RESEARCH PAPER

Reimagining Atopic Dermatitis Care with Roots, Leaves and Pills: A Systemic Analysis of Sacred Plans and Scientific Solutions - A Review

Naman Mohan Sharma[1], Priyadarshini Soni[2*], Varsha Raj[3], Lubhan Singh[4], Akansha Singh[5]

[1]Research Scholar, Swami Vivekanand Subharti University, Meerut, U.P. 250005

[2*]Faculty of Pharmacy, Swami Vivekanand Subharti University, Meerut, U.P. 250005.

Email: Priyadarshinisoni274@gmail.com (Corresponding Author)

[3,4,5]Faculty of Pharmacy, Swami Vivekanand Subharti University, Meerut, U.P. 250005

ABSTRACT

Background:

Atopic dermatitis (AD) is a long-lasting inflammatory disease of the skin, which strikes up to 20% of the children and 7% of adults worldwide, and has yearly health care expenses estimated at over 5 billion dollars. Though traditional medicine has been the current method of treatment, there has been increasing interest in the use of plant-based therapies because of the adverse side effects that conventional drugs may have on the human body in the long term.

Purpose:

This paper will aim to examine the overall comparison between plant-based and conventional medicines to treat AD, which will involve the efficacy, safety profiles, mechanism of action and clinical use. This review summarize the existing literature, recent clinical trials, and emerging treatment modalities released up to 2025 with the TC, novel conventional therapies, and evidence-based plant medicines.

Findings:

Traditional interventions, especially topical corticosteroids, have strong short-term effects but have side effects of skin atrophy and systemic absorption in case of long-term use. Plant-based medicines, such as TCM formulations, or individual botanical extracts, demonstrate encouraging anti-inflammatory effects with an overall good safety record of high quality, although the evidence is more lacking.

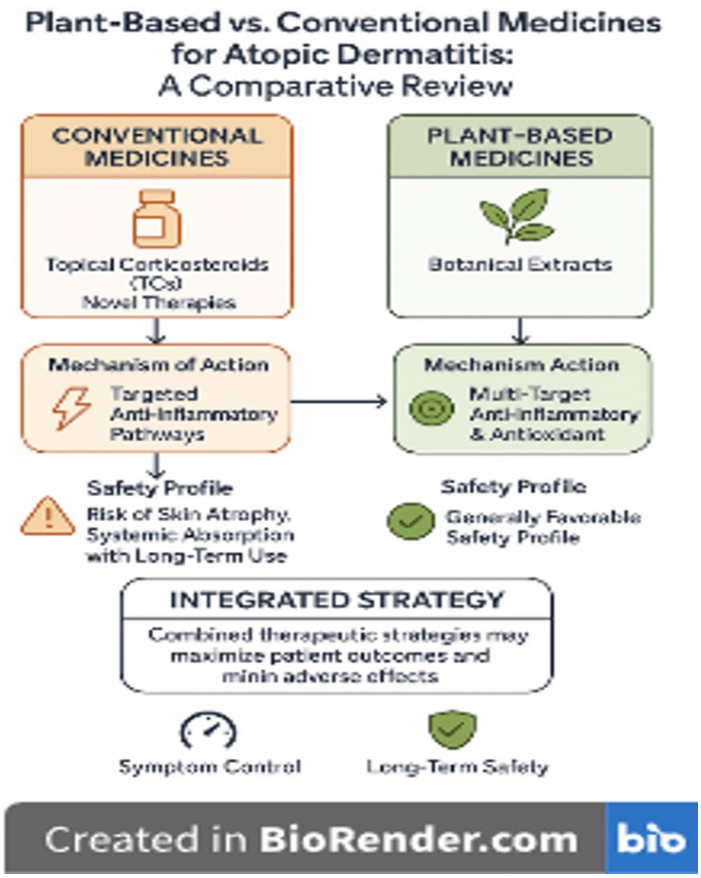
Conclusions:

Each of the two methods has different merits, whereby conventional medicines are fast in controlling the symptoms and plant-based alternative has milder long-term management modalities. Combined strategies could maximize patient outcomes and reduce ill outcomes.

Keywords: atopic dermatitis (AD), topical corticosteroids (TC), Traditional Chinese Medicine(TCM).

How to cite this article: Sharma NM, Soni P, Raj V, Singh L, Singh A. Reimagining Atopic Dermatitis Care with Roots, Leaves and Pills: A Systemic Analysis of Sacred Plans and Scientific Solutions - A Review. Int J Drug Deliv Technol. 2026;16(14s): 840-857. DOI: 10.25258/ijddt.16.14s.96

Figure.1. Graphical Abstract



1. INTRODUCTION

The skin is the largest body organ and the main protective impediment against the environmental hazards and ensures homeostasis through a complex set of physiological activities [1]. The skin is made up of the epidermis, dermis, and hypodermis, which ensure that healthy skin is well hydrated, cool and also monitors immunity [2]. The stratum corneum, the most superficial layer of the epidermis, is a very important permeability barrier made of corneocytes in lipid matrices [2].

Atopic dermatitis (AD), also referred to as eczema, is one of the most widespread chronic inflammatory skin diseases on the global scale. Atopic dermatitis (AD) is a persistent inflammatory skin disorder, which afflicts 20 to 7 percent of children and 7 percent of adults in the world. It is a multifactorial disease, which occurs in all age groups with a high prevalence in pediatric groups where it may have a deep effect on the quality of life of both patients and families[3]. This is a severe pruritus, erythematous lesions and chronic inflammation which may cause insomnia, stigma towards the condition and mental distressness[4].

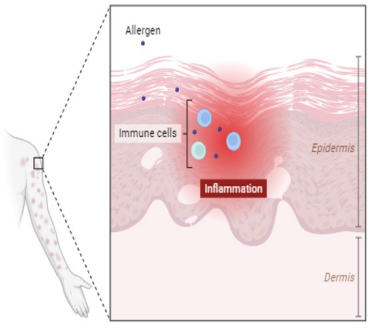


Figure.2. Impact of Atopic dermatitis

THE WORLD DATA ANALYSIS SHOWS THAT:

- Occurs in about 15-20 percent of children and 1-3 percent of adults all over the world [5].
- Increased rates of prevalence seen in developed countries [6].
- In the United States alone, economic cost of 5.3 billion a year [7].
- Preferentially occurs in people of African American and Asian origin [8].

AD is a chronic and apparent condition, which adds further to significant psychological distress, and studies have found that anxiety, depression, and social isolation rates are higher within this group of people [9].

PATHOPHYSIOLOGY

The pathophysiology of AD is characterized by a complicated interplay of genetic predisposition, environmental factors, immune malfunction and skin barrier breakdowns[10]. Atopic dermatitis (AD) is an inflammatory chronic disease of the skin that has been greatly revised in terms of pathophysiology. Conventionally, AD was described by the "inside-out" model in which the triggering event was defined as immune mal-regulation. The Th2 lymphocytic and cytokine domination (IL-4, IL-5, IL-13) was reported to stimulate IgE production, eosinophilic recruitment, and mast cells activation to cause inflammation and itch mediated by histamine[11]. Th1 shift (e.g. IFN-g) was found to facilitate tissue remodeling and lichenification in chronic phases[12]. Barrier dysfunction in the skin was long considered secondary and was caused by impaired keratinocytes due to the action of cytokines and scratching-induced trauma[10]. Modern understandings, however, focus on the theory of the outside-in finding primary epidermal barrier defects to be key initiators. The mutations of filaggrin (FLG) gene and problems with tight junction proteins and lipid metabolism (in particular, ceramides) damage epidermal integrity, resulting in xerosis and allergen penetration increases[13,14]. The alarmins released by damaged keratinocytes (thymic stromal lymphopoietin (TSLP), IL-25, and IL-33) stimulate the type 2 innate lymphoid cells (ILC2s). These cells enhance inflammation through the production of IL-5 and IL-13 preceding the development of adaptive T-cell action[15-17]. The other breakthrough finding is the dysbiosis of microbiome. The AD is worsened by reduced microbial diversity and Staphylococcus aureus overgrowth that causes superantigen release that hyperactivates T-cells, protease-degradation of skin barrier proteins[18,19]. Lastly, itch responses are re-defined, with cytokines as IL-31 and TSLP directly activating sensory neurons, explaining the lack of efficacy of antihistamines and future therapy options. Collectively, these advances indicate that AD is a multifactorial disorder, which combines immune, barrier, microbial, and neuroimmune mechanisms[20,21].

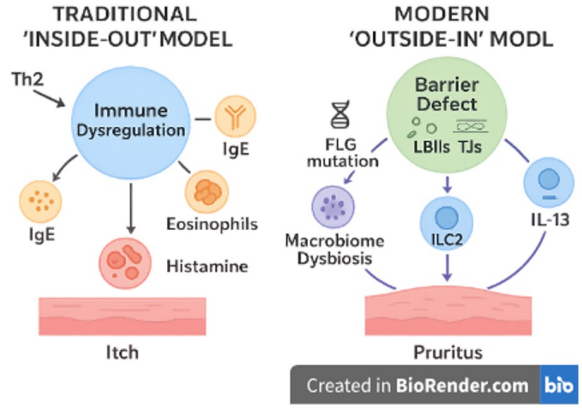


Figure 3. Pathophysiology of atopic dermatitis

Plant and conventional methods of approach

The traditional methods of treatment have developed greatly, as topical corticosteroids have been the mainstay of treatment over decades. Nevertheless, the issue of safety in the long term, as the atrophy of the skin, the inhibition of the hypothalamic-pituitary-adrenal axis, and the development of steroids dependence, has led to the desire to find alternative methods [22]. The last few years have seen the establishment of new conventional therapeutic agents, such as topical calcineurin inhibitors, PDE4 inhibitors, and targeted biologics, with a wider therapeutic armamentarium [23].

Interest in plant-based medicines has at the same time, gone through the roof, due to patient preference of natural medicine, side effects of pharmaceutical drugs, and scientific evidence that indicates the effectiveness of certain botanical interventions. Conventional medicine systems, especially the Traditional Chinese Medicine (TCM), have also made a contribution in this area and some of the herbal formulations have proven to be promising in clinical trials [24].

The purpose of the review is to offer an evidence-based comparison of plant-based and conventional treatments of AD, which are based on their mechanisms, efficacy, safety profiles, and optimal clinical use.

Traditional medical methods

Topical Corticosteroids: Gold methods

Topical corticosteroids (TCS) are the staple of atopic dermatitis (AD) treatment and have been

used to treat the condition over 50 years[25,26]. TCS have been the most commonly prescribed agent against AD since their introduction in dermatology in the 1950s due to their rapid, potent and broad-spectrum anti-inflammatory effects[25-27]. In both an acute flare and in maintenance management of AD, corticosteroids are still considered the so-called gold standard first-line treatment, despite the introduction of newer and more specific targeted therapies, including biologics, JAK inhibitors, and PDE4 inhibitors[28,29]. Their relevance has been secured by their efficacy, comparatively low cost and availability[25,30]. This discussion will give an overview of this pharmacology of TCS, their clinical use in AD, adverse effects, limitations, and recent innovations patented to enhance its safety and efficacy[31-33].

Mechanism of Action:

TCS combine with cytoplasmic glucocorticoid receptors to create complexes which translocate to the nucleus and regulate gene transcription. The result of this process is a reduced synthesis of inflammatory mediators, such as prostaglandins, leukotrienes, and other cytokines of the AD inflammatory cascade [34].

Clinical Efficacy:

Several randomized controlled studies show that TCS have significant activity in the reduction of inflammation, pruritus and severity of lesions in acute and chronic AD [35]. The classification of potencies is Class I (superpotent) to Class VII (least potent) with the ability to apply a specific treatment according to the severity of lesions and anatomical sites [36].

Safety Issues:

TCS is not considered to be very dangerous, but its use can have serious negative effects over the long period. The local complications are atrophy of the skin, striae, telangiectasias and perioral dermatitis[37]. Systemic absorption especially when high potency preparations are used or when used as occlusives, can lead to suppression of the hypothalamic-pituitary-adrenal axis [38].

The recent safety evidence of a 2023 systematic review of long-term TCS use in AD patients also showed that although local side effects appear, they are usually reversible and disappear after the cessation of the treatment. The risk-benefits ratio, however, should be taken into consideration especially in children and in sensitive parts of the body [39].

Topical Calcineurin Inhibitors (TCIs):

Tacrolimus and pimecrolimus are non-steroidal immunomodulators that do not induce skin atrophy and suppress T-cell activation. These agents are especially useful in the face and intertriginous regions as TCS is less safe to use[40].

Innovations are Patented

1. US Patent 6,352,998 B2- Pharmaceutical Compositions

Assignee: Novartis AG

Grant Date: March 5, 2002

Key Innovation: Characterizes topical formulations of emulsions and suspensions based on tacrolimus and other macrolide-based immunosuppressives (FK506 family).

Stabilization: Stabilization of tacrolimus in oil-in-water emulsions with the help of particular solvents (alkane diols, oleyl alcohol, etc.), which enhances the penetration and tolerability.

Clinical Relevance: The formulations are also cosmetic and non-occlusive and hence are especially appropriate in sensitive skin areas like the face and intertriginous areas where corticosteroids induce atrophy.

Evidence on your side: Asserts tacrolimus as a non-steroidal immunomodulator which is used safely in chronic therapy on sensitive skin.

2. EP Patent 1 534 339 B1- The ethanol-free topical pimecrolimus compositions are described in.

Assignee: Novartis AG

Grant Year: 2007 (priority early 2000s)

Critical Innovation: Claims to use pimecrolimus as a single-phase topical gel, foam, semi-solid, without ethanol/water which enhances stability, solubility and penetration into the skin.

Novelty: Vehicles are also lightweight, non-greasy, not-occlusive, to increase patient compliance when used repeatedly on the facial and flexural locations.

Clinical Relevance: Particularly focuses on tolerability and cosmetic acceptability, which address concerns of irritability and greasy residue that older ointments have.

Evidence to your argument: It confirms that pimecrolimus formulations were patented with face/intertriginous application in consideration, the application in which your drug is a safe substitute to corticosteroids in sensitive areas.

PATENT NO.	DRUG	VEHICLE/TYPE FORMULATION	SENSITIVE AREA SUITABLE	OUTCOMES
US Patent 6,352,998 B2	Tacrolimus	oil-in-water emulsions	especially appropriate in sensitive skin areas like the face and intertriginous areas	Asserts tacrolimus as a non-steroidal immunomodulator which is used safely in chronic therapy on sensitive skin
EP Patent 1 534 339 B1	Pimecrolimus	single-phase topical gel, foam, semi-solid, without ethanol/water	facial and flexural locations	It confirms that pimecrolimus formulations were patented with face/intertriginous application and drug is a safe substitute to corticosteroids in sensitive areas

Table.1. Patented innovations

PDE4 Inhibitors:

The latest innovation in the topical AD treatment in 2024 would be the FDA approval of roflumilast 0.15% cream[41]. This phosphodiesterase-4 inhibitor inhibits the production of inflammatory mediators and has an equivalent efficacy to mid-potency corticosteroids without the risks of skin atrophy[42].

JAK Inhibitors:

Topical ruxolitinib is a cytokine signaling pathway JAK-STAT-inhibitor that is approved to be used in AD[43]. This mechanism is a specific approach to the underlying inflammatory cascade, as opposed to the conventional corticosteroids.

Biologic Therapies:

Dupilumab is a monoclonal antibody targeting the IL-4 and IL-13 receptors, which have supplanted the treatment of moderate-to-severe AD[44]. More biologic options. In 2023, tralokinumab-ldrm (Adbry) was approved in children, which also enlarges the scope of biologic agents[45].

Novel Topical Agents:

Tapinarof, an approved aryl hydrocarbon receptor agonist, is a new generation of topical therapy, which regulates immune mechanisms by using environmental sensing signaling[46].

APPROACHES TO PLANT BASED MEDICINES

Formulations of Traditional Chinese Medicine (TCM)

Traditional Chinese Medicine has helped in the development of plant-based AD therapy where a number of standardized preparations have shown clinical effectiveness in clinical trials[47].

Zemaphyte:

Zemaphyte is one of the most widely researched TCM formulations it is a Multi-herb formula, which included Ledebouriella seseloides, Potentilla chinensis, Clematis armandii, Rehmannia glutinosa, Paeonia lactiflora, Lophatherum gracile, Dictamnus dasycarpus, Tribulus terrestris, Glycyrrhiza uralensis and Schisandra chinensis. Its therapeutic potential is exhibited by clinical outcomes which show improvement of up to 60 percent in SCORAD scores, a decrease in reliance on topical corticosteroids as well as enhanced quality of life indicators.[48]

Pentaherbs Formula (PHF)

This five-herb formula Comprising Lonicerae Flos, Mentulae Herba, Cortus Moutanae, Atractylodes Rhizoma, and Bark Ponthelodendron PHF has shown great clinical efficacy. The use of SCORAD has been noted to reduce the SCORAD(Scoring Atopic Dermatitis) scores significantly, owing to its anti-inflammatory and immunomodulatory properties, as reported by randomized controlled trials[49,50]. The formulation is not associated with serious adverse effects and is well tolerated, which can help prove its safety in the pediatric and adult population[49]**.**

Modified Xiaofeng San

It is a traditional formula that contains Saposhnikovia divaricata, Rehmannia glutinosa, Angelica sinensis, Arctium lappa, Sophora flavescens etc. Its effectiveness and safety have been established in AD by high-quality randomized placebo-controlled trials with similar results in terms of disease severity and symptom management[51].

Mechanisms of Action:

TCM preparations normally act on many of the pathways concurrently, such as regulation of Th1/Th2, decreasing the production of inflammatory cytokines, and improving skin barrier functioning[26]. This multi-targeted strategy is in line with the principles of TCM of treating the body as a whole instead of the symptoms[52].

Recent Evidence:

Compounded together, CHM formulations offers a supplemental treatment in the AD therapy. Their

multi-target mechanisms, such as anti-inflammatory, barrier-restorative, and immunomodulatory, have a complex pathophysiology of AD. Nonetheless, standardization of formulations, long term safety, and worldwide acceptance is a big issue that needs to be incorporated into mainstream therapy. A topical Chinese herbal medicine systematic review and meta-analysis study on AD indicate that the intervention is associated with considerable benefits, especially in cases of mild to moderate disease. It was found that TCM formulations worked particularly well as an adjuvant therapy in combination with the conventional therapies[53].

2. KOREAN TRADITIONAL MEDICINE (KTM)

Gamibojungikgitang (GBT):

GBT is a popular multi-herb preparation made of Astragalus membranaceus, Atractylodes macrocephala, Angelica gigas, Poria cocos, Citrus reticulata, Cimicifuga heracleifolia, Bupleurum falcatum and Glycyrrhiza uralensis. According to clinical research, there are major changes in the EASI scores and dramatic changes in the Dermatology Life Quality Index (DLQI), which signify both symptomatic and psychosocial advantages. Mechanically, GBT exhibits immunoregulatory actions, which help to enhance Th1/Th2, and decrease the presence of inflammatory cytokines[54].

Pentaherbs Formula : Korean-modernized

The Korean-modernized version is based on the classical Pentaherbs Formula (PHF) with added Scutellaria baicalensis (Huang Qin) and Cortex Phellodendri (Huang Bai). The additional components increase the anti-inflammatory and antioxidant effects of the formula and expand its therapeutic range. Initial research indicates better clinical effectiveness in the treatment of pruritus, erythema and total severity of the disease and a positive safety profile[55].

MECHANISM OF ACTION

Korean herbal preparations like GBT and PHF have multi-target action in atopic dermatitis. They inhibit Th2-mediated inflammation by lowering IL-4, IL-5 and IL-13 along with the actions of mast cells and eosinophils. Antimicrobial effect (berberine, gallic acid, chlorogenic acid) against Staphylococcus aureus, antimicrobial diversity, increases barrier homeostasis. Both formulae decrease skin thickening, epidermal hyperplasia and mast-cell infiltration in experimental models. Network pharmacology connects their phytochemicals to inhibition of NF-kB, antioxidant activities and enhanced immune response. All of these formulae reestablish the body of skin barrier functionality and regulate immunity, microbiota, and inflammation in AD[55].

Recent evidence

PHF in vitro and ex vivo studies indicate PHF inhibits mast cell and basophil release of inflammatory mediators - mechanistic evidence of diminished instant allergic reactions. In an experimental investigation (Molecules) on berberine (2016), gallic acid and chlorogenic acid were recognized as key anti-inflammatory constituents; oral/topical PHF led to the reduction of epidermal thickening, eosinophil and mast-cell infiltration, and proinflammatory cytokines in models of dermatitis[49,56].

AYURVEDIC POLYHERBAL FORMULATIONS IN ATOPIC DERMATITIS

Ayurveda provides a number of poly-herbal preparations which have anti-inflammatory, immunomodulatory and barrier-restoring effects on the treatment of atopic dermatitis (AD)[57].

Herbavate Topical Formulation

The clinical potential of Herbavate Topical Formulation (Centella asiatica, Juglans regia, Curcuma longa, Azadirachta indica, Wrightia tinctoria) as an alternative medicine using topical application has shown clinical efficacy in the treatment of eczema, which alleviates the symptoms such as erythema, itching, and scaling, and has an excellent safety record in clinical practice[58].

Winsoria Oil

It is an Ayurvedic proprietary formulation that treats psoriasis and eczema with much need and prevents itching, color discoloration, reddening, scaling, and lesions. It has shown clinical effects

in reducing inflammation and regulating skin exfoliation, and its extensive dermatological implications have been indicated[59].

Shirishadi Decoction and Snuhyadi Lepa

It is a classical integrative therapy. The Snuhyadi Lepa (Euphorbia neriifolia, Sesamum indicum) when administered orally as the Shirishadi Decoction (with Albizia lebbeck, Hemidesmus indicus, Tinospora cordifolia) was also effective in improving the Vicharchika (Ayurvedic equivalent of AD), with reduced pruritus, erythema and lichenification. The dual therapy here highlights the synergy of Ayurveda in the systemic and local therapies, which have been proven to be clinically beneficial in AD by systematic reviews[60].

Mechanism of action

In AD, Ayurvedic poly herbal preparations have a multi-target, synergistic mechanism of action. They activate anti-inflammatory and anti-allergic mechanisms by inhibiting degranulation of mast cells, the recruitment of eosinophil as well as Th2 cytokines (IL-4, IL-5, IL-13), thus decreasing pruritus and inflammation. Phytochemicals (e.g., azadirachtin, curcumin, neem limonoids) used as antimicrobial agents prevent the colonization of Staphylococcus aureus and replenish the microbial balance. Restorative herbs like Centella asiatica and Sesamum indicum are used as a barrier because they increase the synthesis of collagen, lipid balance and epidermal repair. Tinospora cordifolia as an oral immunomodulators are used to control systemic immunity and oxidative stress. All these formulations are restorative of the skin barrier, regulate immune responses, re-equilibrium the microbiome, and reduce itch-scratch cycles and provide integrative management of AD[57].

NATURAL THERAPEUTIC AGENTS

Herbs with clinical evidence

Aloe Vera (Aloe barbadensis):

It is a gel of aloe vera, which has more than 75 active compounds, among them, there are anti-inflammatory glycoproteins, polysaccharides, and anthraquinones[58]. Clinical trials show that topical application is associated with considerable gains in the scores of the AD severity, possessing excellent safety rates and very few side effects[59].

Chamomile (Matricaria chamomilla):

German chamomile is a source of anti-inflammatory properties such as chamazulene, bisabolol and flavonoids[60]. Topical preparations of chamomile have demonstrated equivalent effectiveness with low-potency corticosteroids in the treatment of mild-to-moderate AD, and they are better tolerated[61].

Colloidal Oatmeal (Avena sativa):

Oatmeal is an ingredient that is rich in beta-glucans, avenanthramides, and other compounds that have anti-inflammatory and barrier-protective effects[62]. When used as topical preparations, clinical trials show a massive enhancement in skin hydration, barrier functionality, and pruritus[63].

Licorice Root (Glycyrrhiza glabra):

Glycyrrhizin and other related compounds in the licorice root have strong anti-inflammatory activities that inhibit phospholipase A2 and 11b-hydroxysteroid dehydrogenase[64]. Topical licorice extracts have potential as AD inflammation with fewer side effects[65].

Turmeric (Curcuma longa):

The active ingredient in turmeric that is important is curcumin which possesses substantial anti-inflammatory, antioxidant, and antimicrobial activity[66]. Topical and oral preparations of curcumin have both demonstrated some advantage in AD patients, but bioavailability is a restraining factor[67].

Table.2. Natural therapeutic agents

S.NO	PLANTS	ROUTE OF ADMINISTRATION	OUTCOMES
1	ALOE VERA	TOPICAL	Clinical trials indicate that it has great effects in AD severity score done by topical application, as well as excellent safety profiles and little adverse effects.
2	CHAOMILE	TOPICAL	Topical chamomile preparations have demonstrated the same level of efficacy as low-potency corticosteroids in the management of mild-to-moderate AD, and better tolerability profiles.
3	COLLOID OATMEAL	TOPICAL	Clinical trials show that topical preparations of colloid oatmeal improve skin hydration, barrier functioning and pruritus to a significant level.
4	LICORICE ROOT	TOPICAL	Topical licorice preparations are promising in the reduction of AD inflammation with few side effects.
5	TURMERIC	TOPICAL AND ORAL	Both topical and oral preparations of curcumin have been found to be helpful in AD patients but the bioavailability is a limiting factor.

CURRENT USAGES AND DEVELOPMENTS.

Nanoformulations: Enhanced penetration Sustained release Improved stability

Nanoemulsions and lipid-based carriers: nanoemulsions, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), liposomes, ethosomes, transfersomes.

Polymeric nanoparticles (e.g., PLGA-based, chitosan-based) that encapsulate drugs or phytochemicals to improve stability and release profile[68,69]

Hydrogels incorporating nanocarriers, for controlled release, skin hydration, and improved drug depot effect[68].

Mechanisms / Advantages Improved penetration via thickened/damaged skin: Nano-sized particles are able to penetrate through stratum corneum more effectively, or may also bypass the compromised barrier in AD, to access deeper layers, depositing drug / actives[68,70]. Controlled/sustained release: Peak concentration is reduced, thus reducing irritation/side-effects and frequent application[68,69]. Greater stability of phytochemicals, many of which are destroyed by light, oxidation or low solubility. They are guarded by encapsulation[68,71]. Specific delivery of anti-inflammatory drugs: improved reactions and reduced general exposure. As an illustration, nanoparticle-cyclosporine (CsA) in NPs made of PLGA reduced IL-4, IL-5, IFN-g, reduced TEWL, skin thickness and so on in animal models[72,73].

Combination Therapies: Wet-Wrap dressing of herbs extracts. Acupuncture with herbal treatment. Herbal supplementation by probiotics. There is an increase in the use of combination therapies. Wet-wrap dressing with herbal extracts helps to increase the level of hydration and transdermal intake of active ingredients, providing the quick pain relief of inflammation and itching. The combination of acupuncture and herbal therapy has synergetic effects, as it can be used to affect the systemic body immunomodulation and localized skin action[72].

Limitations of Conventional Therapies vs. Advantages of Herbal Formulations in Atopic Dermatitis

Conventional therapies for atopic dermatitis (AD) provide targeted and rapid relief but are often limited by safety concerns, high costs, and restricted accessibility. Topical calcineurin inhibitors such as tacrolimus and pimecrolimus may cause burning and erythema, with long-term malignancy concerns. PDE4 inhibitors like roflumilast and crisaborole carry risks of application site pain, gastrointestinal disturbances, and remain costly with limited long-term data. JAK inhibitors, including topical ruxolitinib, pose risks of systemic absorption leading to infections, thrombosis, or malignancy, requiring close monitoring. Biologics such as dupilumab and tralokinumab have transformed moderate-to-severe AD management, yet they demand subcutaneous injections, are associated with ocular side effects, and remain prohibitively expensive for many populations. Newer agents like tapinarof show promise but lack sufficient long-term safety data.

In contrast, herbal and polyherbal formulations offer several advantages. Their multi-target actions simultaneously modulate inflammation, immune responses, barrier function, and microbiome balance, unlike single-target conventional drugs. They are generally safer for long-term use, even in sensitive skin regions, without risks of atrophy or malignancy. Additionally, they are more affordable, accessible, and culturally acceptable, especially in resource-limited settings. With lower risk of tolerance and holistic benefits such as oxidative balance and barrier repair, natural therapies hold promise as sustainable alternatives or complements to conventional treatments[70-73].

ASPECT	CONVENTIONAL	HERBALS / POLYHERBALS
Efficacy	Deliver speedy, focused therapy	Multi-target inflammatory
Safety	Burns to skin, erythema, infection, malignancy, ocular side effects, systemic toxicity	Generally safe when used long-term, even in sensitive areas; no chance of atrophy or malignancy.
Cost & Accessibility	Expensive (e.g., biologics, PDE4, JAK inhibitors); not very accessible in low-resource countries	Affordable, highly available, particularly in conventional medicine systems
Administration	Topicals (there is a risk of irritation), subcutaneous injections (biologics).	Oral, topical preparation, or decoctions; good patient acceptance.
Long-term use	Safety limited, tolerance limited, and monitoring needed.	Prolonged use is safe; risk of tachyphylaxis (loss of efficacy) is low.
Holistic Benefits	Only symptom control; only narrow action mechanism	Barrier repair, antioxidant effects, overall immune balance, quality of life.
Cultural Acceptance	Appears artificial; restricted traditional acceptance	Basing on Ayurveda/TCM; culturally familiar and accepted.

OUTLOOKS OF PLANT-BASED THERAPEUTICS

Cannabis-Derived Compounds:

Non-psychoactive cannabis compounds (e.g., cannabidiol [CBD]) have potential in the AD therapy by affecting endocannabinoid receptors of inflammation and pruritus[74]. Initial clinical experiments have indicated effectiveness in the treatment of AD severity and related symptoms[75].

In development:

There are a number of plant-based compounds that are in clinical development, such as resveratrol, green tea polyphenols and a range of mushroom extracts. These agents are aimed at various stages of the pathophysiology of AD, including the improvement of the barrier functions or
immune compartment[76].

Mentha spicata(Spearmint)-Derived Compounds:
The anti-inflammatory, antioxidant, and antimicrobial effects of bioactive compounds of Mentha spicata, especially rosmaminic acid, carvone, and flavonoids have been shown to apply to atopic dermatitis (AD). These compounds regulate inflammatory mediators, and lower oxidative stress, and potentially induce skin barrier rejuvenation. There is preliminary research indicating possible applications in relieving pruritus, erythema and barrier dysfunction in AD[76].

In development:
Mentha spicata extracts and individual actives are currently under study use as a dermatological agent. The existing experimental models emphasize their immunomodulatory and skin protective properties, but again, clinical results in AD have not been done extensively as compared to other botanicals. Controlled clinical trials are required to confirm efficacy, optimize compounds (e.g. topical creams, gels or oral supplements), and determine safety profiles of long-term use[75].

COMPARISON ANALYSIS:EFFICACY AND SAFETY

Efficacy Comparison

Acute Treatment:
The conventional therapies, especially the topical corticosteroids, are better in rapid action than most plant-based alternatives[77]. TCS may achieve considerable relief in symptoms in 24-48 hours, whereas plant-based therapies may take weeks to months to achieve maximum effects[78].

Chronic Management:
TCM D Plant-based therapies have shown some specific enhancement in long-term AD management, some TCM formulations have been shown to have sustained effects months post discontinuation of treatment[79]. This is unlike the traditional therapies that in most cases need constant use to sustain their benefits.

Effects of Severity:
Traditionally, conventional treatments prove to be more effective with moderate-to-severe AD, whereas plant-based ones present the best effects with mild-to-moderate disease[45]. The variance can be indicative of the multi-mechanistic yet less aggressive effect of botanical compounds in contrast to the strong pharmaceutical compounds[80].

Safety Profile Comparison

Traditional Therapy Safety:
Traditional therapies are effective, but have also been well documented to be dangerous. TCS may lead to local skin atrophy, the effects of systemic absorption, and the possible dependence on steroids[81]. Other more recent agents, such as JAK inhibitors and biologics, have other safety issues, such as infection risks and potential malignancy associations[82].

Safety of the Plant-Based Therapy:
As a rule, the plant-based therapy has a better safety profile and fewer serious adverse effects[83]. Safety is, however, not universal and there are botanicals that produce an allergic effect, or photosensitivity, or drug interactions[84]. Quality control and standardization are still a major problem in herbal medicine[85].

Pediatric Considerations:
Plant-based treatment has been particularly beneficial in pediatric patients and issues of side effects of conventional therapy are more pronounced in this group of patients[86]. Nevertheless, safety information in children are still low in most botanical agents[87].

Mechanistic Considerations

Single vs Multi-Target Action:
Traditional medicines aim at specific pathways with high potency and plant based medicines have a multi target action with medium potency[88]. This disparity could be the reason why the combination of both strategies can produce better outcomes at times[89].

Resistance and Tolerance:
Topical corticosteroids have been shown to develop tachyphylaxis (decreased response with repeat use) in order to counter this problem[90]. Plant-based therapies seem to have less chance of tolerance development, perhaps because they are multi-component[91].

Table.3. Efficacy and safety comparison

PARAMETERS	CONVENTIONAL THERAPIES	PLANT-BASED / HERBAL THERAPIES
Efficacy - Acute Treatment	Acute Treatment Rapid relief; TCS improve considerably in 24-48 hours old	Slower progression; it may take weeks or months before full response
Efficacy - Chronic Management	The formulation is required to maintain effect and relapse is frequent upon withdrawal	Persistent effects have been observed that last several months after withdrawal of some TCM formulations
Efficacy - Severity	In moderate-to-severe AD	More effective; in mild-to-moderate AD, not so aggressive, but multi-mechanistic
Safety - General	Risks: skin atrophy (TCS), systemic absorption, steroid dependence; JAK inhibitors/biologics are less risky	Substantially fewer side effects; risks: allergic reaction, photosensitivity or herb-drug interactions
Safety - Pediatric Use	Systemic risks and atrophy more intense in the child (androgenic)	Favorable safety in pediatrics; however, no strong child safety data available
Mechanism - Target Specificity	Activity on single or restricted pathways with high potency	Multi-target activities: inflammation, immunity, repair of barriers, oxidative balance
Tolerance/Resistance	Tachyphylaxis seen with TCS (attenuated response with repeat use)	Less chance of tolerance, because of multi-component effect
Quality/Standardization	Controlled dosage formulations (standardized doses)	Major limitation: Quality control and standardization is lacking

CLINICAL USES AND THREAT SYSTEMS

Evidence-Based Treatment Recommendation

Mild AD:

In the case of mild AD plant-based therapies can be used as an initial intervention, especially in those who are attracted to natural treatment or who are worried about the side effects of corticosteroids[92]. The preparation of aloe vera, chamomile and colloidal oatmeal, demonstrates specific opportunities in this context[93].

Moderate AD:

Median AD normally needs traditional therapy to be managed in the first place, and plant-based agents have useful adjuvant functions[94]. There is a specific potential in TCM preparations in combination with low- to moderate-potency topical corticosteroids[95].

Severe AD:

Severe AD usually requires traditional systemic treatment, but the use of vegetable solutions can play an important supportive role[96]. Plant-based maintenance therapy may also have better long-term outcomes in some patients who undergo conventional acute therapy[97].

Integrated Treatment Approaches

Sequential Therapy:

Rapid acute control with conventional agents, followed by maintenance therapy with plant-based therapy could be the best way to improve efficacy and safety[98]. This is a strategy that builds on the fact that the onset of conventional therapies is quick and reduces the risks of long term exposure[99].

Combination Therapy:

The combination of conventional and plant-based therapy can be synergistic[100]. As an illustration, the effectiveness of the combination of low-potency topical corticosteroids and TCM formulations has been found to be better than that of either method by itself[101].

Personalized Medicine:

Selection of treatment must be based on patient preferences, the severity of the disease, age, comorbidities, and previous response to the treatment[102]. Genetic factors in the metabolism and response to treatment are also becoming more commonly accepted as factors of importance[103].

ECONOMIC CONSIDERATIONS

Cost-Effectiveness Analysis

Direct Costs:

Traditional treatments, especially newer biologics, are associated with high direct expenses[107].

Dupilumab therapy is estimated to cost over 30,000 per year, whereas plant-based therapies are estimated to be much cheaper[108].

Nevertheless, this potential increase in expenditures by less medical work can be covered by the increased efficacy of traditional agents in severe disease[109].

Indirect Costs:

AD entails a high indirect cost in terms of lost productivity, caregiver load and diminished quality of life[110].

These indirect costs can be greatly minimized with effective treatment using either of these two methods, albeit comparative economic analysis is not prolific[111].

Healthcare System Impact:

The increasing AD healthcare burden on societies across the globe calls on affordable treatment methods[112].

In particular, plant-based therapies can be of special importance in resource-restricted environments or long-term maintenance therapy[113].

PARAMETER	CONVENTIONAL THERAPIES	PLANT-BASED / HERBAL THERAPIES
Direct Costs	Very high, particularly with biologics (e.g., Dupilumab > $30,000/year)	TCS and topical agents much cheaper in general; cost benefit in long-term use
Cost vs. Efficacy Trade-off	Greater expenditures can be defensible by high efficacy, especially in the case of severe AD	Less potent and slower efficacy; can be most effectively used in mild-moderate or maintenance treatment
Indirect Costs	Reduced lost productivity, caregiver burden, loss of QoL; however, dependence/tolerance flares can add costs	Same effect but sustained control can reduce relapses and hospital stays
Healthcare System Impact	Added to increasing global AD health burden, particularly that of biologics and monitoring requirements	More cost-effective and sustainable in resource-constrained settings; more appropriate to long-term community-based care

Table.4. Cost effective analysis

REGULATORY AND ETHICAL CONSIDERATIONS

Regulatory Frameworks

Traditional Regulation of Drugs:

Traditional AD treatments are thoroughly reviewed by regulatory agencies, manufactured in the same manner, quality controlled, and their safety is monitored[114]. This oversight regulation gives healthcare providers and patients a certain assurance that the products are of quality and safe[115].

Regulation concerning botanical medicine:

The regulation of plant-based medicines is markedly different across the world with some countries considering them as dietary supplements, but others enforcing pharmaceutical quality standards[117]. This regulatory heterogeneity poses a difficulty to quality and consistency assurance of products[118].

Standardization Challenges:

Plant-based medicines also have intrinsic issues in standardization because of natural variability of active compound[119]. These difficulties are being overcome by progressive analytical chemistry and good manufacturing practices, although a lot of work still needs to be done[120].

Safety Monitoring and Quality Control.

The product contains traces of adulteration and contamination.

Adulteration and Contamination:

Plant-based medicines can also have adulterants, contaminants, or unknown pharmaceutical ingredients[121]. Strict quality control procedures, such as the third-party testing and certification schemes are important in guaranteeing the safety of the products[121].

Drug Interactions:

The botanical medicines may interact with traditional medicines in different ways[121]. Medical practitioners need to understand the possible interactions and observe patients appropriately[120].

FUTURE RESEARCH AND DIRECTIONS

Emerging Research Areas

Microbiome-Targeted Therapies:

The increasing recognition of the role of skin microbiome in AD has provided new therapy targets. The conventional and plant-based methods are under development to regulate the skin microbiome in a beneficial way.

Personalized Medicine:

The next stage of drug-genome interaction studies might allow more accurate choice of treatment. This would streamline the traditional and non-traditional therapy options on a case-by-case basis.

Nanotechnology Applications:

Nanotechnology presents chances to improve conventional and plant-based delivery of therapy. New formulations have the potential to enhance bioavailability, decrease side effects and allow local delivery.

Research Priorities

Comparison Effectiveness Research:

They require large comparative effectiveness studies that are carried out over a long period of time to determine the best treatment algorithms that include both traditional and plant-based solutions. These studies must involve the investigation of clinical outcomes, as well as patient-reported measures.

Mechanism-based approach towards drug development:

Evidence of improved learning about AD pathophysiology has still been used to find new therapeutic targets. Synthetic and natural product libraries both can be used in mechanism-based drug discovery.

Pediatric Research:

This is necessary as the prevalence of AD in children is high and thus there is a need to give specific attention to children in research studies. There is a paucity of both conventional and plant-based interventions in pediatric groups on safety and efficacy data.

CLINICALS PRACTICE GUIDELINES and RECOMMENDATIONS

Evidence-Based Treatment Selection

According to the existing evidence, the following guidelines can guide clinical practice:

First-Line Therapy:

Mild AD:

Plant-based interventions (aloe vera, chamomile, colloidal oatmeal) can be viewed as a first-line treatment option, especially with patients who can favor the use of natural treatments.

Moderate AD:

Low-to-moderate topical corticosteroids have potency that are still first-line, and in addition to plant-based adjuvant.

Severe AD:

Topical corticosteroids of high potency are needed or systemic treatment, and plant-based supportive treatment.

Maintenance Therapy:

The plant-based methods have a specific potential in terms of long-term maintenance, which may decrease the need to be under constant conventional therapy and its related side effects.

Special Populations:

Children: A vegetarian therapy can be a safer solution in the long term.

Pregnancy/lactation: Botanical drugs have to be carefully assessed in terms of safety.

Older patients: Take into account the drug interactions and polypharmacy.

Severity / Stage	Conventional Therapies	PLANT BASED/NATURAL THERAPIES	ROLE IN PRACTICES
Mild AD	Not necessarily necessary; low-potency TCS can be used	aloe vera, chamomile, colloidal oatmeal, and other botanical extracts are gentle	may be used as initial standalone treatment of mild disease, particularly where the patient favors a natural treatment
Moderate AD	Low-to-moderate potency topical corticosteroids are still the standard of care	Used as an adjuvant treatment to TCS as a barrier repair, anti-inflammatory, and soothing agent	by itself or with steroids reduced steroid dependence
Severe AD	Topical corticosteroids of high-potency, systemic agents (e.g., JAK inhibitors, biologics)	supporting barrier protection, inflammation control, and reduce relapse reduction Side effects, increased tolerability	Add-on therapy should be used to complement other treatment
Maintenance / Long-Term	High-risk of corticosteroids or systemic use	Strong role in long-term maintenance (e.g., emollient botanicals, polyherbals)	Helps prevent flares, increase remission, and reduce dependence on conventional medication

Table.4. Severity comparison table

Monitoring and Follow-up

Ortiz reports as a patient experiencing no issues with mobility or energy.

Traditional Therapy Surveillance:

- Frequent evaluation in regard to local side effects (skin atrophy, telangiectasias)
- High-potency or long-term TCS Systemic surveillance.
- Immunosuppressive therapies: screening of infection.

Monitoring of plant-based therapy:

The patient does not use medications and drugs that could result in drowsiness and sedation.

- Allergic Evaluation or Sensitization.
- Treatment effectiveness and escalation of therapy monitoring.
- Monitoring interaction of drugs.

CONCLUSION

Treatment of atopic dermatitis has changed considerably to have more choices in both traditional and plant-based therapeutic processes. The traditional medicines especially topical corticosteroids and the emerging targeted therapies show high efficacy and are well-characterised in terms of safety. Long-term side effects and preference of natural treatments by the patient however has led to interest in the use of plant based alternatives.

Plant-based medicines, not only Traditional Chinese Medicine preparations, but also single botanical agents have potential therapeutic utility and are generally safe. Although they might take longer before they become effective, they are shown to be especially useful in the maintenance therapy mode in the long term and might also lead to a decrease in the continuous use of conventional medications.

It can be assumed that the best solution to AD is a personalized treatment option that might include both traditional and plant-based methods. Progressive combination of traditional agents during acute control and maintenance with plant agents or combination methods with the advantages of both therapeutic classes may not only yield a better effect but also reduce the side effects.

The research needs to be conducted on comparative effectiveness, the creation of evidence-based treatment algorithms, and exploration of personalized medicine methods in the future. The safety and efficacy of plant-based medicines are dependent on the quality control and standardization that is still an essential issue that needs to be solved.

Medical professionals are supposed to be aware of traditional and plant based treatment alternatives, taking into account the choice of the patient, acuteness of the illness, and personal risk factors in formulating the treatment strategies. As research and development continue in both fields, future therapies of AD will offer more effective and individualized treatment methods

REFERENCES

1. Proksch E, Brandner JM, Jensen JM. The skin: an indispensable barrier. Exp Dermatol. 2008;17(12):1063-1072
2. Madison KC. Barrier function of the skin: "la raison d'être" of the epidermis. J Invest Dermatol. 2003;121(2):231-241
3. Nutten S. Atopic dermatitis: global epidemiology and risk factors. Ann Nutr Metab. 2015;66 Suppl 1:8-16.
4. Silverberg JI, Hanifin JM. Adult eczema prevalence and associations with asthma and other health and demographic factors: a US population-based study. J Allergy Clin Immunol. 2013;132(5):1132-8.
5. Nutten S. Atopic dermatitis: global epidemiology and risk factors. Ann Nutr Metab. 2015;66(suppl 1):8-16.
6. Asher MI, Montefort S, Björkstén B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet. 2006;368(9537):733-743.
7. Mancini AJ, Kaulback K, Chamlin SL. The socioeconomic impact of atopic dermatitis in the United States: a systematic review. Pediatr Dermatol. 2008;25(1):1-6.
8. Shaw TE, Currie GP, Koudelka CW, Simpson EL. Eczema prevalence in the United States: data from the 2003 National Survey of Children's Health. J Invest Dermatol. 2011;131(1):67-73.
9. Cheng BT, Silverberg JI. Depression and psychological distress in US adults with atopic dermatitis. Ann Allergy Asthma Immunol. 2019;123(2):179-185.
10. Leung DYM, Bieber T. Atopic dermatitis. Lancet. 2003;361(9352):151–60.
11. Hamid Q, Boguniewicz M, Leung DYM. Differential in situ cytokine gene expression in acute versus chronic atopic dermatitis. J Clin Invest. 1994;94(2):870–6.
12. Grewe M, Walther S, Gyufko K, Czech W, Schöpf E, Krutmann J. Analysis of the cytokine pattern expressed in situ in inhalant allergen patch test reactions of atopic dermatitis patients. J Invest Dermatol. 1995;105(4):407–10.
13. Palmer CNA, Irvine AD, Terron-Kwiatkowski A, Zhao Y, Liao H, Lee SP, et al. Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. Nat Genet. 2006;38(4):441–6.
14. De Benedetto A, Rafaels NM, McGirt LY, Ivanov AI, Georas SN, Cheadle C, et al. Tight junction defects in patients with atopic dermatitis. J Allergy Clin Immunol. 2011;127(3):773–86.
15. Soumelis V, Reche PA, Kanzler H, Yuan W, Edward G, Homey B, et al. Human epithelial cells trigger dendritic cell–mediated allergic inflammation by producing TSLP. Nat Immunol. 2002;3(7):673–80.
16. Schmitz J, Owyang A, Oldham E, Song Y, Murphy E, McClanahan TK, et al. IL-33, an interleukin-1-like cytokine that signals via the IL-1 receptor–related protein ST2 and induces T helper type 2–associated cytokines. Immunity. 2005;23(5):479–90.
17. Camelo A, Barlow JL, Drynan LF, Neill DR, Ballantyne SJ, Wong SH, et al. IL-33, IL-25, and TSLP induce a distinct phenotypic and activation profile in human type 2 innate lymphoid cells. Blood Adv. 2017;1(10):577–89.
18. Kong HH, Oh J, Deming C, Conlan S, Grice EA, Beatson MA, et al. Temporal shifts in the skin microbiome associated with disease flares and treatment in children with atopic dermatitis. Genome Res. 2012;22(5):850–9.
19. Leung DYM, Harbeck R, Bina P, Reiser RF, Yang E, Norris DA, et al. Presence of IgE antibodies to staphylococcal exotoxins on the skin of patients with atopic dermatitis. Evidence for a new group of allergens. J Clin Invest. 1993;92(3):1374–80.
20. Dillon SR, Sprecher C, Hammond A, Bilsborough J, Rosenfeld-Franklin M, Presnell SR, et al. Interleukin 31, a cytokine produced by activated T lymphocytes, induces dermatitis in mice. Nat Immunol. 2004;5(7):752–60.
21. Wilson SR, Thé L, Batia LM, Beattie K, Katibah GE, McClain SP, et al. The epithelial

cell–derived atopic dermatitis cytokine TSLP activates neurons to induce itch. Cell. 2013;155(2):285–95.
22. Ference JD, Last AR. Choosing topical corticosteroids. Am Fam Physician. 2009;79(2):135-40.
23. Current and emerging immunobiologic therapies for atopic dermatitis. Drugs Ther Perspect. 2024;40:247-259.
24. Topical Chinese herbal medicine in treating atopic dermatitis: A systematic review and meta-analysis. J Ethnopharmacol. 2023;308:116292.
25. Coondoo A, Phiske M, Verma S, Lahiri K. Side-effects of topical steroids: A long overdue revisit. Indian Dermatol Online J. 2014;5(4):416–25.
26. Sinha A, Sardana K. Topical corticosteroids in dermatology: A review on the evolution of topical formulations, adverse effects, and newer innovations. Indian J Dermatol Venereol Leprol. 2011;77(5):552–67.
27. Burns DA. The history of cortisone and of topical steroids. Clin Exp Dermatol. 1983;8(4):349–58.
28. Katoh N, Saeki H, Imafuku S, et al. Clinical practice guidelines for the management of atopic dermatitis 2021. J Dermatol. 2022;49(12):1292–324.
29. Ashcroft DM, Dimmock P, Garside R, Stein K, Williams HC. Efficacy and tolerability of topical pimecrolimus and tacrolimus in the treatment of atopic dermatitis: meta-analysis of randomized controlled trials. BMJ. 2005;330(7490):516.
30. Hengge UR, Ruzicka T, Schwartz RA, Cork MJ. Adverse effects of topical glucocorticosteroids. J Am Acad Dermatol. 2006;54(1):1–15.
31. Ference JD, Last AR. Choosing topical corticosteroids. Am Fam Physician. 2009;79(2):135–40.
32. Hajar T, Leshem YA, Hanifin JM, Nedorost S, Lio PA, Paller AS. The use of topical corticosteroids for atopic dermatitis in children: A systematic review of adverse effects. J Am Acad Dermatol. 2015;72(4):733–40.
33. Hengge UR, Ruzicka T, Schwartz RA, Cork MJ. Adverse effects of topical glucocorticosteroids. J Am Acad Dermatol. 2006;54(1):1–15.
34. Rhen T, Cidlowski JA. Antiinflammatory action of glucocorticoids--new mechanisms for old drugs. N Engl J Med. 2005;353(16):1711-23.
35. Hoare C, Li Wan Po A, Williams H. Systematic review of treatments for atopic eczema. Health Technol Assess. 2000;4(37):1-191.
36. Topical Corticosteroids: Choice and Application. Am Fam Physician. 2021;103(6):337-343.
37. Corticosteroids for Atopic Dermatitis. American Academy of Pediatrics.
38. Tempark T, Phatarakijnirund V, Chatproedprai S, et al. Exogenous Cushing's syndrome due to topical corticosteroid application: case series and review literature. Endocrine. 2010;38(3):328-34.
39. Harvey A, et al. The long-term safety of topical corticosteroids in atopic dermatitis: A systematic review. Skin Health Dis. 2023;3(4):e268.
40. Paller AS, et al. Tacrolimus ointment is more effective than pimecrolimus cream with a similar safety profile in the treatment of atopic dermatitis: results from 3 randomized, comparative studies. J Am Acad Dermatol. 2005;52(5):810-22.
41. 2024 Eczema Treatment Roundup. National Eczema Association. 2025.
42. 2024 Key Insights: Atopic Dermatitis. Dermatology Times. 2025.
43. FDA approves Opzelura (ruxolitinib) cream for atopic dermatitis. FDA News Release. 2021.
44. Simpson EL, et al. Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis. N Engl J Med. 2016;375(24):2335-2348.
45. Atopic Dermatitis Market Forecast Report 2025-2034. Globe Newswire. 2025.
46. Advances in Atopic Dermatitis: A 2024 Recap and 2025 Outlook. DermSquared.
- Zhao Y, Guo C, Zhang H, et al. Chinese herbal medicine for atopic

dermatitis: A systematic review and meta-analysis. *Dermatol Ther (Heidelb).* 2021;11(4):1229–44.

- Sheehan MP, Rustin MH, Atherton DJ, et al. Efficacy of traditional Chinese herbal therapy in adult atopic dermatitis. *Lancet.* 1992;340(8810):13–7.
- Hon KL, Leung TF, Ng PC, et al. Pentaherbs capsule as a treatment option for atopic dermatitis in children: an RCT. *J Altern Complement Med.* 2011;17(2):109–14.
- Li XM, Brown L. Efficacy and mechanisms of Pentaherbs Formula in eczema. *Molecules.* 2016;21(4):519.
- Xie Y, Zhuang Y, He T, et al. Modified Xiaofeng San in the treatment of atopic dermatitis: A systematic review. *Complement Ther Med.* 2015;23(3):469–76.
- Bae JM, Choi YY, Park CO, et al. Herbal medicine for atopic dermatitis: An evidence-based systematic review. *Allergy Asthma Immunol Res.* 2013;5(6):461–70.
- Tan HY, Zhang AL, Chen D, et al. Chinese herbal medicine for atopic dermatitis: A systematic review. *Australas J Dermatol.* 2013;54(4):241–52.
- Kim J, Lee J, Kim J, et al. Gamibojungikgitang improves symptoms and quality of life in atopic dermatitis: A clinical trial. *J Ethnopharmacol.* 2014;155(1):145–51.
- Park JH, Lee J, Kim JH. Korean Pentaherbs Formula and atopic dermatitis: pharmacological insights. *Phytomedicine.* 2017;24:1–9.
- Li XM, Sampson HA. Berberine, gallic acid, and chlorogenic acid as anti-inflammatory agents in experimental dermatitis. *Molecules.* 2016;21(4):519.
- Patwardhan B, Vaidya AD, Chorghade M. Ayurveda and natural products drug discovery. *Curr Sci.* 2004;86(6):789–99.
- Kaur C, Sarkar R, Sharma S, et al. Clinical evaluation of a polyherbal topical formulation (Herbavate) in the management of eczema. *J Altern Complement Med.* 2009;15(11):1189–94.
- Winsoria Oil: Proprietary Ayurvedic formulation for dermatological disorders. *Ayurveda Pharmacol Rev.* 2012;6(2):89–94.
- Sharma PV, Dash B. Clinical evaluation of Shirishadi decoction and Snuhyadi Lepa in eczema (Vicharchika). *AYU.* 2010;31(2):196–200.

47. Reuter J, et al. Botanicals in dermatology: an evidence-based review. Am J Clin Dermatol. 2010;11(4):247-67.
48. Home treatment and remedies for eczema (atopic dermatitis). Medical News Today. 2025. Available at: https://www.medicalnewstoday.com/articles/324228
49. Singh O, et al. Chamomile (Matricaria chamomilla L.): An overview. Pharmacogn Rev. 2011;5(9):82-95.
50. Patzelt-Wenczler R, Ponce-Pöschl E. Proof of efficacy of Kamillosan(R) cream in atopic eczema. Eur J Med Res. 2000;5(4):171-5.
51. Reynertson KA, et al. Bioactive depsides and anthocyanidins from jaboticaba (Myrciaria cauliflora). J Nat Prod. 2006;69(8):1228-30.
52. Reynertson KA, et al. Anti-inflammatory activities of colloidal oatmeal (Avena sativa) contribute to the effectiveness of oats in treatment of itch associated with dry, irritated skin. J Drugs Dermatol. 2015;14(1):43-8.
53. Saeedi M, et al. Herbal treatment of atopic dermatitis: A comprehensive review. Biomed Pharmacother. 2019;110:293-303.
54. Reuter J, et al. Investigation of the anti-inflammatory potential of Aloe vera gel (97.5%) in the ultraviolet erythema test. Skin Pharmacol Physiol. 2010;23(1):40-59.

55. Vaughn AR, et al. The role of curcumin in dermatologic disease: A review of the literature. J Am Acad Dermatol. 2016;75(4):814-821.
56. Antiga E, et al. Oral curcumin (Meriva) is effective as an adjuvant treatment and is able to reduce IL-22 serum levels in patients with psoriasis vulgaris. Biomed Res Int. 2015;2015:283634.
57. Bonifácio BV, Silva GMM, Santos JBC, et al. Nanotechnology-based drug delivery systems and herbal drugs: a review. *Pharmaceutical Nanotechnology.* 2013;1(4):227–43. (PMC) ["Nanosized drug delivery systems for herbal drugs can potentially enhance the biological activity and overcome problems associated with plant medicines."] PMC
58. Jalili A, Dinarvand R, et al. Current advances in nanotechnology-mediated delivery of phyto/herbal medicines. *Frontiers in Pharmacology / related review.* 2023. [Outlines types of nanocarriers (lipid, polymeric, hydrogels) and challenges] PMC
59. Khogta S, Bansal H, Bansal G. Herbal nano-formulations for topical delivery: a review. *Journal of Controlled Release / related*. 2020. [Examines nanoformulation penetration in skin] ScienceDirect
60. Puspadewi R, Nurhayati I, et al. Nanoparticle-Encapsulated Plant Polyphenols and Flavonoids: Enhanced stability, bioavailability, and skin penetration. *Pharmaceuticals (MDPI).* 2025. [Discusses how encapsulation improves stability & penetration] MDPI
61. Win SY, Lee BJ, et al. Encapsulation of Cyclosporine A-Loaded PLGA Nanospheres: controlled release and anti-inflammatory effect. *ACS Omega.* 2024. [Example of nanoparticle CsA design, though not specifically AD] ACS Publications
62. Tang L, Wang Q, et al. Immunosuppressive activity of size-controlled PEG-PLGA nanoparticles with cyclosporine. *Journal / PMC article.* 2012. [Demonstrates that CsA in PEG-PLGA NPs retains immunosuppressive effect]
63. Eberlein B, et al. Adjuvant treatment of atopic dermatitis: assessment of an emollient containing N-palmitoylethanolamine (ATOPA study). J Eur Acad Dermatol Venereol. 2008;22(1):73-82.
64. Natural Products and Their Derivatives as Anti-inflammatory Agents. MDPI. 2023. Available at: https://www.mdpi.com/2079-6382/12/2/243
65. Berth-Jones J, Damstra RJ, Golsch S, et al. Twice weekly fluticasone propionate added to emollient maintenance treatment to reduce risk of relapse in atopic dermatitis: randomised, double blind, parallel group study. BMJ. 2003;326(7403):1367.
66. Enshaieh S, et al. The efficacy of 5% topical tea tree oil gel in mild to moderate acne vulgaris: a randomized, double-blind placebo-controlled study. Indian J Dermatol Venereol Leprol. 2007;73(1):22-5.
67. Hon KL, et al. Long-term efficacy and safety of a Chinese herbal formula (Pentaherb) for childhood eczema. Br J Dermatol. 2008;158(2):394-6.
68. Hanifin JM, et al. Long-term safety and efficacy of topical tacrolimus for the treatment of atopic dermatitis in children. J Am Acad Dermatol. 2005;53(2 Suppl 2):S240-51.
69. Severity Assessment Tools for Atopic Dermatitis. National Eczema Association.
70. Hajar T, et al. A systematic review of topical corticosteroid withdrawal ("steroid addiction") in patients with atopic dermatitis and other dermatoses. J Am Acad Dermatol. 2015;72(3):541-9.e2.
71. Safety of JAK inhibitors in dermatology: Current evidence and future considerations. J Am Acad Dermatol. 2023;89(4):783-791.
72. Ernst E, White AR. The BBC survey of complementary medicine use in the UK. Complement Ther Med. 2000;8(1):32-6.
73. Zaccara S, et al. Phototoxic reactions to herbal remedies. Dermatol Online J. 2016;22(1):13030/qt7rq4n3p8.
74. Quality Control Methods for Medicinal Plant Materials. World Health Organization.
75. Zhang W, et al. Traditional Chinese medicine for children with atopic dermatitis: A

systematic review. Complement Ther Med. 2013;21(4):253-9.
76. Safety considerations for herbal medicines in pediatric dermatology. Pediatr Dermatol. 2020;37(5):823-828.
77. ulti-target approaches in drug discovery for inflammatory diseases. Drug Discov Today. 2019;24(7):1337-1350.
78. Integrative approaches to atopic dermatitis treatment. Integr Med Res. 2018;7(4):297-308.
79. Hajar T, et al. A systematic review of topical corticosteroid withdrawal ("steroid addiction") in patients with atopic dermatitis and other dermatoses. J Am Acad Dermatol. 2015;72(3):541-9.e2.
80. Tolerance development in herbal medicine: A systematic review. Phytother Res. 2018;32(10):1883-1900.
81. First-line treatments for atopic dermatitis. Am Fam Physician. 2020;101(10):590-598.
82. Evidence-based treatment of atopic dermatitis with topical therapies. J Am Acad Dermatol. 2014;71(1):116-32.
83. Moderate atopic dermatitis treatment approaches. Dermatol Ther. 2021;34(6):e15087.
84. Combined treatment approaches in atopic dermatitis. Curr Opin Allergy Clin Immunol. 2019;19(4):349-356.
85. Severe atopic dermatitis: Management strategies and emerging therapies. J Allergy Clin Immunol Pract. 2018;6(4):1162-1172.
86. Long-term management of atopic dermatitis: A systematic approach. Dermatol Clin. 2017;35(3):301-313.
87. Sequential therapy in dermatology: Optimizing treatment outcomes. J Am Acad Dermatol. 2016;74(6):1071-1077.
88. Treatment sequencing in atopic dermatitis. Curr Allergy Asthma Rep. 2020;20(7):32.
89. Combination therapies in atopic dermatitis: A comprehensive review. Dermatol Ther. 2018;31(6):e12715.
90. Synergistic effects of combined conventional and herbal treatments. Integr Med Res. 2017;6(3):283-291.
91. Personalized treatment approaches in atopic dermatitis. J Allergy Clin Immunol. 2019;143(5):1751-1764.
92. Pharmacogenomics in dermatology: Current applications and future directions. Pharmacogenomics. 2018;19(16):1287-1297.
93. Economic burden of atopic dermatitis in adults: A systematic review. J Am Acad Dermatol. 2018;78(4):653-672.e7.
94. Cost-effectiveness of dupilumab for atopic dermatitis. Pharmacoeconomics. 2019;37(8):1043-1054.
95. Healthcare utilization and costs in atopic dermatitis. J Allergy Clin Immunol Pract. 2017;5(4):1064-1072.e5.
96. Indirect costs of atopic dermatitis: A systematic review. Br J Dermatol. 2016;175(5):919-930.
97. Economic evaluations of treatments for atopic dermatitis: A systematic review. Pharmacoeconomics. 2020;38(5):479-502.
98. Global burden of atopic dermatitis: Economic implications. Allergy. 2018;73(8):1631-1645.
99. Cost-effective approaches to atopic dermatitis in resource-limited settings. Int J Dermatol. 2019;58(9):1031-1038.
100. Regulatory oversight of topical dermatologic drugs. FDA Guidance.
101. Quality assurance in pharmaceutical manufacturing. WHO Technical Report Series.
102. Regulatory frameworks for herbal medicines: A global perspective. WHO.
103. Harmonization of herbal medicine regulations. Drug Inf J. 2012;46(4):425-435.
104. Standardization of herbal medicines: Current status and future prospects. Evid Based Complement Alternat Med. 2013;2013:454783.
105. Good manufacturing practices for herbal medicines. WHO Guidelines.
106. Adulteration of herbal medicines: Current status and mitigation strategies. Phytother Res. 2020;34(11):2872-2886.
107. Quality control of herbal medicines: Third-party testing and certification. J Pharm Biomed Anal. 2019;174:273-279.

108. Herb-drug interactions: Clinical relevance and mechanisms. Br J Clin Pharmacol. 2019;85(1):1-18.
109. Monitoring herb-drug interactions in clinical practice. Drug Saf. 2018;41(4):347-364.
110. Skin microbiome in atopic dermatitis: Therapeutic implications. Microorganisms. 2020;8(5):728.
111. Microbiome-targeted therapies for atopic dermatitis. Front Immunol. 2021;12:676274.
112. Pharmacogenomics of atopic dermatitis treatments. Pharmacogenomics J. 2020;20(3):392-405.
113. Biomarkers for personalized atopic dermatitis treatment. J Allergy Clin Immunol. 2021;147(4):1345-1354.
114. Nanotechnology in dermatology: Current applications and future prospects. Nanomedicine. 2019;14(9):1213-1233.
115. Nanoformulations for topical drug delivery in dermatology. Expert Opin Drug Deliv. 2018;15(10):1003-1022.
116. Comparative effectiveness research in dermatology: Current state and future directions. J Invest Dermatol. 2017;137(12):2498-2502.
117. Patient-reported outcomes in atopic dermatitis research. Dermatitis. 2018;29(5):238-242.
118. Novel therapeutic targets in atopic dermatitis. Nat Rev Drug Discov. 2019;18(2):99-120.
119. Natural product drug discovery for inflammatory skin diseases. Drug Discov Today. 2020;25(11):1996-2008.
120. Pediatric atopic dermatitis: Current understanding and future research priorities. J Allergy Clin Immunol. 2020;145(4):1102-1109.
121. Safety of atopic dermatitis treatments in pediatric populations. Pediatr Dermatol. 2019;36(6):855-862.