in itching and sleep. These patients also were followed up for 1 year, with reports of continued improvement and no serious adverse effects, although the patients who discontinued treatment noted a relapse in their condition (Sheehan and Atherton 1994). Although the sample sizes were limited, initial results were promising for patients for whom standard therapy had failed. The main limiting issue seemed to be the taste and the preparation of the decoction. It should be emphasized that although no serious adverse effects were noted in this study, careful monitoring of complete blood cell count and liver function is recommended, as liver failure and even death have been reported with these TCM herbs when baseline laboratory values were not followed (Graham-Brown 1992; Mostefa-Kara et al. 1992; Koo and Arain 1998). It is known that the specific herbs used in these studies have anti-inflammatory, antibacterial, antifungal, antihistaminic, immunosuppressant, and corticosteroid-like effects. A few of the ingredients are also smooth muscle relaxants, and inhibit the platelet-activating factor. Several studies have attempted to elucidate the mechanism of action of this group of 10 herbs (Zemophyte, manufactured by Phytotech Limited, Godmanchester, England) in treating atopic dermatitis. Patients with atopic dermatitis are known to have

elevated levels of the low-affinity IgE receptor CD23 expressed on circulating monocytes. In studies of IL-4-induced CD23 expression on monocytes, there appeared to be a reduction in CD23 expression when the cells were exposed to the aqueous herb extracts (Latchman et al. 1994, 1996). Another study examined immunologic markers for T cells, macrophages, Langerhans cells, and low-affinity and high-affinity IgE receptors in biopsy specimens of lesional skin treated with Zemophyte compared with biopsy specimens of nonlesional skin (Xu et al. 1997). The investigators found clinical improvement similar to that seen in the aforementioned Sheehan studies, and also found that the improvement was associated with a statistically significant reduction in CD23 antigen-presenting cells. However, an attempt to replicate the Zemophyte double-blind randomized placebo-controlled study in Hong Kong failed to achieve a statistically significant effect of Zemophyte over placebo (Fung et al. 1999). A different TCM herbal mixture called PentaHerbs formula, with *Paeonia suffruticosa* root bark, Class

1; *Phellodendron chinensis* bark, Class 2b; *Lonicera japonica* flower, Class 1; *Mentha haplocalyx* aerial part, Class 1; and *Atractylodes lancea* rhizome Class 1 in a ratio of 2:2:2:1:2, known clinically to be useful in the management of atopic dermatitis, was tested on rat peritoneal mast cells and found to suppress histamine release and prostaglandin D2 synthesis (Chan et al. 2008). The bark of the birch tree (*Betula platyphylla* var. *japonica*), which is used to treat atopic dermatitis, was studied in NC/Nga mice. It decreased scratching and skin inflammation, as well as decreasing IgE and IL-4 messenger ribonucleic acid (mRNA) levels, suggesting that it suppresses the T-helper 2 cellular response (Kim et al. 2008). Other TCM herbal mixes for dermatitis are listed by Xu (2004).

Jewelweed (*Impatiens biflora*) is alleged to be useful topically for treating poison ivy contact dermatitis, but research results are conflicting. In one study, treatment with jewelweed was found to be comparable with standard treatment for poison ivy contact dermatitis, and in 108 of 115 patients studied, the symptoms cleared within 2–3 days (Lipton 1958). However, in another study, jewelweed extract failed to decrease symptoms of poison ivy dermatitis (Guin and Reynolds 1980). In yet another study, no prophylactic effect of jewelweed in treating poison ivy dermatitis was reported (Long, Ballentine, and Marks 1997). Jewelweed has been said to be most effective if applied to the area where the poison ivy touched as soon as possible after contact, but this aspect was not addressed by the aforementioned studies.

There have been no reports of topical jewelweed causing adverse effects (Peirce, Fargis, and Scordato 1999, 365).

Several herbs contain a substance called —mucilage, which is useful topically to soothe and act as an emollient on skin. Heartsease (*Viola tricolor*), Class 1; marshmallow (*Althea officinalis*); English plantain (*Plantago lanceolata*), Class 1; fenugreek (*Trigonella foenum-gaecum*), Class 2b; mullein (*Verbascum thapsus*), Class 1; slippery elm (*Ulmus fulva*), Class 1; and flax (*Linum usitatissimum*) contain mucilages, which act as emollients on and soothe the skin. Mucilage quickly swells into a gooey mass when exposed to water, thereby ameliorating dry or mildly inflamed skin. Mucilage also dries as a mild adhesive and can be used as an herbal bandage for minor wounds (McGuffin et al. 1997; Peirce, Fargis, and Scordato 1999; Fleming 2000).

Oats (*Avena sativa*) have been used topically in baths for hundreds of years for their soothing and antipruritic properties, and they are approved for this use by the German regulatory authority Commission E and are listed as Class 1 (McGuffin et al. 1997; Fleming 2000; Bisset and Wichtl 2001).

Colloidal oatmeal turns to a gooey sticky mass when mixed with liquid which can be used to coat the skin and sealing in moisture. This soothing and moisturizing property is attributed to the gluten content of the plant. This can be useful in treating atopic dermatitis as well as idiopathic pruritus of the elderly.

Pansy flower (*V. tricolor* hybrids) infusion is recommended as a nontoxic treatment for seborrheic dermatitis, especially in infants. The infusion is made by mixing 1–2 tsp of flowers per cup of water and is used as a wet dressing. Salicylic acid in concentrations of about 0.3% appears to be the active ingredient. It also contains saponins and mucilage, which have softening and soothing effects. No adverse effects have been reported with topical use, and pansy is included in Class 1 (McGuffin et al. 1997; Peirce, Fargis, and Scordato 1999).

1.4 HERPES SIMPLEX

Lemon balm (*Melissa officinalis*) is a lemon-scented member of the mint family. An essential oil can be steam-distilled from the cut leaves. Topical uses include treatment of herpes simplex and minor wounds. In a randomized, double-blind trial of 116 patients with herpes simplex lesions, 96% reported complete clearing of lesions at day 8 after using 1% balm extract cream five times a day (Wobling and Leonhardt 1994). In another trial where balm extract was placed on lesions within 72 hours of the onset of symptoms, the size of the lesions and healing time were found to be statistically better in the group treated with balm (Brown and Dattner 1998). Tannin and polyphenols appear to be responsible for the antiviral effect of the balm (Peirce, Fargis, and Scordato 1999). Balm is included in Class 1, and is very safe to use both topically and orally (McGuffin et al. 1997; Peirce, Fargis, and Scordato 1999).

Other herbal preparations that have reported in-vitro activity against herpes simplex include *Echinacea* spp., sweet marjoram, peppermint, and propolis, although clinical studies for the latter three have not yet been performed (Peirce, Fargis, and Scordato 1999). A small, randomized, placebo-controlled crossover clinical trial found no statistically significant differences between *Echinacea* extract of 800 mg twice per day for 6 months and placebo controls in treating recurrent genital herpes (Basch et al. 2005). The TCM herbal mixtures for treating herpes simplex are listed by Xu (2004).

1.5 PSORIASIS

Aloe vera (*Aloe vera*), which is Class 1 internally and Class 2d externally (McGuffin et al. 1997), has been used for centuries in wound healing and was recently found to be a potential treatment for psoriasis. In a double-blind placebo-controlled study, 60 patients with slight to moderate plaque psoriasis were treated topically with either 0.5% hydrophilic aloe cream or placebo. The aloe-treated group showed statistically significant improvement (83.3%) compared with the placebo group (6.6%). There were no adverse effects reported in the treatment group (Syed et al. 1996).

Capsaicin is the main ingredient in cayenne pepper (*C. frutescens*), which is Class 1 internally but Class 2d externally (McGuffin et al. 1997); it has also been studied for the treatment of psoriasis. In vitro, capsaicin was found to inhibit phorbol ester-induced activation of transcription factors NF- κ B and AP-1 (Surh et al. 2000). Two trials showed that 0.025% cream used topically is effective in treating psoriasis. The first study showed a significant decrease in scaling and erythema during a 6-week period in 44 patients with moderate and severe psoriasis (Bernstein et al. 1986). The second was a double-blind study of 197 patients in whom psoriasis was treated with the capsaicin cream four times daily for 6 weeks, with a significant decrease in scaling, thickness, erythema, and pruritus (Ellis et al. 1993). The main adverse effect reported was a brief burning sensation at the application site. Capsaicin is contraindicated on injured skin or near the eyes, and the German authority Commission E suggests it should not be used for more than 2 consecutive days, with a 14-day lapse between applications.

A survey of patients with psoriasis at a large university dermatology practice revealed that 51% of patients used one or more alternative therapeutic modalities (Fleischer et al. 1996). This is consistent with previous Norwegian surveys of patients with psoriasis (Jensen 1990). Herbal therapy is one of the most frequently chosen alternative therapies. Psoriasis has been treated for centuries with herbal preparations, both topical and oral.

There are many herbal preparations composed of furocoumarins, which act as psoralens when combined with ultraviolet A (UV-A, 320–400 nm).

Furocoumarins derived from *Ammi majus* and related plants that produce 8-methoxy-psoralen when applied topically or taken orally intercalate with DNA. Further, when coupled with exposure to UV-A from the sun or an ultraviolet light-box, the photoactivation causes cross-linkages with the thymine in the DNA, inducing cell death (van Wyk and Wink 2004). This, in turn, inhibits hyperproliferation in psoriatic lesions.

One commonly used TCM, *Radix Angelicae dahurica*, included in Class 1 (McGuffin et al. 1997), contains the furocoumarins imperatorin, isoimperatorin, and alloimperatorin. In a study involving 300 patients with psoriasis, this TCM, taken orally, was combined with UV-A therapy and was compared with the standard treatment of psoralen—UV-A with methoxsalen. The efficacy of the two treatments was equivalent; however, there were fewer adverse effects such as nausea and dizziness in the group treated with TCM and UV-A (Koo and Arain 1998). In addition, there are topical preparations made from herbs that show systemic efficacy against psoriasis, but are too toxic when given systemically (Ng 1998). Topical TCM of the plant

Camptotheca acuminata in an open trial including 92 patients with psoriasis found that this TCM was statistically more effective than 1% hydrocortisone. A disadvantage was that allergic contact dermatitis was seen in 9–15% of the patients in the TCM group. Comparison of TCM mixtures in clinical trials is difficult, because the mixture of herbs prescribed varies individually depending on the subtype of psoriasis (–blood-heat type, –blood deficiency dryness type, and –blood stasis type), which is determined in TCM by many findings, including lesions of psoriasis, the pulse, and the condition of the tongue (Koo and Arain 1998). Some types of TCM may act in part on the microcirculation of the psoriatic lesion (Zhang and Gu 2007). Additional TCM herbal mixtures for psoriasis are listed by Xu (2004).

About 5% curcumin is present in turmeric (*Curcuma longa*), which is included in Classes 2b and 2d (McGuffin et al. 1997; see also Chapter 13 on turmeric). Turmeric has been used for centuries in India to provide glow and luster to the skin. It has antimicrobial, antioxidant, astringent, and other useful effects that help to heal wounds and reduce scarring (Chaturvedi 2009). In vitro, the purified turmeric extract curcumin has been found to inhibit phorbol ester-induced activation of transcription factors NF- κ B and AP-1 (Surh et al. 2000). The resulting suppression of phosphorylase kinase activity correlates with the resolution of psoriasis when curcumin is applied topically to the lesions (Heng et al. 2000). Microencapsulation of curcumin reduces the yellow staining produced by application of topical curcumin on the skin, while prolonging the bioavailability of curcumin (Aziz, Peh, and Tan 2007).

Tars have been used for centuries to treat psoriasis. Tars derived from birch (*Betula* spp.), beech (*Fagus* spp.), or juniper (*Juniperus* spp.) trees (van Wyk and Wink 2004) are antipruritic and antiproliferative. They are used in a 5–10% concentration in creams, gels, and soaps. They are photosensitizing compounds, so judicious exposure to sunlight can be beneficial, or they can be used in conjunction with ultraviolet B (UV-B; 250–320 nm) or narrowband UV-B (311 nm).

WOUNDS AND BURNS

Aloe vera (*A. vera*) leaves produce a gel and a juice or latex. The gel is obtained from the central core of the leaf and has been used topically for centuries for the treatment of wounds and burns. The juice or latex is a bitter yellow fluid extracted from the inner leaf skin and is generally sold dried as a powder that has very potent laxative effects (Peirce, Fargis, and Scordato 1999). Several case reports and animal studies demonstrate that aloe vera decreases burning, itching, and scarring associated with radiation dermatitis (Klein and Penneys 1988). Aloe vera was also found to accelerate healing of chronic leg ulcers, surgically induced wounds, and frostbite. The mechanism of action has been studied in vivo in animal studies. Aloe vera decreases thromboxane A₂, thromboxane B₂, and prostaglandin 2 α , which cause vasoconstriction and platelet aggregation. By increasing dermal perfusion, tissue loss from ischemia is reduced (Klein and Penneys 1988). In vitro studies have also demonstrated a carboxypeptidase that inactivates bradykinin, decreasing pain at the treatment site (Fujita and Shosike 1976). Salicylic acid present in aloe vera acts as an analgesic and anti-inflammatory agent by inhibiting prostaglandin production (Robinson, Heggors, and Hagstrom 1982). Magnesium lactate is also present in aloe vera and is thought to be antipruritic by inhibiting histidine decarboxylase, which controls the conversion of histidine to histamine in mast cells (Klein and Penneys 1988). Reduction in inflammation is also thought to result from the immunomodulatory properties of the gel polysaccharides present, especially the acetylated mannans (Reynolds and Dweck 1999). Aloe vera also demonstrates bactericidal and antifungal activity in vitro. The main adverse effect of topical aloe vera gel is that it causes allergic contact dermatitis. There are also reports of delayed healing after laparotomy or a Cesarean section. Taken orally, aloe vera is considered very safe when used properly. It is Class 1 internally and Class 2d externally (McGuffin et al. 1997).

Asiaticoside in low concentrations has been found to enhance the healing of burn wounds, with evidence suggesting that enhanced angiogenesis may occur as a result of stimulation of vascular endothelial growth factor production (Kimura et al. 2008).

Honey has been used topically for centuries to assist healing of wounds, including burns, decubitus ulcers, and infected wounds (Greenwood 1993). It has been found in vitro to have antibacterial and antifungal activity against organisms that commonly infect surgical wounds (Efam and Udoh 1992). A study was performed on nine infants with large, open, culture-positive postoperative wound infections for whom standard treatment consisting of appropriate intravenous antibiotics and cleansing with chlorhexidine for more than 14 days had failed. The wounds were then treated with 5–10 mL of fresh, unprocessed honey twice a day. There was marked clinical improvement by day 5, and by day 21, the wounds were all closed, clean, and

sterile (Vardi et al. 1998). In a randomized controlled trial, honey-impregnated gauze was compared with a polyurethane film (OpSite, manufactured by Smith & Nephew, North Humberside, England) for partial-thickness burns. The honey-treated wounds healed statistically earlier, with a mean of 10.8 days versus 15.3 days for film-treated wounds and with equal numbers of complications such as infection, excessive granulation, and contracture compared with the polyurethane-film-treated wounds (Subrahmanyam 1993). The wound-healing properties of honey are believed to result from the debriding properties of the enzyme catalase, absorption of edema due to honey's hygroscopic properties, its ability to promote granulation and reepithelialization from the wound edges, and its antimicrobial properties (Efam 1988). There have been no reports of significant adverse effects, although there are reports of contact dermatitis to honey (Efam 1988).

Marigold (*Calendula officinalis*) has been used topically since ancient times and is approved by the German regulatory authority Commission E as an antiseptic and for wound healing (Bisset and Wichtl 2001). A topical preparation of marigold continues to be recommended for the treatment of wounds, ulcers, burns, boils, rashes, chapped hands, herpes zoster, and varicose veins. Marigold gargles are used for mouth and throat inflammation (Peirce 1999). Marigold is also widely used as a topical treatment for diaper dermatitis and other mild skin inflammations (Brown and Dattner 1998). The treatment consists of an application several times a day of an ointment or a cream made by mixing 2–5 g of the flower heads with 100 g of ointment. A gargle or lotion is made by mixing 1–2 tsp (5–10 mL) of tincture with 0.25–0.5 L of water (Peirce 1999). The main adverse event is allergic contact dermatitis. No serious adverse effects have been reported, and it is considered safe to use both topically and orally. It is Class 1 (McGuffin et al. 1997). The anti-inflammatory effects of marigold are ascribed to the presence of triterpenoids. In animal studies, *Calendula* was suggested to stimulate granulation and increase glycoproteins and collagen at wound sites (Brown and Dattner 1998). Marigold also shows in vitro antimicrobial and immune-modulating properties (Peirce 1999).

There are many herbs containing tannins that act as astringents, helping to dry oozing and bleeding wounds. Some of the more commonly reported tannin-containing herbs that may be helpful for the topical treatment of wounds include English walnut leaf, goldenrod, Labrador tea, lavender, mullein, oak bark, rhatany, Chinese rhubarb, St. John's wort, and yellow dock.

2. ADVERSE EFFECTS OF HERBAL THERAPY

Herbal therapies vary greatly in their safety class ratings. For example, some are consumed as foods and have high safety ratings, whereas others are highly biologically active and toxic and must be used very carefully. The safety classes of the herbs mentioned in this chapter are addressed in each section, and further discussion of interactions of herbal therapies that may be encountered in dermatology is detailed in the remaining sections of the chapter. Many cutaneous reactions to herbal preparations have been reported, with the most common cutaneous adverse event being allergic contact dermatitis. More serious cutaneous reactions have been reported. Two patients developed erythroderma after using topical herbal treatments for psoriasis and atopic dermatitis, and one patient developed Stevens-Johnson syndrome after taking –golden health blood-purifying tablets, which contained multiple herbs, including red clover, burdock, queen's delight, poke root, prickly ash, sassafras bark, and *Passiflora* (Monk 1986). Bullous and nodular lichen planus were reported to be induced by ingestion of native African herbal medicines (Soyinka 1973). A young woman was also described with leukemia-related Sweet syndrome elicited by a pathergic response to topical arnica cream (Delmonte et al. 1998).

Serious systemic adverse effects have been reported with the use of TCM herbal mixtures for the treatment of dermatologic disorders. The most common are hepatotoxic effects. Although most patients recover without serious consequences as long as the medication is stopped, there have been reports of patients with acute liver failure leading even to death. There are also reports of renal failure and agranulocytosis (Graham-Brown 1992; Mostefa-Kara et al. 1992; Koo and Arain 1998). One patient was described with adult respiratory distress syndrome after administration of a TCM, kamisyoyo-san, for seborrheic dermatitis (Shota et al. 1961). A patient was reported with reversible dilated cardiomyopathy after receiving treatment for her atopic dermatitis with a Chinese herbal tea (Ferguson, Chalmers, and Rowlands 1997). There are also reports of Chinese and Indian herbal medicines containing as contaminants heavy metals, such as lead, arsenic, and mercury. Prescription medications have also been found in over-the-counter herbal formulations from other countries. Some herbs are mislabeled or misidentified.

There are many possible drug interactions with herbs and prescription medications. It is crucial for patients to share information about what herbs, supplements, and other over-the-counter remedies they are taking or applying to their skin with their physicians. The most important drug interactions in the dermatologic setting are the immune-upmodulating effects of *Echinacea*, *Astragalus*, licorice, alfalfa sprouts, and vitamin E, and zinc may decrease the efficacy of corticosteroids and immunosuppressants (Miller 1998). Some herbs are reported to cause hepatic damage, and they should not be used in combination with medications such as methotrexate.

These include many of the ingredients in TCM preparations, as well as *Echinacea*, chaparral, germander, ragwort, and life root (Ferguson,

Chalmers, and Rowlands 1997; Borins 1998). Herbs containing γ -linolenic acid, such as evening primrose oil, which has been used for treating dermatitis, psoriasis, and xerosis, lower the seizure threshold; thus, dosages of anticonvulsants may need to be increased (Ferguson, Chalmers, and Rowlands 1997). Rue (*Ruta graveolens*) and other herbs containing psoralens can cause phototoxic reactions externally on the skin (Eickhorst, Deleo, and Csaposs 2007). In addition to making them aware of the adverse effects already discussed, patients should be counseled on the relative lack of regulation for herbal medicines. There are minimal quality-control requirements currently in place in the United States to ensure the purity, concentration, or safety of herbal supplements. Although herb manufacturers are restricted from making efficacy statements, there are no regulations on claims for what symptoms these herbs can alleviate. In the United States, there are also minimal regulations on which herbs can be restricted in formulations

CAVEATS CONCERNING HERBAL THERAPY AND DERMATOLOGIC SURGERY

Herbs may affect blood coagulation. A number of medicinal herbs contain coumarin, salicylate, or other platelet-inhibiting substances that can increase the risk of interoperative and postoperative bleeding. Some coumarin-containing herbs include danshen (*Salvia miltiorrhiza*), dong quai (*Angelica sinensis*), horse chestnut bark (*Aesculus hippocastanum*), sweet clover (*M. officinalis*), sweet vernal (*Anthoxanthum odoratum*), sweet-scented bedstraw (*Galium triflorum*), tonka beans (*Dipteryx odorata*), vanilla leaf (*Trilisa odoratissima*), and woodruff (*Asperula odorata*). Salicylate-containing herbs include black cohosh (*Cimifuga racemosa*), meadowsweet (*Spirea ulmaria*), poplar bark (*Populus* spp.), sweet birch bark (*Betula* spp.), willow bark (*Salix* spp.), and wintergreen (*Gaultheria procumbens*). Other platelet function inhibitors include bromelain (*Ananas comosus*), cayenne (*C. frutescens*), Chinese skullcap (*Scutellaria baicalensis*), feverfew (*Tanacetum parthenium*), garlic (*A. sativum*), ginger (*Zingiber officinale*), ginkgo (*G. biloba*), ginseng (*Panax ginseng*), onion (*A. cepa*), papain (*Carica papaya*), reishi fruit (*Ganoderma lucidum*), and turmeric (*C. longa*; Pribitkin 2005).

Herbs may also affect blood pressure. Potentially hypertensive plants include black cohosh, ephedra or ma huang (*Ephedra* spp.), licorice (*G. glabra*), and yohimbe (*Pausinystalia yohimbe*). Potentially hypotensive plants include garlic

CONCLUSIONS

Many herbal therapies have been used for centuries, which show good anecdotal results. A few randomized, controlled trials have also demonstrated significant results in the use of herbal therapies for the treatment of dermatologic disorders. Some countries, such as Germany, now require standardization of herbal preparations and specific recommendations as to the use and efficacy of herbs in the treatment of disease. It is important to know what common herbal alternatives exist and which potential adverse effects or interactions can occur to permit more effective counseling of patients.

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