



Complementary therapy for atopic dermatitis and other allergic skin diseases: facts and controversies

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Abstract The term complementary or alternative medicine encompasses numerous diverse therapeutic concepts, ranging from as herbal medicine, diet with essential fatty acids, and probiotics, to acupuncture. The main focus of these treatment methods is inflammatory skin disease, in particular atopic dermatitis. Although integrative medicine enjoys increasing popularity, particularly in industrialized countries, clinical studies that meet the double-blind, placebo-controlled standard are rare or nonexistent. The aim of this contribution is to provide the various concepts of integrative medicine.

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Complementary or alternative medicine (CAM) is defined as “diagnosis, treatment and/or prevention which complements mainstream medicine by contributing to a common whole, by satisfying a demand not met by orthodoxy or by diversifying the conceptual frameworks of medicine.”¹

Use of CAM

CAM is becoming increasingly popular for the treatment of inflammatory skin diseases, primarily atopic dermatitis (AD). AD is one of the most chronic inflammatory skin diseases, with a prevalence of about 18% to 25% in children.^{2,3} A Danish study that compared the prevalence of AD between children in 1986 and 2001 demonstrated a significant increase.² Other studies verified the increasing incidence worldwide, particularly in industrial nations.⁴⁻⁶

Risk factors are mainly sensitizations to food allergens and inhalation allergens. Other inflammatory skin diseases where CAM becomes more and more popular are contact dermatitis, hand dermatitis, and psoriasis.⁷

CAM encompasses a number of different treatment methods, including acupuncture, homeopathy, diets, probiotics, essential fatty acids, autologous blood injection, bioresonance treatment, aromatherapy, massage therapy, hypnotherapy, and tea and herbal preparations. A series of studies have demonstrated the enormous popularity of CAM in France (49%), Germany (46%), Australia (48.5%), and the United States (34%) among patients with inflammatory skin diseases.^{8,9} The high incidence in France and Germany was verified by an independent study.¹⁰ Taking a look on the physician's site and the preferred treatment regimen, a study that compared treatment patterns in Japan, the United States, and the United Kingdom identified the prescription of alternative remedies to be highest in Japan.¹¹

Usage of CAM does not seem to depend on the type of dermatologic condition¹² but is found to be, in addition to the above-mentioned geographic factors, positively associated with disease severity and duration.^{12,13} A survey executed by the British Broadcasting Corporation as well

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as a Danish study identified higher-educated, middle-aged women as the most frequent users of CAM.^{14,15} Not to be underestimated are the enormous individual and general expenses created by CAM. Total annual costs (US \$) were estimated to be \$13.7 billion in the United States,¹⁶ \$588,000 in Australia,⁹ and \$2.4 billion in the United Kingdom.¹² In a Swiss study including 202 patients from a rehab hospital, 37% indicated use of CAM. The mean age was 26 years, 62% were women, and the average expense was €674 (range, €15 to €6132).¹⁷

Specific treatments

Herbal medicine

Traditional Chinese medicine (TCM) encompasses numerous alternative therapeutic options that can be administered in oral, topical, or injectable forms. An integral part is the use of herbs that are combined in different formulations. Any plant part may be used, such as the root, bark, stem, seeds, flowers, or leaves.

Sheehan conducted one of the first double-blind, placebo-controlled studies with TCM to demonstrate its positive effects for the treatment of AD in both children and adults.^{18,19} Sheehan worked with a Chinese herbalist in London to create a drink mixture composed of at least 10 plant extracts, including *Potentilla chinensis*, *Tribulus terrestris*, *Rehmannia glutinosa*, *Lophatherum gracile*, *Clematis armandii*, *Ledebouriella seseloides*, *Dictamnus dasycarpus*, *Paeonia lactiflora*, *Schizonepeta tenuifolia*, and *Glycyrrhiza glabra* (Zemaphyte). In a crossover study design that included 47 children and 40 adult patients, a significant improvement of erythema and surface involvement by nearly 90% in the adult group and 63% in the children's group was shown in patients who continued treatment for 1 year. Itching and sleep were also improved. Liver and renal function tests demonstrated no abnormalities. In contrast, a subsequent randomized trial with the same mixture in Hong Kong failed to demonstrate any beneficial effect.²⁰

A trial that compared two different preparations of Zemaphyte showed both preparations improved erythema and surface damage.²¹ The composition of these 10 herbs had a modulating effect on dendritic cells from atopic donors, as these dendritic cells exposed to this herbal mixture exhibited diminished stimulatory activity towards autologous antigen-specific and allogeneic T cells while secreting high amounts of interleukin 10 (IL-10).²² A decrease in cutaneous Langerhans cells, circulating serum immunoglobulin E (IgE), and vascular adhesion molecules was also shown.^{23,24}

Other studies that used an herbal combination of *Eleutherococcus senticosus*, *Achillea millefolium*, and *Lamium album* also demonstrated no difference between the verum and placebo group.²⁵ In turn, a randomized, placebo-controlled clinical trial with the capsulated Pentaherb

mixture containing extracts of 5 raw herbs (*Flos lonicerae*, *Herba menthae*, *Cortex moutan*, *Rhizoma atractylodis*, and *Cortex phellodendri*) showed a clear efficacy.²⁶ In another study, in vitro and in vivo immunomodulatory effects on peripheral blood mononuclear cells (PBMC) and reduced secretions of brain-derived neurotrophic factor (BDNF), interferon- γ (IFN- γ) and tumor necrosis factor- α (TNF- α) in response to phytohemagglutinin were noted.²⁷ Modulating effects of Pentaherb on cytokine production was demonstrated in a study with rat peritoneal mast cells, implying that the inhibition of an inflammatory mediator release is part of the therapeutic effect.²⁸

Psoriasis is another common chronic inflammatory skin disease where alternative treatment methods have been studied. TCM commonly classifies psoriasis into the three main syndromes: blood heat, blood dryness, and blood stasis.²⁹ The 10 herbs mostly used in treating psoriasis are *Rehmannia glutinosa*, *Angelica sinensis*, *Salvia miltiorrhiza*, *Dictamnus dasycarpus*, *Smilax glabra*, *Oldenlandia diffusa*, *Lithospermum erythrorhizon*, *Paeonia lactiflora*, *Carthamus tinctorius* and *Glycyrrhiza uralensis*.²⁹ A different mixture of herbs is suggested according to the subtype of psoriasis.

Studies about the effect of these herbs and their combinations are published in the Chinese literature and are uncontrolled. Some of them demonstrated an equivalent to Western traditional approaches.³⁰ Pathophysiologic effects include inhibited secretion of TNF- α from mast cells by *Rehmannia glutinosa*, inhibition of interferon- γ and IL-12 secretion from macrophages by *Salvia miltiorrhiza*, and inhibition of TNF- α , IL-1 α , IL-1 β , and IL-6 from monocytes by *Carthamus tinctorius*.

Adverse effects of herbal drugs include the adulteration of creams with corticosteroids such as dexamethasone.³¹⁻³³ Other documented adverse effects are allergic contact dermatitis, photosensitivity, arsenic and mercury poisoning, Sweet syndrome, pellagra, and Stevens-Johnson syndrome. Recently, reports have mounted about hepatotoxicity of herbal remedies.³⁴ Exacerbations of the treated skin disease also have been reported.³⁵ The pattern of side effects is similar to that observed by the use of conventional medicine.³⁶

Another herb used for treatment of AD is St. John's wort extract (*Hypericum perforatum* L). In a randomized, double-blind, placebo-controlled study with 21 patients, a significant positive therapeutic effect compared with placebo was found for mild-to-moderate atopic eczema.³⁷ In a partially double-blind, randomized study done as a half-side comparison, Kamillosan cream was tested vs 0.5% hydrocortisone cream and the vehicle cream as placebo in patients with moderate AD. After a 2-week treatment, Kamillosan cream showed a mild superiority vs 0.5% hydrocortisone and a marginal difference vs placebo. Kamillosan cream contains chamomile extract as active principle manufactured from the chamomile variety of Manzana. Depending on the composition of ethereal oils, different varieties of chamomile (*Matricaria chamomilla* L)

are distinguished.³⁸ In another study with a topical ointment consisting of *Mahonia aquifolium*, *Viola tricolor*, and *Centella asiatica* for the treatment of mild-to-moderate AD, no statistically significant effect could be demonstrated.³⁹ A lack of efficacy was also found in a study with *Eleutherococcus senticosus*, *Achillea millefolium*, and *Lamium album*.²⁵ A Japanese study investigated the effect of Oolong tea in the management of atopic eczema and found a marked-to-moderate improvement. A good response to treatment was still observed in 54% of the patients tested at 6 months.⁴⁰

No controlled studies have proved the efficacy of other common herbal agents such as *Arnica montana*, *Calendula officinalis*, and *Melaleuca alternifolia* (tea tree); however, reports have been published demonstrating their potency as contact allergens. An experimental study showed that tea tree oil can induce histamine-induced skin inflammation.⁴¹

Indigo naturalis was demonstrated to be of beneficial effect in the treatment of psoriasis.⁴² Another topical treatment successfully tested in a small study was vitamin B₁₂ containing avocado oil.⁴³

Diet with essential fatty acids

The idea that a deficiency in essential fatty acids (EFA) might be important in the pathogenesis of AD arose in 1937 when decreased levels of arachidonic acid were detected in the serum of children with AD.⁴⁴ Healthy human skin is unable to convert linoleic acid into γ -linoleic acid (GLA), the precursor of prostaglandin E₁, due to a lack of δ -6-desaturase. Therefore, when a diet high in GLA is consumed, its metabolic products prostaglandin E₁ and 15-hydroxy-eicosatrienoic acid, which have anti-inflammatory properties, should rise in the skin. Because prostaglandin E₁ is involved in T-cell maturation and differentiation, IgE production might be influenced by prostaglandin E₁, and alleviation of AD might be attained.

A meta-analysis of 22 studies, however, could not confirm that supplementation with GLA has a significant effect on the severity of AD.⁴⁵ A recent study that compared breast-fed children with those who have never been breast-fed found that an increase of AD is concurrent with the duration of breast-feeding. Yet, AD was most often observed in mixed-fed infants. No effect on the development of AD was detected when mothers who breast-fed their infants received GLA supplementation.⁴⁶

Probiotics

Metchnikoff⁴⁷ proposed that many diseases were related to the action of gut bacteria and that consuming lactic acid-producing bacteria was beneficial because it prevented growth of putrefactive bacteria in the gut. At birth, the human body is sterile. Colonization starts with the first breath, and quantity and species vary markedly during the first 2 years of life.⁴⁸ Variations in gastrointestinal flora

during the first 2 years of life have implications for the functional ability of gut flora to optimize the myriad activities in nutrition/metabolism, defense, and development of the immune system. The term “probiotics” has been defined as nonpathogenic microorganisms that exert a positive influence on host health when ingested.

Cesarean section is associated with a decrease in the beneficial obligate anaerobes *Bacteroides* and *Bifidobacterium*, along with an increase in *Clostridium* spp.⁴⁹ Pronounced changes are again noted in breast-fed vs bottle-fed infants.⁵⁰ Breast-fed infants benefit from the immunoregulatory nutrients present; they also benefit from the metabolic (EFAs) and prebiotic (oligosaccharide) effects of breast milk. Furthermore, in many cases, alterations in gut flora precede the development of illness, including atopic diseases.⁵¹ As a consequence, the idea surfaced that gastrointestinal flora can be modified by diet and environmental factors to affect health.⁵²

Nearly 70% of the human immune system is localized in the digestive tract. Gut flora can down-regulate dendritic cell maturation, thus preventing the activation of effector T cells (Th₁ and Th₂).⁵³ Because of the dynamic interplay between gut flora and gut-associated lymphoid tissue, the immunologic response can be modified by dietary change in the form of prebiotics and beneficial bacteria in the form of probiotics.

Prebiotics were first defined a “non-digestible food ingredients that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health.”⁵⁴ Probiotics are defined as products containing a sufficient number of viable organisms to alter the host’s microflora to produce beneficial health effects. Because of the apparent role of probiotics early in life in regulating systemic immunologic development, interest in the effects of probiotics on AD in young children has grown. Lactic acid bacteria, in particular specific *Lactobacilli* and *Bifidobacteria* spp, are the most widely used including *L rhamnosus* GG (LGG).

For the treatment of AD in young children, several studies demonstrated a significant reduction of the Severity Scoring of AD (SCORAD) index. Two studies suggested that probiotics are only effective in children with food sensitization. In a Finnish randomized, controlled study, LGG was effective in preventing the development of eczema in a breast-fed child when the mother was given LGG 4 weeks prenatally and 6 months postnatally. In a double-blind, prospective, randomized study with breast-fed children and cow’s milk allergy, a significant increase of interferon- γ was measured.⁵⁵ Another study that enrolled children with AD, allergic rhinitis, asthma, and food allergies, measured a significant reduction of CD34+ cells.⁵⁶ One effect could also be the stimulation of a low-grade inflammation that supports tolerance.⁵⁷ In a long-term, randomized, double-blind study, the safety of probiotic and prebiotic treatment has been proven.⁵⁸

Acupuncture

Nine kinds of needles are described in ancient acupuncture texts.⁵⁹ The four kinds still applied today are the filiform, bloodletting, cutaneous, and ear needle. In dermatology, the filiform needle is generally used for the points Xuehai (Sp10), Quchi (LI 11), and Zhubin (Ki 9) for the treatment of AD.⁶⁰ In refractory cases, cutaneous needle puncture on the lesion has been reported to be effective.⁶⁰ A related method of acupuncture without using needles, known as moxibustion, has also been reported to be effective.⁶⁰ In combination with an herb cake on the lesion site once a day during a period of 1 week, an improvement occurred after 2 weeks in 55% and a cure in 45%.⁶¹ For the treatment of psoriasis, the stimulation of Dazhui (Du 14), Fengmen (UB 12), Zusanli (St 36), Sanyinjiao (Sp 6), Xuehai (Sp 10), Quichi (LI 11), Weizhong (UB 40), and related points with filiform needles was effective in a study of 61 patients who were resistant to therapy with standardized methods.⁶²

Miscellaneous

Massage therapy resulted in a reduction of redness, scaling, and itching in studies with children with AD.^{63,64} Hypnotherapy was also described as effective in a study with children.⁶⁵ Nevertheless, these studies do not meet the required criteria for clinical studies.

To study the popular method of autologous blood therapy for treating AD in some European countries such as the United Kingdom and Germany, a randomized, double-blind, placebo-controlled study including 30 individuals with AD was performed.⁴³ Beneficial effects were found in the primary outcome measures that were not verified by the secondary patient-rated outcome.

Homeopathy was developed by Samuel Hahnemann (1755-1843) and is based on the law of similars and the law of infinitesimals. It is a regulatory therapy where high dilutions of particular compounds are thought to induce a counter-reaction in the organism. In dermatology, homeopathy is often used in AD, other forms of eczema, psoriasis, and many other conditions. To date, however, there is no convincing evidence of therapeutic effect. There are only a few controlled trials, most of them with negative results. The few studies with positive results have not been reproduced. Acceptance by the patient seems largely based on counseling and emotional care, rather than on objective responses to the homeopathic drugs.⁶⁶

Aroma therapy is also popular, but no studies prove and objectify the beneficial effects reported by patients. However, several reports have been published on contact dermatitis in the context of aromatherapy.^{67,68}

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