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## Review Article

# Review of Herbal Interventions for Atopic Dermatitis/ Eczema: Types, Etiology, Evaluation and Treatments

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### ABSTRACT

Eczema is a chronic inflammatory skin disease that affects 2-3% of the global population. It is characterized by skin that is excessively dry, itchy, and has rashes. About 15% to 20% of children and 1% to 3% of adults worldwide suffer with eczema. Several theories have been put out because the precise etiology of eczema has not been found. Two theories are put forth: (i) the inside-out hypothesis, which suggests that an immunological malfunction that permits patients to develop an IgE sensitivity may be the cause of the illness; and (ii) the outside-in hypothesis, which maintains that a disruption in the skin barrier may be the cause of the illness. Its manifestation is brought on by environmental and genetic factors that compromise the integrity of the skin barrier, making it more vulnerable to increased penetration by different allergens and pathogens. This exacerbates the condition and increases the risk of deadly hypersensitivity reactions, making it one of the most serious illnesses in the world. The use of synthetic medications is associated with the worst side effects and long-term negative reactions that negatively impact quality of life. Based on existing literature, medicinal plants possess a variety of chemically configured chemicals, such as alkaloids, phenolic compounds, sterols, terpenoids, and free fatty acids, which are intended to modify various pathological situations. Several well-known substances are used to treat skin infections, including nimbolide, morgolon, tocopherols, unsaturated fatty acids, oleic acid, linoleic acid, rosmarinic acid, and gamma linoleic acid. These substances have the exceptional ability to treat eczematous skin and the lesions connected to atopic eczema by preserving the integrity of the skin, preserving its ability to remain hydrated and normal, regulating the pH of the skin, and promoting the microbial flora. They have been observed to offer complete relief in a relatively short amount of time with almost no side effects by securing the outer layers of the epidermis

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from pathogenic bacteria, fungi, viruses, and many other invaders because they have an effective penetration tendency and can seep into the stratum.

## INTRODUCTION

Eczema, or atopic dermatitis, is the most common form of dermatitis. Many factors, including genetic and environmental factors, are thought to play a part in the pathogenesis of eczema. It is most commonly seen in children but can be seen in adults as well. People with eczema tend to have dry, itchy skin prone to infection. The condition is commonly known as the "itch that rashes" because dry, itchy skin leads to a rash due to scratching or rubbing the skin[1]. The pathophysiology of atopic dermatitis and other inflammatory skin diseases is associated with an immune mechanism that involves T lymphocyte activation. This mechanism is the consequence of intricate interactions between various cells, including keratinocytes, endothelium cells, eosinophils, Langerhans cells, T lymphocytes, and numerous cytokines and mediators. Skin cells produce interleukins in atopic skin conditions, which trigger inflammatory responses. Different organs and systems experience signs of inflammation as a result of the release of leukotrienes, prostaglandins, and proteases. An elevated value of trans epidermal water loss (TEWL) is observed in clinically healthy skin and in areas of dry skin that are not affected by inflammation in patients with atopic dermatitis. This may be related to a decreased concentration of lipids in the skin, specifically ceramides, and the loss of natural moisturizing factor (NMF) ingredients[2]. The potential of medicinal plants in treating various diseases is considerable. These plants contain a wealth of active components and can offer a safer and more cost-effective approach to treating a variety of skin conditions.

Inflammation is a complex but vital process for the body's defense mechanism. Excessive production of certain inflammatory agents can lead to chronic ailments. Natural plant substances can exhibit anti-inflammatory properties that target different stages of the inflammation process. They can hinder the production of cytokines and eicosanoids, prevent the initiation of the inflammatory response cascade, and alleviate symptoms such as skin burning, itching, or excessive peeling[3].

## ECZEMA

Eczema is a condition that causes your skin to become dry, itchy and bumpy. This condition weakens your skin's barrier function, which is responsible for helping your skin retain moisture and protecting your body from outside elements.

## ETIOLOGY

The exact etiology of eczema is not entirely understood, but it is believed to be a combination of genetic and environmental factors[4].

### Genetic Factors

Eczema has a significant genetic element, with affected individuals often having a family history of eczema, asthma, or allergies. Researchers have pinpointed various genes linked to eczema, including those that play a role in skin barrier function and the immune system.

### Filaggrin Gene

The filaggrin gene (FLG) is a commonly recognized gene linked to eczema. It is responsible for producing the filaggrin protein, which plays a vital role in preserving the skin's barrier function. Mutations in this gene have been associated with eczema and other skin disorders

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and are believed to raise the vulnerability to environmental irritants and allergens[5][6].

### **Other Skin Barrier Genes**

Other than the filaggrin gene, there are other genes related to the skin barrier function that have been linked to the onset of eczema. These genes encompass those involved in lipid production and movement, such as the ceramide synthase gene and the ABCA12 gene[7].

### **Immune-related Genes**

Eczema has been linked to various genes associated with the immune response, such as those responsible for regulating T-cells, cytokines, and immunoglobulins. Examples of these genes are interleukin (IL)-4, IL-13, IL-31, signal transducer and activator of transduction (STAT)3, and Fc fragment of immunoglobulin (Ig)E receptor Ig (FCER1G). The genetic factors contributing to eczema are intricate and likely involve multiple genes and genetic pathways. While eczema is not typically diagnosed using genetic testing, understanding the genetic underpinnings of the disease can help in identifying individuals at higher risk and in determining effective treatment strategies.

### **Environmental Factors**

Eczema development is also influenced by environmental factors. Eczema patients' skin barrier function is compromised, which increases their vulnerability to allergens and environmental irritants as well as increased water loss. Exposure to allergens like dust mites, pet dander, and certain foods, as well as irritants like detergents, soaps, and solvents, can cause flare-ups of eczema. Eczema symptoms can also be made worse by stress, humidity and temperature changes, and infections.

### **Immune System Activation**

Apart from genetic and environmental factors, there is a belief that the immune system contributes to the development of eczema. Eczema patients' hyperactive immune systems

react to environmental stimuli, causing inflammation and skin damage[8].

### **SYMPTOMS**

Itching - There may be severe itching. Scratching during eczema frequently results in skin damage.

Scaling - The skin may appear rough and scaly as a result of surface flakes.

Redness - Bleeding and blotchy skin are possible symptoms of the affected skin.

Fluid-filled blisters - Crusts may form and they may seep out.

Cracking - Severe skin damage can lead to the development of deep, painful cracks known as fissures[9].

### **EVALUATION**

Clinical diagnosis is usually made on the basis of the patient's history and the way the rash looks. Typically, routine laboratory work is not advised. Patch testing and allergy testing may be done if the diagnosis is ambiguous. Topical anti-inflammatory drugs for flare-ups and adequate hydration are the mainstays of eczema management and treatment regimes. Treatment priorities include concentrating on a daily moisturizing routine for the skin and utilizing a fragrance-free ointment with minimal preservatives. Lotions include a large ratio of oil to water, which makes an ointment better than a cream. Any triggers should be recognized and dealt with by both the patient and the caregiver. It is important to advise them to stay away from harsh detergents, soaps, scents, and materials that are rough or do not breathe in the environment. Topical anti-inflammatory drugs, including topical steroids, or steroid-free treatments like pimecrolimus, tacrolimus, or Eucirsa, can be used to treat skin flare-ups. Children typically experience more evening itching. For itch-related sleep disturbances, oral antihistamines can be used sporadically before bed; however, antihistamine use during the day is no longer advised for eczema irritation. Patients who have



unmanaged eczema are more susceptible to skin infections. To reduce cutaneous infections, patients and caregivers may be advised to use intranasal mupirocin or diluted bleach baths[10].

## TYPES OF ECZEMA

### 1. Atopic dermatitis [11]

With eczema, atopic dermatitis is the most prevalent type. Between the ages of two months and five years, it usually begins in childhood and usually gets milder or goes away by adulthood. Nonetheless, it is possible for symptoms to resurface later in life or to appear for the first time.

#### Symptoms

Symptoms typically appear on your arms or in the creases of your elbows or knees. Children may develop symptoms on their scalp and cheeks. It's important not to scratch any bumps, rashes, or lesions, as this may lead to infection.

#### Causes

It is unknown what specifically causes atopic dermatitis. But the illness arises from a weakening of your skin's natural barrier. This implies that your skin's ability to shield you from allergens and irritants is diminished. Atopic dermatitis is most likely brought on by a number of variables, including:

- Genes that cause dry skin;
- Immune system problems; and
- Triggers like stress, irritants, and dry skin.

### 2. Contact dermatitis [12]

Contact dermatitis results from a reaction to substances you touch. There are two types:

- **Allergic contact dermatitis:** This is an immune system reaction to an irritant, like latex or metal.
- **Irritant contact dermatitis:** This starts when a chemical or other substance directly damages your skin.

#### Symptoms

Symptoms of contact dermatitis may take up to 48 hours to appear after coming into contact with a trigger. In contact dermatitis, you may experience:

- itchy skin that turns red, pink, or magenta. In darker skin tones, this can appear as brown, purple, or gray.
- skin that burns or stings
- hives
- fluid-filled blisters
- thick, leathery skin

#### Causes

Contact dermatitis happens when you touch a substance that irritates your skin or causes an allergic reaction. The most common irritants include: detergents, bleach, jewelry, latex, nickel, paint, poison ivy and other poisonous plants, skin care products, including makeup, soaps and perfumes, solvents, tobacco smoke.

### 3. Dyshidrotic eczema [13]

Dyshidrotic eczema, also known as pompholyx, causes small blisters to form on your hands and feet.

#### Symptoms

Symptoms of dyshidrotic eczema may last between 2–3 weeks at a time. You may experience fluid-filled blisters that could itch, hurt, crack, and flake. These may appear on your: fingers, toes, palms, soles of the feet.

#### Causes

Dyshidrotic eczema can be caused by: allergies, damp hands and feet, exposure to substances such as nickel, cobalt, or chromium salt, stress, smoking tobacco products

### 4. Seborrheic dermatitis [14]

Seborrheic dermatitis is sometimes referred to as scalp eczema because it typically affects your scalp. Seborrheic dermatitis in infants is commonly called cradle cap, and it does not reappear later. In teens and adults, however, seborrheic dermatitis will most likely be an ongoing skin issue.



### **Symptoms**

Seborrheic dermatitis may cause scaly, oily patches of skin that produce dandruff-like flakes. These patches often appear where there are more sebaceous glands on the body, such as the: scalp, hairline, upper back, nose. In people with darker skin tones, these patches may be darker than their skin, but in people with lighter skin tones, the patches may be lighter.

### **Causes**

Seborrheic dermatitis may be due to a combination of environmental and genetic factors. First, a trigger like stress or illness sets off an inflammatory reaction in the skin. This sends the oil-producing glands in the body into overdrive, which allows too much *Malassezia* yeast to grow. This is an organism that lives on the skin's surface. When yeast grows too rapidly, the immune system reacts and causes a series of skin changes. This leads to the development of the patches of skin common with seborrheic dermatitis. Aside from stress and illness, other triggers of seborrheic dermatitis may include: Hormonal changes, illness, harsh detergents or chemicals, cold, dry weather, certain medical conditions, like Parkinson's disease, psoriasis, HIV, and acne, medications, including interferon and lithium.

### **5. Neurodermatitis [15]**

A form of eczema known as neurodermatitis, also called lichen simplex chronicus, typically results in the development of one to two eczema patches. It entails excruciating itching that gets worse the more you itch.

### **Symptoms**

Thick, scaly, and occasionally extremely itchy patches can develop on your arms, legs, back of your neck, scalp, bottoms of your feet, backs of your hands, and genitalia as a result of neurodermatitis.

It's crucial to refrain from picking at the exposed skin. This could exacerbate your symptoms and result in infection and bleeding.

### **Causes**

As of yet, neurodermatitis underlying cause is unknown. However, the AAD states that the condition typically begins with an itching, and the more you scratch it, the worse the rash gets.

### **6. Nummular eczema [16]**

Nummular eczema, also known as discoid eczema, causes round, coin-shaped spots to form on your skin. It looks different than other types of eczema and could be very itchy.

### **Symptoms**

Symptoms of nummular eczema may last up to several years without treatment. The first sign of nummular eczema is usually a group of small bumps on the skin. These may appear red or pink on lighter skin tones and dark brown on darker skin tones. These small bumps then usually grow coin-shaped skin lesions that may be itchy, flaky, or cracked.

### **Causes**

The exact cause of nummular eczema is not known. However, it may result from having very dry skin. You're also more likely to develop nummular eczema if you have another type of eczema, such as atopic dermatitis.

### **7. Stasis dermatitis [17]**

Stasis dermatitis is more common in people who have poor circulation, according to the AAD. It happens when fluid leaks out of weakened veins into your skin. This fluid may cause: swelling, redness in lighter skin tones, brown, purple, gray, or ashen color in darker skin tones, itching, pain.

### **Symptoms**

Symptoms of stasis dermatitis are most likely to affect your legs and ankles. For example, the lower part of your legs may swell, especially during the day when you've been walking. Your legs may also ache or feel heavy. Other

symptoms of stasis dermatitis may include: varicose veins, dry, itchy skin, open sores.

### Causes

Stasis dermatitis happens in people who have blood flow problems in their lower legs. If the valves that normally push blood up through your legs toward your heart malfunction, blood can pool in your legs.

### COMPLICATIONS

Complications of atopic dermatitis (eczema) may include:

- Asthma and hay fever. Many people with atopic dermatitis develop asthma and hay fever. This can happen before or after developing atopic dermatitis[18].
- Food allergies. People with atopic dermatitis often develop food allergies. One of the main symptoms of this condition is hives (urticaria).
- Chronic itchy, scaly skin. A skin condition called neurodermatitis (lichen simplex chronicus) starts with a patch of itchy skin. You scratch the area, which provides only temporary relief. Scratching actually makes the skin itchier because it activates the nerve fibers in your skin. Over time, you may scratch out of habit. This condition can cause the affected skin to become discolored, thick and leathery[19].
- Patches of skin that's darker or lighter than the surrounding area. This complication after the rash has healed is called post-inflammatory hyperpigmentation or hypopigmentation. It's more common in people with brown or Black skin. It might take several months for the discoloration to fade.
- Skin infections. Repeated scratching that breaks the skin can cause open sores and cracks. These increase the risk of infection from bacteria and viruses. These skin infections can spread and become life-threatening.

- Irritant hand dermatitis. This especially affects people whose hands are often wet and exposed to harsh soaps, detergents and disinfectant at work.
- Allergic contact dermatitis. This condition is common in people with atopic dermatitis. Allergic contact dermatitis is an itchy rash caused by touching substances you're allergic to. The color of the rash varies depending on your skin color[20].
- Sleep problems. The itchiness of atopic dermatitis can interfere with sleep.
- Mental health conditions. Atopic dermatitis is associated with depression and anxiety. This may be related to the constant itching and sleep problems common among people with atopic dermatitis.

### HERBAL MEDICINE FOR ECZEMA

Herbal medicine, also known as botanical medicine, involves the use of plant-based remedies to treat various health conditions. Herbs have been used for centuries to treat a wide range of ailments, including skin conditions like eczema[21]. Here are some of the most popular herbal remedies for eczema:

**Aloe vera (Aloe barbadensis):** Aloe vera is a succulent plant that is well known for its healing properties. It contains compounds that can help reduce inflammation and soothe irritated skin. Aloe vera gel can be applied directly to the affected area to help calm eczema flare-ups[22].

**Arnica (Arnica montana):** Arnica is derived from the dried flowers of Arnica montana or other arnica species. Although oral administration can cause severe health hazards even in small amounts, preparations for external use are very safe and effective. It is also an ingredient found in many seborrheic dermatitis and psoriasis preparations). The active ingredients of arnica are the sesquiterpene lactones such as helanalin, 11 $\alpha$ ,13-dihydrohelenalin, chamissonolid, and their ester derivatives. These components reduce



inflammation by inhibiting the transcription factor nuclear factor  $\kappa$ B (NF- $\kappa$ B)[23]. German chamomile (*Matricaria recutita*), Chamomile is a popular herb that is often used to treat skin conditions like eczema. It contains anti-inflammatory compounds that can help reduce redness and inflammation. The anti-inflammatory, wound-healing, and antimicrobial effects of German chamomile are attributed to an essential blue oil that contains sesquiterpene alcohol,  $\alpha$ -bisabolol, chamazulene, and flavanoids. In animal experiments, these compounds exhibited anti-inflammatory and antispasmodic qualities, partly because they inhibited lipoxygenase and cyclooxygenase in vitro. In addition, the flavanoids work by preventing antigen-stimulated human basophilic polymorphonuclear leukocytes from releasing histamine. Additionally, the compound  $\alpha$ -isabolol showed that it promoted granulation tissue in the healing of wounds[24].

**Calendula (*Calendula officinalis*):** Calendula, also known as marigold, is a flowering herb that has been used for centuries to treat various skin conditions. It contains anti-inflammatory compounds that can help soothe irritated skin and reduce redness. Calendula cream or ointment can be applied topically to the affected area.

**Licorice (*Glycyrrhiza glabra*):** Licorice root contains compounds that can help reduce inflammation and itching, making it an effective remedy for eczema. Licorice root can be taken internally in the form of tea, or applied topically as a cream or ointment[25].

**Lavender (*Lavandula angustifolia*):** Lavender is a popular herb that is often used for its calming and relaxing properties. It contains compounds that can help reduce inflammation and promote healing. Lavender oil can be applied topically to the affected area, or it can be added to a warm bath to promote relaxation and soothe irritated skin[26].

**Evening primrose oil (*Oenothera biennis*):** Evening primrose oil is natural oil that is high in Gamma Linolenic Acid (GLA), an essential fatty acid that is known to help reduce inflammation. It can be taken internally in the form of supplements, or applied topically as a cream or ointment[27].

**Jewelweed (*Impatiens biflora*):** Although research on jewelweed (*Impatiens biflora*) is inconsistent, it is said to be helpful topically in treating poison ivy contact dermatitis. In one study, the use of jewelweed as a treatment for poison ivy contact dermatitis was found to be similar to usual care; in 108 out of 115 patients, the symptoms subsided in two to three days. Jewelweed extract however failed to lessen the symptoms of poison ivy dermatitis in another research. Another trial revealed that jewelweed had no preventive impact on treating poison ivy dermatitis. Although the aforementioned studies did not address this element, jewelweed has been reported to work best if administered as soon as feasible following poison ivy contact. There are no known side effects from topical jewelweed usage[28].

**Oats (*Avena sativa*):** Due to their calming and antipruritic qualities, oats (*Avena sativa*) have been applied topically in baths for hundreds of years. Commission E, the German regulatory body, has approved this use and they are classified as Class 1. When combined with liquid, colloidal oatmeal transforms into a gooey, sticky mass that can be applied to the skin to seal in moisture. This calming and hydrating quality is linked to the plant's gluten content. Both idiopathic pruritus in the elderly and atopic dermatitis may benefit from this[29].

**Pansy flower (*V. tricolor*):** An infusion of pansy flowers (*V. tricolor*) is advised as a safe remedy for seborrheic dermatitis, particularly in young children. As a wet dressing, the infusion is prepared by combining 1-2 tsp of flowers with a

cup of water. Approximately 0.3% concentrations of salicylic acid seem to be the active component. Additionally, it has mucilage and saponins, which have calming and softening properties. Since topical application has not been associated with any negative effects, pansy falls under Class 1[30].

**Birch tree (*Betula platyphylla* var. *japonica*):** NC/Nga mice were used to study the bark of the birch tree (*Betula platyphylla* var. *japonica*), which is used to treat atopic dermatitis. It may suppress the T-helper 2 cellular response because it reduced skin inflammation and scratching as well as IgE and IL-4 messenger ribonucleic acid (mRNA) levels[31].

### CONCLUSION

In an attempt to reduce patient discomfort, the review is presented as a sort of showcase for medicinal plants with particular therapeutic potential for treating eczema. In fact, the distinct active ingredients found in the plants were in charge of various pharmacological effects and assisted in regulating physiological processes such as inflammation, permeability, and skin barrier homeostasis, which in turn gave the patient relief. Moreover, certain plant extracts moisturized the dry skin by acting as humectants. In the current era of evidence-based medicine, more in vitro and in vivo studies are needed to evaluate and validate the safety and efficacy of these herbs. The therapeutic field is expected to explore new frontiers.

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