



Atopic Dermatitis: Advances in Pathogenesis, Management, and Future Directions

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Authors' contributions

This work was carried out in collaboration among all authors. Author AAM conceived and designed the study. Authors AAO and MJA collected the data and conducted the experiments. Author AMS analyzed the results. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The goal of this review is to give a complete update on atopic dermatitis (AD), including its causes, risk factors, symptoms, diagnosis, and treatment. It will focus on new treatments and future directions in personalised care.

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Study Design: This is a narrative review of the most recent research on the genetic, immunological, and environmental factors that cause AD and the new ways to treat it.

Place and Duration of Study: The review took place at the Department of Dialysis Technique at Northern Technical University from January to May 2025.

Methodology: The review looks at genetic predisposition, immune dysregulation, and environmental triggers in a study that used databases like PubMed, Scopus, and ScienceDirect. It talks about clinical diagnostic criteria, differential diagnoses, treatment options, non-drug strategies, and daily habits that can help prevent the disease.

Results: There is evidence that both a weak skin barrier and Immunodeficiency play a role in the development of AD. Mutations in the filaggrin gene, living in a city, and being exposed to things early in life are all strong risk factors. Management strategies now include both drug-based (like dupilumab and crisaborole) and non-drug-based (like moisturising and avoiding allergens) treatments. Personalised care plans and new treatments like herbal agents and microbiome-targeted therapies look promising. AD has a big impact on quality of life and is linked to other problems like anxiety and trouble sleeping.

Conclusion: Atopic dermatitis is still a complicated disease with many causes, so it needs to be treated in a way that is specific to each person and involves many different types of professionals. Recent improvements in biologic therapies, barrier-repair agents, and preventive strategies may help patients get better. More research is needed to confirm that new treatments work and are safe in the long term.

Keywords: Atopic dermatitis; eczema management; risk factors; skin barrier dysfunction; pathogenesis.

1. INTRODUCTION

Atopic dermatitis (AD) or atopic eczema (AE) is a chronic, recurring, itchy, inflammatory skin condition that starts in early childhood (Bieber, 2020; Eyerich et al., 2018). Although the cause of AD is not well understood, it is believed that genetic and other factors may play a role, with mutations in the filaggrin (FLG) gene being a significant contributor to the development of the condition (McAleer & Irvine, 2013). The incidence of AD has been rising in the last few years, and the exact cause is still not well understood. Some of the studies indicate that there are other factors that may have contributed to the increase in the prevalence. Some of the factors that have been suggested as the possible risk factors include: Higher use of antibiotics, migration from the rural to the urban areas, contact with outdoor allergens, indoor air pollutants, and environmental tobacco smoke (Al-Shobaili et al., 2016). AD is a major public health problem worldwide, affecting about 1% to 20% of the population of the world. Specifically, it affects about 1% to 3% of adults and 10% to 20% of children (Nutten, 2015). The disease has a significant impact on the quality of life of patients with moderate to severe AD and their families. The burden of disease includes physical lesions, intractable itching, skin damage, discomfort, and sleep disturbances and the need for frequent medical visits, special clothing, and continuous

application of topical treatments. Although the exact pathogenesis of AD is not well understood, it is believed to be the result of a combination of genetic factors, allergic and non-allergic factors, and environmental factors (Chu et al., 2024, Hameed et al., 2025). However, the effectiveness of the treatment options for AD is still unclear in some instances (Al-Shobaili et al., 2016). Atopic dermatitis (AD) is a frequent chronic inflammatory disease of the skin which occurs in 10%–20% of the population, and its prevalence is increasing in developing countries (Al-Shobaili et al., 2016). Two major theories have been proposed to explain its development: Inside-Out Hypothesis: This concept implies that immune system dysfunction is the first cause of AD. Immune response activation results in the down-regulation of filaggrin production, which in turn weakens the skin barrier function (McAleer & Irvine, 2013). Outside-In Hypothesis: According to this model, the primary defect lies in the skin barrier which allows allergens and pathogens to penetrate and trigger an immune response. FLG mutations support this hypothesis, as FLG deficiency leads to increased permeability and immune sensitization (Chu et al., 2024).

Research indicates that eczema affects 15% to 30% of children and 2% to 10% of adults throughout their lifetimes. The first year of life marks the time when 60% of AD cases appear while urban areas show higher rates of the

condition than rural areas. The distribution pattern shows how lifestyle and environmental elements might affect AD pathogenesis. The "atopic march" describes how allergic diseases like asthma and allergic rhinitis follow atopic dermatitis as part of its progression. Research shows that asthma develops in 50% of severe eczema patients and allergic rhinitis occurs in 75% of these patients (Spergel & Paller, 2003). The assessment of AD incidence and prevalence has relied on both general population surveys and age-specific research in previous studies. The symptoms of AD persist into adulthood for only 25% of children who received their diagnosis. The majority of childhood-onset AD cases disappear before the adolescent period according to research findings (Wan et al., 2019). The most frequent symptom of AD is pruritus (itching) which affects 21% to 100% of patients according to research data (Weisshaar et al., 2023). Research findings demonstrate a strong link between atopic dermatitis and mental health conditions including depression and anxiety. The Hospital Anxiety and Depression Score (HADS) showed clinical anxiety in 41% of patients with AD according to Mizara et al. (Silverberg et al., 2019; Abdul et al., 2025).

Patients with atopic dermatitis experience frequent sleep disturbances because their itching causes nighttime wakings and they have trouble falling asleep. The sleep disturbances result in patients needing sleep aids which in turn diminishes their daily functioning and concentration and productivity levels (Al-Shobaili et al., 2016).

2. PATHOPHYSIOLOGY OF ATOPIC DERMATITIS

The exact mechanisms behind AD pathophysiology remain unclear but research shows that skin barrier problems and immune system dysregulation play essential roles in AD development (Fig. 1). The epidermis functions as both a physical and functional barrier and skin barrier defects represent the primary pathological findings in AD skin (Abdel-Mageed, 2025; Ahmed et al., 2025). The epidermal function depends on four essential proteins which include FLG and transglutaminases together with keratins and intracellular proteins. The malfunction of these proteins allows allergens and microorganisms to penetrate through the skin (Facheris et al., 2023; Ali et al., 2025).

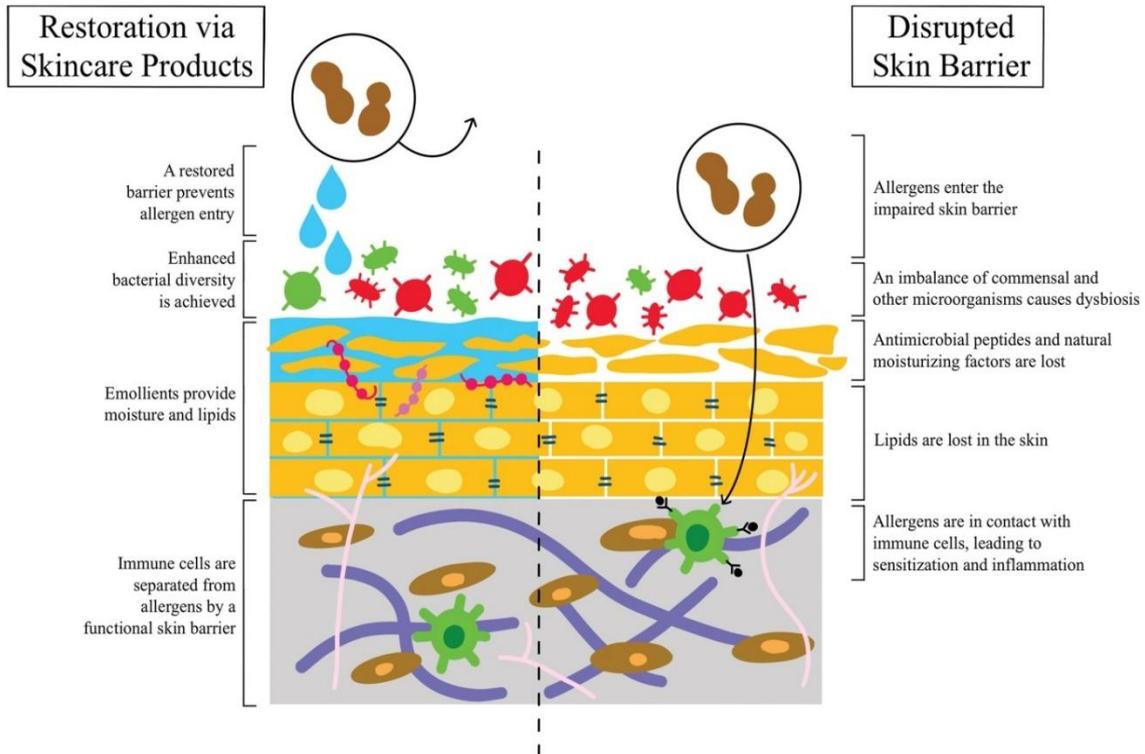


Fig. 1. Disrupted skin barrier in AD and goals to be reached through consistent and effective miniaturisation (Chovatiya & Hebert, 2025)

Atopic dermatitis (AD) begins with skin barrier problems and immune system problems which are both influenced by genetic factors. The protective epidermis loses its barrier function because of FLG gene mutations together with immune system problems and microbial imbalance. The initial application of moisturizers helps fix the skin barrier but most cases of AD need topical and systemic treatments. The antimicrobial defense system becomes weaker because of pattern recognition receptors (PRRs) and Toll-like receptor (TLR) mutations which leads to increased susceptibility to *Staphylococcus aureus* infections. The FLG gene mutations create two problems for the skin barrier while simultaneously increasing the risk of asthma and allergic rhinitis as associated atopic conditions (Facheris et al., 2023).

3. RISK FACTORS OF ATOPIC DERMATITIS

The development of atopic dermatitis (AD) has multiple risk factors. The discovery of the filaggrin (FLG) gene is the most significant development so far in our understanding of the role of genetics in this disease. It has been shown that having a positive family history of atopic or allergy disease in either parent increases the risk of developing AD in addition to FLG gene mutations (Osawa et al., 2011). Like how *Staphylococcus aureus* colonizes more in people with atopic dermatitis, secondary bacterial infections are common in people with weakened immune systems, including those with viral infections like COVID-19, where *S. aureus* and *K. pneumoniae* are the most common (Mohammed et al., 2023).

3.1 Genetic Risk Factors

Atopic dermatitis (AD) develops significantly because of genetic predisposition. The mutation in the filaggrin (FLG) gene stands as the most well-established genetic risk factor because this gene produces a vital protein for skin barrier function. The impaired skin barrier function caused by FLG mutations results in both excessive water loss through the skin and better entry of allergens and microbes which activates immune responses (Palmer et al., 2006; Hamasalih et al., 2025). People who have relatives with atopic diseases including asthma, allergic rhinitis or eczema face a substantially increased chance of

developing AD. The hereditary aspects of this condition become clear through these findings which support the requirement for early detection and prevention methods for genetically susceptible people (Facheris et al., 2023).

3.2 Environmental Triggers

The "hygiene hypothesis" and "biodiversity hypothesis" demonstrate that environmental diversity protects against allergies and inflammatory diseases because industrialized countries' reduced microbial exposure leads to higher atopic illness risk and because varied natural environments strengthen the immune system (Kalmari et al., 2025; Salih et al., 2025). The prevalence and severity of atopic dermatitis (AD) strongly depend on climate factors which include temperature and humidity and UV radiation and pollution levels. The skin barrier becomes impaired when weather conditions become extreme and humidity levels drop but UV exposure may provide some protective effects on the immune system (Thyssen et al., 2015). Environmental pollutants cause AD to worsen through their ability to harm skin barriers and create oxidative stress. The compromised skin barrier allows dust mites pollen pet dander and mold allergens to activate immune responses which leads to chronic inflammation in AD pathogenesis. The management and prevention of AD flare-ups together with improved quality of life for patients depend on early intervention strategies that include improving indoor air quality and using hypoallergenic products (Tan et al., 2024; Salih et al., 2021).

3.3 Lifestyle Factors

The severity of eczema and its management depends heavily on lifestyle choices. Smoking causes increased inflammation and damages skin barriers which results in more frequent and severe eczema outbreaks. Drinking alcohol leads to skin dehydration which increases its sensitivity to irritation and intensifies symptoms. Stress functions as a major factor because it activates inflammatory processes which worsen eczema symptoms (Lee et al., 2016; Salih et al., 2019). The condition of obesity with its associated increased waist circumference leads to more serious eczema cases because of its inflammatory effects. Physical exercise helps patients by lowering stress levels and reducing body-wide inflammation but intense

sweating can occasionally cause eczema symptoms to worsen. The diet directly affects eczema because particular foods may cause symptoms but an anti-inflammatory eating pattern can assist with condition management (Ascott et al., 2021; Mahmood et al., 2021). The quality of sleep stands as a vital factor because inadequate rest disrupts skin restoration mechanisms which leads to worsening eczema symptoms throughout time. Statistical research confirms these relationships between lifestyle elements and eczema severity which enables healthcare providers to create individualized treatment plans and lifestyle adjustments for improved disease control (Chu et al., 2024).

4. CLINICAL PRESENTATION AND DIAGNOSIS

Atopic dermatitis (AD) causes chronic eczematous lesions which result in intense pruritus and erythema and xerosis (dry skin) and lichenification because of repeated scratching. Lesions from AD affect different body regions depending on the patient's age group: Infants show lesions mainly on their face and extensor surfaces but older children and adults develop lesions in flexural areas including the antecubital and popliteal fossae (Napolitano et al., 2022). The combination of skin barrier damage and scratching leads to frequent bacterial infections among patients. The severity of AD symptoms shows periodic changes because environmental triggers and allergens and psychological stress factors affect the condition (Baidya & Mabalirajan, 2025).

The diagnosis of AD relies on clinical evaluation which uses established criteria. The Hanifin and Rajka criteria consist of major features which include pruritus and chronic or relapsing dermatitis alongside personal or family atopy history and typical lesion distribution and morphology and minor features that include xerosis and ichthyosis and elevated serum IgE levels and early onset (De et al., 2006). The UK Working Party criteria present a simplified version that requires patients to show pruritus together with three or more supporting clinical findings. The diagnosis of atopic dermatitis can be supported by serum IgE measurement and skin-prick testing but these tests remain optional (Baidya & Mabalirajan, 2025). The process of differential diagnosis serves to identify atopic dermatitis from other skin conditions which

present with similar symptoms. The condition known as seborrheic dermatitis requires distinction from atopic dermatitis because it produces greasy yellowish scales which mainly occur on the scalp and face. Contact dermatitis shows well-defined lesions because of allergen or irritant exposure but psoriasis produces thick silvery plaques mainly found on extensor surfaces (Jackson et al., 2024). The differential diagnosis should include scabies together with fungal infections (tinea) and dermatitis that occurs in immunodeficient patients. The process of accurate diagnosis and effective management of atopic dermatitis requires complete clinical evaluation together with patient history and specific laboratory or histopathological tests when needed (Ascott et al., 2021). Researchers have also looked into infectious agents like *Giardia lamblia* in children to see how they can be used for diagnosis. This shows how molecular diagnostics are becoming more important in dermatology-related conditions (Jassim et al., 2025).

5. TREATMENT STRATEGIES FOR ATOPIC DERMATITIS

The treatment of atopic dermatitis (AD) demands multiple therapeutic strategies because it represents a chronic inflammatory skin condition. The main objective of treatment involves both barrier function recovery of the epidermis and inflammation reduction (Puar et al., 2021). The treatment of skin inflammation requires both topical anti-inflammatory agents including corticosteroids and calcineurin inhibitors and skin moisturization. The combination of topical corticosteroids and calcineurin inhibitors applied twice weekly to previously affected areas has proven effective in shortening the duration until the next eczematous flare occurs. The treatment plan includes wet wrap therapy together with anti-histamines and vitamin D supplements. *Staphylococcus aureus* bacterial colonization represents a major factor that leads to both eczematous flares and overt infections (Saeki et al., 2009).

5.1 Non-Pharmacological Approach

Non-pharmacological management approaches form an essential part of atopic dermatitis (AD) care since they provide crucial support in disease control and prevention of flare-ups. The fundamental aspect of educational interventions consists of giving patients and their caregivers comprehensive knowledge about AD's chronic

Table 1. Considerations for moisturizer choice in AD (Chovatiya & Hebert, 2025)

Moisturizer property	Purpose	Mechanism	Example ingredients
Barrier repair	A healthy skin barrier retains moisture and protects against allergen penetration	Stratum corneum lipid barrier dysfunction	Ceramides; lactic acid; urea
Hydration	A well hydrated SC is intact and healthy	Loss of hydration from the SC results in increased permeability	Ceramides; lactic acid; petrolatum; pyrrolidone carboxylic acid; urocanic acid
Protection	Temporary protection can be used to prevent further damage and allow the damaged skin to heal	Protectant ingredients can create an occlusive barrier that reduces TEWL and blocks external irritants	Colloidal oatmeal; dimethicone; lanolin; mineral oil; petrolatum
Anti-pruritic	Dysfunction of the skin barrier, coupled with immune dysregulation, leads to inflammation and activation of sensory neurons	Anti-pruritic ingredients can reduce itching sensation, leading to a lower scratch drive	Ceramides; colloidal oatmeal
Anti-inflammatory	Dysfunction of the skin barrier as a result of AD leads to the release of inflammatory cytokines	Anti-inflammatory ingredients can inhibit the release of cytokines and reduce the downstream inflammatory response	Colloidal oatmeal; licochalcone A

nature together with proper skincare practices and treatment plan compliance (Puar et al., 2021). The regular application of moisturizers combined with barrier repair therapies helps both restore skin hydration and strengthen skin protective capabilities which results in reduced transepidermal water loss and minimized irritation. Acute flare-ups benefit most from wet wrap therapy that includes emollient application followed by damp bandages because this method both hydrates the skin and decreases inflammation. Proper skin hygiene practices that include bathing with lukewarm water and using mild fragrance-free cleansers help preserve skin integrity and reduce skin irritation (Lodén, 2003). The prevention of disease exacerbations requires patients to identify trigger factors that include allergens together with harsh soaps and environmental irritants. Psychological interventions that incorporate stress management and cognitive behavioral therapy help patients manage the mental impact of AD since stress is a known symptom-worsening factor. Patients with AD can achieve better life quality and better treatment results through the combination of these non-pharmacological care strategies in their daily routines (Purnamawati et al., 2017).

Reduced microbial exposure in industrialized societies according to the "hygiene hypothesis" leads to an increased risk of atopic illnesses but environmental diversity serves as a crucial protective factor (Lodén, 2003). The "biodiversity hypothesis" demonstrates that different natural environments provide immune system benefits through human microbiome enhancement. The prevalence and severity of atopic dermatitis (AD) experience significant changes due to climate elements that include temperature and humidity as well as ultraviolet (UV) radiation and pollution. Symptoms of the skin condition become worse due to extreme weather conditions and insufficient moisture in the air but UV rays offer potential immune system regulation benefits (Roslund et al., 2022). The combination of environmental pollutants causes AD worsening through their destructive impact on the skin barrier as well as their ability to trigger oxidative stress and promote inflammation. The compromised skin barrier allows allergens such as dust mites and pollen and pet dander and mold to activate immune responses which leads to sustained chronic inflammation in AD pathogenesis. The quality of life for patients with AD improves through early intervention methods that include improving indoor air quality together

with hypoallergenic practice implementation for preventing AD flare-ups (Liddicoat et al., 2016). Within components that improve the cutaneous barrier, treat immunological and neurological dysregulation, and encourage microbial variety along the external surface, modern moisturizer compositions are aesthetically pleasing and logically constructed. This enables them to maintain SC acidity, minimize water loss, encourage a healthy microbiota, minimize flare-ups, optimize the skin barrier to defend against environmental triggers, and even perhaps prevent AD when administered early in life to children who are at risk. The key to managing AD is choosing moisturizers carefully in order to preserve the skin barrier and, eventually, support cutaneous homeostasis (Chovatiya & Hebert, 2025). AD patients now have access to an increasing variety of over-the-counter moisturizers, which may be confusing and leave them unsure of how to choose the best one. HCPs in dermatology must be vital educators who provide patients with clinically supported advice (Purnamawati et al., 2017). Adequate knowledge of OTC moisturizer formulations and ingredients is key in helping patients choose the most appropriate product for their skin type, AD needs, and overall skin barrier status. (Rajkumar et al., 2023). Table 1. Summarizes the aim and mechanism of clinically significant moisturizing characteristics and emphasizes notable individual components in prevalent over-the-counter moisturizers (Aziz et al., 2025).

5.2 Pharmacological Management

The skin barrier dysfunction of atopic dermatitis (AD) leads to both water loss and ceramide deficiency. The main goal of AD management involves both barrier repair and inflammation reduction. The treatment of AD requires ceramide-based moisturizers together with occlusives such as petroleum jelly and humectants including glycerin. The treatment requires patients to stay away from harsh soap products and fragrances as well as from allergens such as dust mites and particular foods (Gabros et al., 2025). The initial treatment plan for AD includes topical corticosteroids which span from hydrocortisone 1%–2.5% for facial use to clobetasol propionate 0.05% for severe cases involving thickened skin. The calcineurin inhibitors pimecrolimus (Elidel) and tacrolimus (Protopic) serve as suitable alternatives for treating sensitive skin regions when corticosteroids are not suitable (Moncayo-Hida, 2024).

Severe cases require additional treatments which include phototherapy and immunosuppressants and biologics like dupilumab that target particular immune pathways in AD (Chu et al., 2024). Systemic immunosuppressive drugs become an option for patients who fail to respond to topical treatments particularly during acute flare-ups or when dealing with severe localized AD lesions. The emerging therapeutic options which include JAK inhibitors and probiotics provide new long-term disease management possibilities that enhance the flexibility of caring for this chronic skin condition. The selection of corticosteroids should be based on AD severity and location to achieve the best treatment results while reducing adverse effects (Butala et al., 2023).

6. PREVENTIVE MEASURES AND LIFESTYLE MODIFICATIONS

Genetic history plays a major role in determining atopic dermatitis (AD) development because children born to two affected parents have a greater risk of developing the condition. Research indicates that children with two atopic parents will develop atopic allergies in 40–50% of cases but children with one atopic parent will have a 20–30% risk and those with no atopic parents will have a 10% risk. Atopy from the mother proves to be a more significant risk factor for AD than atopy from the father (Oszukowska et al., 2015; Mohammed et al., 2020). Environmental factors beyond genetic influences appear crucial because AD incidence has been increasing in affluent nations throughout the past several decades. People who relocate become more prone to developing AD in their new environment according to observations. The main goal of prevention measures focuses on lowering atopic dermatitis risks for children who are genetically predisposed (Butala et al., 2023; Omar et al., 2025).

The hygiene hypothesis from the 1980s proposes that insufficient early infection contact because of high sanitation practices and antibiotic use and decreased infections might boost the development of atopic disorders. Research indicates that children enrolled in daycare and following the Anthropozoic philosophy with restricted antibiotic use and fermented food consumption show reduced AD risk (Levin et al., 2020; Rahman et al., 2021). The prevention of atopic disorders requires immediate intervention for individuals at high risk since food allergies (FA) tend to appear after atopic dermatitis (AD) (Tsakok et al., 2016).

Healthy mucosal barriers which present antigens to the immune system before compromised skin can help stop food allergies from developing. The prevention of eczema depends on breastfeeding together with proper early nutrition (Greer et al., 2019; Rasul et al., 2025). A minimum of four months of exclusive breastfeeding offers protection against eczema development particularly for infants at risk. The introduction of allergenic foods including peanuts and eggs during the fourth to sixth month of life lowers allergy probabilities (Logan et al., 2023). Omega-3 fatty acids present in maternal diets during pregnancy and breastfeeding create additional protection against eczema development. Each child requires unique dietary approaches because their genetic makeup along with environmental factors determine how early nutrition affects the development of eczema (Kang et al., 2021).

7. FUTURE DIRECTIONS AND RESEARCH GAPS

The treatment of atopic dermatitis (AD) undergoes transformation through personalized medicine which uses genetic and immunological and environmental characteristics to customize therapy approaches. The approach leads to better treatment results while reducing adverse effects. The biologic agents Dupilumab and Nemolizumab specifically target immune pathways in AD to treat inflammation and pruritus (itching) symptoms. The oral JAK inhibitor baricitinib delivers quick relief to patients who do not respond to standard treatments while the topical PDE4 inhibitor crisaborole offers steroid-free maintenance therapy. The medical community shows increasing interest in using herbal treatments as additional therapies because they demonstrate promising advantages regarding treatment effectiveness and safety and patient tolerance. A thorough evaluation of herbal treatments for eczema stresses the need for strict safety and effectiveness assessments to fulfill current unmet requirements in AD treatment. New ways of diagnosing chronic inflammatory conditions, like nanotechnology-based imaging with pH-responsive SPIONs to find tumors, could lead to new noninvasive ways of diagnosing inflammatory skin diseases like atopic dermatitis (A. A. Mahmood et al., 2019; Wei et al., 2017). Nanoparticle-based treatments are becoming more popular for both skin and parasitic diseases. Notably, biosynthesised Ag and ZnO nanoparticles have shown to be more effective at killing parasites in vitro than

traditional drugs. This suggests that they could be used to treat skin infections and inflammation (Attiah et al., 2023).

8. CONCLUSION

Atopic dermatitis (AD) represents a multifaceted chronic inflammatory skin disease which results from the combination of genetic predisposition and immune system dysregulation together with environmental elements and personal lifestyle choices. The physical manifestations of AD create substantial psychological distress which negatively affects patients' life quality. The development of targeted treatments including biologics and JAK inhibitors became possible because of improved knowledge about skin barrier defects and immune system reactions. The current situation requires evidence-based individualized management approaches for patients. The treatment plan for effective management includes both medication-based interventions and non-drug approaches which include patient education and regular moisturizer use and trigger avoidance and mental health support. Early medical intervention together with lifestyle modifications can help stop disease progression or minimize its severity. The current understanding of new treatments faces challenges regarding their long-term safety profile and the development of standardized diagnostic standards and environmental and psychosocial risk factor management. Future research should concentrate on personalized medicine approaches combined with prevention strategies and novel therapies including herbal and microbiome-based treatments to enhance disease management and patient outcomes.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The authors of this article have not conducted any research involving humans or animals; rather, it is a review of previously published literature. Consequently, ethical clearance was not necessary.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image

generators have been used during writing or editing of this manuscript.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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