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Review

Phytotherapeutic potential of natural herbal medicines for the treatment of mild-to-severe atopic dermatitis: A review of human clinical studies



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ABSTRACT

For many decades, natural herbal medicines, polyherbal formulations and/or decoctions of plant-derived materials have widely been accepted as alternative complementary therapies for the treatment, cure or prevention of a wide range of acute and chronic skin diseases including chronic herpes, prurigo, acute and chronic wounds, psoriasis and atopic dermatitis (AD). This review was aimed to summarize and critically discuss about the therapeutic viability and clinical applicability of natural herbal medicines for the treatment of AD in human. The critical analysis of the literature revealed that oral (in the form of capsules, syrup or granules) and/or topical application (alone or in conjunction with wet-wrap dressing and/or acupuncture) of natural herbal medicines exhibit remarkable potential for the treatment of mild-to-severe AD in adults, children, infants and in the pregnant women. In this review, the clinical efficacy of various herbal formulations such as Chinese herbal therapies, Korean medicines, Iranian medicines, honey, natural herbal oils (coconut oil, olive oil and mineral oil), beeswax, dodder seeds and whey for the treatment of AD has been discussed. The clinical anti-AD efficacy of these complementary therapies has been observed in terms of down-regulation in Scoring Atopic Dermatitis (SCORAD) index, erythematous intensity, Children's Dermatology Life Quality Index (CDLQI), Dermatology Life Quality Index (DLQI), pruritus and itching frequency, transepidermal water loss (TEWL) and expression of AD-mediated chemokines. Conclusively, we recognized that natural herbal medicines demonstrate remarkable clinical efficacy when used alone or in conjunction with other complementary therapies for the treatment of AD in patients of all ages as well as pregnant women.

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Abbreviations: AD, atopic dermatitis; CAMs, complementary and alternative medicines; TNF- α , tumor necrosis factor- α ; IFN- γ , interferon gamma; IL, interleukins; TGF- β 1t, issue growth factor- β 1; IgE, immunoglobulin-E; IgG, immunoglobulin-G; GOT, glutamic oxaloacetic transaminase; GPT, glutamic pyruvic transaminase; NF- κ B, nuclear factor- κ B; MAPK, mitogen-activated protein kinase; TEWL, transepidermal water loss; SCORAD, scoring atopic dermatitis index; EASI, eczema area severity index; QOL, quality of life index; CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; O-SSI, objective-SCORAD severity index; TARC, thymus and activation-regulated chemokine; VCO, virgin coconut oil; VOO, virgin olive oil; TCHM, traditional Chinese herbal medicine; TCHT, traditional Chinese herbal therapy; KM, Korean medicines; TIM, traditional Iranian medicines.

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1. Introduction

Complementary and alternative medicines (CAMs) have been growing throughout the healthcare industry, spurred by patient empowerment within the communities. Historically, allopathic medicines were once considered as the alternative form of treatment because healthcare providers were practitioners who dealt primarily with herbal interventions. The switch from alternative herbal-based medicine to the present allopathic regimens only occurred in the past century. Presently, only 10–30% of healthcare services are being delivered by allopathic practitioners; whereas, the remaining 70–90% of services are still being conquered by the CAMs practising healthcare providers (World Health Organization). These alternative modalities range from self-care according to folk principles to care given in an organized health care system based on a traditional or common practice.

Natural herbal medicines have been numerous used for the treatment of a wide range of acute, chronic and mild-to-severe diseases. Natural medicines have been evidenced to effectively treat various diseases including cancer, gastrointestinal diseases, skin inflammatory disorders, eye infections, blood disorders, joint problems, respiratory issues, urinary tract infections, nerve problems, muscle problems, and bone disorders. Numerous animal and human clinical studies have explored the promising efficacies of natural herbal medicines, herbal products and phytomedicines for the treatment of atopic dermatitis (AD) [1–10].

AD is a type of chronic eczematous skin inflammation characterised by an excessive infiltration of immunoglobulin (Ig)-E, T-lymphocytes and mast cells. The common symptoms of AD include dry inflamed skin, intense pruritus, itching, skin lichenification, sleep disturbance and emotional distress [11,12]. It is a common, often chronic, skin disease that affects a large percentage of the world's population. AD is not restricted to a specific age group, it can occur in any age. Recent studies demonstrated that the prevalence of AD is continuously increasing, affecting 15 to 30% of urban children and 1 to 3% of adults [13–15]. It usually appears during early childhood and periodically relapses throughout the life of a patient [16].

The prime cause of AD is unclear yet; however, it is considered to have a multi-factorial pathogenesis with genetic defects [17–19], immune deregulation, environmental triggers and impaired skin barrier integrity being the principal causative factors [20–22]. For many years, an abnormal T-helper cells adaptive immune response to largely innocuous environmental irritants was considered as the major dynamic in the development of AD [23–25]. Other studies proposed that the skin barrier defects and an abnormal immune response are the highly plausible mechanisms which underline atopic diseases [26,27].

Owing to the complex pathogenic interplay between patient's susceptible genes, skin barrier abnormalities and immune deregulation, there is no absolute therapy for the treatment of AD. Nevertheless, various pharmacological and non-pharmacological approaches including, identification and avoidance of causative allergens, skin hydration (e.g., taking baths or using moisturisers), topical anti-inflammatory or immunosuppressant therapies, antipruritic medications, and anti-bacterial measures (e.g., taking bleach baths, applying antiseptics or disinfectants) have been reported to be very effective either used alone or in combination for the treatment of mild-to-severe AD [28,29]. Mild

clinical cases can potentially be managed with skin care or emollient therapy only; however, moderate-to-severe patients require intensive therapy. It is worth mentioning that these approaches can achieve control over AD with varying degrees; however, several challenges associated with the use of these conventional therapies, which include off-target effects, systemic toxicity, patients' non-adherence, and therapy-related phobia are still debatable. Furthermore, almost every pharmacological agent is associated with various adverse effects and thus their therapeutic feasibility is limited. These drawbacks and shortcomings of conventional pharmacological agents demand the development of CAMs for the treatment of AD with improved patient compliance and therapeutic outcomes and subsequently, minimising off-target adverse effects.

The current review was therefore aimed to summarize the available literature for the pharmaceutical significance and therapeutic feasibility of natural herbal medicines for the treatment of mild-to-severe AD. Various types of herbal medicines used for the treatment of AD, route of administration/application, dosage form, patient information (ages, gender, and severity index), and number of patients involved in clinical trial, experimental model, therapeutic outcomes and the clinical efficacy of herbal medicines have also been critically discussed.

2. Pathophysiology of AD

AD is a typical example of inflammatory skin disease involving complicated inflammatory reaction of the skin particularly, in the epidermal and dermal layers. "Atopic" generally refers to skin allergy due to inherited tendency to develop allergic reactions in response to sensitizing environmental allergens such as pollen, house dust mites, and food allergens; whereas, dermatitis means inflammation of the skin [30]. The common symptoms of AD include dry, inflamed skin, intense pruritus, itching and skin hypersensitivity. In some instances, AD can also cause recurring rashes, persistent scratching, erythematous plaques, and small bumps like blisters that may leak extracellular fluid. In chronic severe cases, AD causes sleep disturbance which may leads to insomnia, psychological and emotional distress, and low quality of life. Patients' elbow folds, back of the knees, and front of the neck or face are the most susceptible parts of the body to develop AD-like skin lesions [28,29]. AD can be grouped into three clinical stages [30]. The first stage can be the AD of infancy that is typically experienced by susceptible infants. It is commonly characterized by the presence of AD-like skin lesions often localised on the face, scalp, and extensor aspects of the arms and legs, and in severe cases, it can also involve the whole body of the infants. These AD-like skin lesions are characterised by erythema, papules, vesicles, excoriations, oozing, and formation of crusts. The second stage is the AD of childhood that commonly occurs in toddlers or older children. At this stage, the AD-like skin lesions often confined to the flexures of the elbows and knees as well as the wrists and the ankles. In general, these AD-like skin lesions become drier and lichenified with excoriations, papules, and nodules at this stage. The third stage is AD of adolescence and adulthood that is typically experienced by the adult patients. At this stage, AD-like skin lesions are typically localised on to the face and neck, head and hands. These types of lesions vary from mild-to-severe skin lesions and required intensive therapy.

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