



# HerbClip™

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**File: ■ Dermatology**

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**RE: Use of Herbal Preparations in Dermatology**

Reuter J, Merfort I, Schempp CM. Botanicals in dermatology: an evidence-based review. *Am J Clin Dermatol.* 2010;11(4):247-267.

This review focuses on the scientific evidence for the use of herbal preparations in dermatology.

The authors searched the PubMed database for studies on herbal preparations in dermatology and recovered 1,263 articles. They included all clinical trials in the review, regardless of quality. Each study was classified using the United Kingdom National Health Service's levels of evidence (LOE) system. "Consistent randomized, controlled clinical trials and cohort studies" were classified LOE-A, and "consistent retrospective cohorts, exploratory cohorts, outcomes research, case-control studies, or extrapolations from LOE-A studies" were classified LOE-B. Case series and extrapolations from LOE-B studies were classified LOE-C, and expert opinions were classified LOE-D.

Traditional acne treatments include German chamomile (*Matricaria recutita*), calendula (*Calendula officinalis*), wheat bran (*Triticum aestivum*), witch hazel (*Hamamelis virginiana*), garden daisy (*Bellis perennis*), heartsease (*Viola tricolor*), dandelion (*Taraxacum officinale*), duckweed (*Lemna minor*), and couch grass (*Elymus repens*). Horsetail (*Equisetum* spp.) tea and the "yellow milk from fresh leaves" of Cape aloe (*Aloe ferox*) are used due to their silicic acid and anthranoid constituents, respectively (LOE-D). Germany's Commission E recommends 40 mg/day of chaste tree (*Vitex agnus-castus*) extract for the treatment of acne,<sup>1</sup> but it is not recommended for pregnant or nursing women. Licorice (*Glycyrrhiza glabra*) and usnic acid from usnea (*Usnea barbata*) possess in vitro antibacterial effects against *Propionibacterium acnes*, an anaerobic bacterium involved in the pathogenesis of acne. African basil (*Ocimum gratissimum*) essential oil (2%) prepared in a hydrophilic base reduced acne lesions, but the results were not statistically significant (LOE-B). Commission E approves the topical use of bittersweet nightshade (*Solanum dulcamara*) and oral brewer's yeast (*Saccharomyces cerevisiae*) for acne.<sup>1</sup> Oregon grape (*Mahonia aquifolium*) root is traditionally used to treat "skin eruptions or rashes associated with pustules" and contains antimicrobial compounds, berberine and jatrorrhizine (LOE-D). Berberine reduces sebaceous gland lipogenesis in vivo. Tea tree (*Melaleuca alternifolia*) oil is traditionally used by the Australian aborigines to treat bruises and skin infections, and it possesses antimicrobial and anti-inflammatory properties. Two clinical trials (LOE-A and LOE-B) have demonstrated that tea tree oil effectively treats mild-to-moderate acne.

The acute stage of atopic dermatitis is traditionally treated with cold wet packs made with oak bark (*Quercus* spp.), witch hazel (*Hamamelis virginiana*), black tea (*Camellia sinensis*), and German chamomile. The subacute stage is traditionally treated with creams and ointments made from balloon vine (*Cardiospermum halicacabum*), bittersweet nightshade, witch hazel, and oat straw (*Avena sativa*). In addition, borage (*Borago officinalis*) and evening primrose (*Oenothera biennis*) oils are used topically and internally, and bacterial superinfections are treated topically with chamomile tea and St. John's wort (*Hypericum perforatum*) oil. A double-blind, randomized, controlled clinical trial (RCT) has shown that a cream containing the 'Manzana' variety of chamomile is more effective than 0.5% hydrocortisone cream, but not superior to a placebo cream, in the treatment of atopic dermatitis (LOE-A). Witch hazel possesses antimicrobial effects (LOE-C), as well as anti-inflammatory, hydrating, and barrier-stabilizing effects that make it potentially useful in the maintenance phase of atopic dermatitis. A recent RCT (n=72, LOE-A) found that witch hazel was not effective in treating moderately severe atopic dermatitis. A European St. John's wort cream has demonstrated efficacy in treating atopic dermatitis in an RCT (n=28, LOE-A).

A small clinical trial (n=7, LOE-B) has found that the Kampo medicine drug Shiunko reduces bacterial counts in patients with atopic dermatitis. An open-label clinical trial (n=42) has shown that Oregon grape root cream improves atopic dermatitis (LOE-B). Glycyrrhetic acid from licorice has anti-inflammatory properties in vivo (LOE-D), and a double-blind phase II RCT has found a 2% licorice gel effectively treats atopic dermatitis (n=90, LOE-A). A cream combining 2% glycyrrhetic acid, grape (*Vitis vinifera*) extract, allantoin, and telmestaine improved the symptoms of sodium lauryl sulfate-induced irritant contact dermatitis in a small clinical trial (n=20, LOE-A), and its efficacy in treating atopic dermatitis in adults and children has been demonstrated in three RCTs (LOE-A for all). An open-label trial has shown that drinking one liter per day of oolong tea improves recalcitrant atopic dermatitis (n=121, LOE-B).

The Kampo formula Hochu-ekki-to has been shown to improve the suppression of atopic dermatitis (LOE-C), and Japanese herbal medicine has been shown to improve the blood eosinophil counts and serum immunoglobulin E levels in patients with recalcitrant atopic dermatitis (LOE-D). In one RCT, a traditional Chinese medicine (TCM) improved the quality-of-life of children with atopic dermatitis and decreased their reliance on topical corticosteroid drugs, but symptoms were not significantly improved (LOE-A). Another RCT has found that TCM improves atopic dermatitis symptoms (n=40, LOE-A). Double-blind RCTs have shown that topical sea buckthorn (*Hippophae rhamnoides*), nigella (*Nigella sativa*), and borage oil, as well as an orally administered combination of eleuthero (*Eleutherococcus senticosus*), yarrow (*Achillea millefolium*), and white nettle (*Lamium album*), are not superior to a placebo in the treatment of atopic dermatitis.

Conventional treatment for psoriasis includes the topical application of salicylic acid, found in willow bark (*Salix* spp.) and other plants, and the drug anthralin, which was originally derived from chrysoarobin from the araroba tree (*Andira araroba*, LOE-A). Psoralens like methoxsalen derived from bishop's weed (*Ammi majus*) and other plant sources inhibit abnormal keratinocyte growth and treat psoriasis when co-administered with ultraviolet (UV) A radiation (LOE-A). A recent monograph and review have found Oregon grape root effective in the topical treatment of mild-to-moderate psoriasis (LOE-B), and a recent clinical trial (n=200) has found 10% Oregon grape root cream standardized to 0.1% berberine effective in improving the severity of psoriasis and sufferers' quality-of-life (LOE-A). Avocado oil combined with vitamin B<sub>12</sub> was equivalent to calcipotriene in the topical treatment of psoriasis in a recent study (LOE-A). Topical creams containing 0.01- 0.025% capsaicin from

chili peppers (*Capsicum* spp.) was found to significantly alleviate psoriasis symptoms in two double-blind RCTs (n=197 and n=44, LOE-A for both).

Bitter melon's (*Momordica charantia*) traditional use as a topical psoriasis treatment has not been confirmed in controlled clinical trials. Studies on aloe (*Aloe vera*) in the treatment of psoriasis have produced mixed results. One double-blind RCT of a 0.5% aloe cream found it to be more effective than the placebo (n=60, LOE-A), while another double-blind RCT found "only a modest effect of a commercial, aloin-free" aloe gel that was not superior to the placebo (n=41, LOE-A). The lack of aloin in the latter product may have reduced its efficacy. Oil from the kukui nut tree (*Aleurites moluccanus*) was ineffective against psoriasis in an RCT (n=30, LOE-A). More research is needed to confirm the efficacy of TCM in psoriasis treatment, but a recent RCT has shown efficacy for a TCM preparation containing Radix Scutellariae and Cortex Phellodendri (n=108, LOE-A). A prospective non-randomized study and an RCT have shown efficacy for indigo naturalis powder made from *Baphicacanthus cusia* in the treatment of psoriasis (LOE-B and LOE-A, respectively).

Tea tree oil, hyperforin from St. John's wort, and coriander (*Coriandrum sativum*) oil possess in vitro antimicrobial effects (LOE-D for all). Dodecenal isolated from coriander is effective against *Salmonella choleraesuis*. Japanese Kampo formulations and the following plants have in vitro antimicrobial effects against bacteria and yeasts of dermatological relevance: *Boswellia serrata*, beard lichen, rosemary (*Rosmarinus officinalis*), and sage (*Salvia officinalis*) (LOE-D for all). Snow gum (*Eucalyptus pauciflora*) essential oil possesses broad spectrum antifungal effects against human pathogenic fungi, and an uncontrolled clinical study has shown efficacy against tinea pedis, tinea corpus, and tinea cruris (LOE-B). Garlic (*Allium sativum*) contains the antifungal trisulfur compound ajoene. An uncontrolled study has shown efficacy for ajoene in the treatment of tinea pedis (LOE-B). A double-blind RCT has shown that a cream made with lemon balm (*Melissa officinalis*) is effective in treating recurrent herpes simplex labialis (LOE-A). Podophyllotoxin from mayapple (*Podophyllum peltatum*) is an established treatment for genital warts caused by the human papilloma virus, and a recent RCT has indicated that podophyllotoxin formulated in a solid lipid nanoparticle gel is more effective than standard podophyllotoxin gel (LOE-A). Three multicenter RCTs (total n=1,508) have demonstrated that the standardized green tea extract Polyphenon E (Mitsui Norin Co. Ltd.; Tokyo, Japan) effectively treats external genital and perianal warts (LOE-A). Common warts have been traditionally treated topically with thuja (*Thuja occidentalis*) tincture and greater celandine (*Chelidonium majus*) juice and internally with extracts of echinacea (*Echinacea purpurea*) and eleuthero (LOE-D), but clinical trials are needed for confirmation.

Three small studies that enrolled between 9 and 21 subjects have found that orally and topically administered tropical cabbage palm fern (*Phlebodium aureum*) extract possesses photoprotective effects against UV radiation-induced skin damage, including sunburn (LOE-B for one trial and LOE-C for two trials). Topical sage ointment and witch hazel distillate have anti-inflammatory effects against UV-induced erythema (LOE-A for both). The oral administration of mixed carotenoids and synthetic lycopene has been used to protect against UV-induced erythema (LOE-A and LOE-B, respectively; however, solubilized tomato extract was more protective than synthetic lycopene at 12 weeks at equivalent lycopene dosage). Orally and topically administered green tea extract has demonstrated protective effects against inflammation and carcinogenesis induced by chemicals and UV radiation in multiple studies (LOE-A). Antioxidant theaflavins from black tea and antioxidant compounds in coffee (*Coffea arabica*) extract may also possess photoprotective and chemopreventative effects (LOE-D). A small study (n=30) has found that a cream containing coffee extract is effective against actinic skin damage, including fine lines and wrinkles (LOE-A). In an uncontrolled study, high flavanol cocoa (*Theobroma cacao*) powder reduced UV-induced erythema (LOE-

B). Potential photoprotective agents awaiting confirmation from clinical trials include silymarin from milk thistle (*Silybum marianum*), apigenin, curcumin from turmeric (*Curcuma longa*), proanthocyanidins from grape seeds, rosemary extract, propolis, genistein from soy (*Glycine max*), and pomegranate (*Punica granatum*) (LOE-D for all). Betulin derived from the outer bark of birch (*Betula* spp.) trees was effective in the treatment of actinic keratoses in two prospective clinical trials (LOE-B for both), but RCTs with histological examinations are needed for confirmation. Two double-blind phase II RCTs have demonstrated that topically applied ingenol mebutate from spurge (*Euphorbia peplus*) effectively treats actinic keratoses (LOE-A).

A single-blind clinical trial has indicated that crude onion juice (*Allium cepa*) improves hair growth when compared to tap water, but the study had a high withdrawal rate (LOE-B). A small RCT has found that a product containing beta-sitosterol and saw palmetto (*Serenoa repens*) extract is effective in treating androgenic alopecia (LOE-A), but a larger trial is needed for confirmation. Tropical cabbage fern extract combined with narrowband UVB treatment was more effective in repigmenting the skin of vitiligo patients than narrowband UVB treatment plus placebo in a double-blind RCT (LOE-A). Another double-blind RCT has shown that ginkgo (*Ginkgo biloba*) extract reduced the rate of vitiligo progression and aided repigmentation (LOE-A). Topical applications of German chamomile, calendula, and arnica (*Arnica montana*) have been traditionally used to treat wounds. St. John's wort "is believed to reduce scars by inhibition of keloid formation." Calendula has a long history of use in the treatment of wounds and Germany's Commission E has approved this use.<sup>1</sup> A large prospective RCT has shown that 10% calendula ointment prevents acute radiodermatitis (LOE-A). Hydrotherapy combined with topical arnica was effective in treating chronic venous insufficiency in a double-blind RCT (LOE-A). A systematic review has found four clinical trials that support the use of aloe to treat chronic wounds and burns (LOE-A). Multiple botanical extracts have demonstrated wound healing activity in animal studies that await confirmation in clinical trials, including teak (*Tectona grandis*), *Allamanda cathartica*, *Vitex trifolia*, *Vitex altissima*, Madagascar periwinkle (*Catharanthus roseus*), gotu kola (*Centella asiatica*), and holy basil (*Ocimum sanctum*).

The authors warn, "Virtually all herbal remedies may provoke allergic reactions and several botanicals hold the risk of photosensitization." Cosmetics containing plant extracts have been linked to contact sensitization and phytocontact dermatitis. Furocoumarins like the psoralen methoxsalen are associated with phototoxic reactions. Plants from the Asteraceae family are particularly associated with the risk of allergic contact dermatitis, but the authors comment that the sensitizing effect of arnica "may be overestimated." Oxidized degradation products of monoterpenes in essential oils like tea tree oil and lavender (*Lavandula* spp.) oil are also associated with allergic reactions.

There are many botanical remedies with a long history of traditional use in dermatology, and research has shown efficacy for some. "Many more controlled clinical studies with well-defined botanical extracts and preparations are needed to determine the efficacy and risks of popular plant-derived products in dermatology."

—Marissa Oppel-Sutter, MS

#### Reference

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The American Botanical Council has chosen not to reprint the original article.

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