

Novel Formulation of *Aloe vera* and Quercetin in the Management of Dermal Disease: Eczema

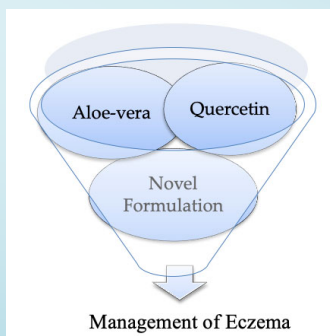
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ABSTRACT

Eczema, also known as atopic dermatitis, is a state that compels your skin inflamed or irritated. Scientific investigations claim that aloe vera, an admired natural plant product may aid to manage the eczema. There is not much research evaluating the use of aloe vera for eczema. But it is well known to have anti-bacterial and anti-fungal properties, along with anti-inflammatory properties, could be particularly applicable to manage the eczema. Quercetin efficaciously inhibits the secretion of histamine and pro-inflammatory markers along with evident to decrease eczema. Thus, amalgamated effect of aloe vera and quercetin may synergize the therapeutic efficacy in the management of eczema. Topical treatment is often the first-line remedy for mild to moderate eczema. Dermal formulations (Cream, ointment, gel etc.) are still the main therapeutic approach for the treatment of skin disorders. Present studies emphasize the types, etiology, symptoms, prevention and herbal therapeutic options for the management of eczema.



Keywords: Skin disorders, Eczema, Aloe vera, Topical formulation, Quercetin

INTRODUCTION

Eczema is a dermal disorder wherein blemish of skin begin dry, broken, and rough. Some types can also cause blebs. Eczema is usually, chronic, non-contagious skin disorder. The main indication of this inflammatory disease is a very itchy rash. There is generally no cure for eczema, but it can be managed with consistent medical care and a systematic treatment plan. Some types of eczema can be prevented by avoiding stress, infliction, and belongings that cause allergic response [1]. Eczema may produce potential for complications, such as a secondary bacterial or fungal infection of the eczema rash.

Aloe vera (*A. vera*) evolve wild in tropical, semi-tropical, and arid climates worldwide. It is cultivated for agricultural and medicinal applications. *A. vera* is one of the most paramount plants used in traditional medicine. *A. vera* contains enzymes, minerals, vitamins, acids, amino acids,

lipids, lectin, lactates, salicylates, phenolics, polysaccharides, urea. *A. vera* is conventionally applied to relieve itching and inflammation, wound healing as well as antimicrobial properties [2,3]. Aloenin is an important compound of *A. vera* used in skin allergies, burns and insect bites. Aloenin is efficacious in healing damaged dermal situation [4].

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Quercetin is able to reduce wheal, flare and itching of damaged skin. It may also help to restore skin barrier function and integrity. Quercetin is a natural flavonoid. It is obtained from several plants and foods, such as onions, apples, green tea, Ginkgo biloba, berries, St. John's wort, American elder, and others. It functions as antioxidants and plays an important role to combat free radical damage, which is related to various diseases [5,6].

Dermal formulation is the most common and popular approach to manage skin diseases [7]. *A. vera* herbal formulations available in the form of cream, gel, facial solution, moisturizer etc. Quercetin is formulated in different dermatological preparations as gel, emulgel and microemulsion gel. Combination, sequential and rotational ways are often more promising and better over single-agent remedies in the management of ailments [8]. There are a variety of novel remedies or topical formulations such as nano emulsions, microemulsion, multiple emulsion, liposomes, aerosol foams, hydrogel, organogel, nanogel etc. available that are frequently applied in order to target concurrent multiple pathogenic factors [9]. Therefore, *A. vera* and quercetin combination in novel topical formulation are proposed as viable remedies for effective eczema management.

ECZEMA AND ITS MANAGEMENT

Eczema is a common incendiary skin amitosis that is increasing in acclaim. The inception of eczema (also known as atopic dermatitis or atopic eczema/dermatitis syndrome) commonly takes place in the first few months of life and generally within the first year of life. The exact rationale of

eczema is unknown, but factors that may trigger or aggravate the condition include food and environmental allergens or annoyance, heat or cold, stress, and genetic susceptibility. Severe eczema can give rise to notable morbidity and have crucial social, emotional and financial influences on children and their families [10]. Histologically, three features of eczema are observed (**Figure 1**). Expansion of the stratum corneum is due to disruption to the cornification process, abnormal accumulation of fluid occurs due to destruction of the proteins involved in tight junctions, thereby leading to uncontrolled gesture of fluids in the paracellular space, infiltration of the dermis by immune cells is an indication of the primary immune reaction itself or in response to the ingress of allergens through a cracked dermal barrier [11].

Eczema has been an engrossing challenge for it is proficient of remissions and worsening. Evidently, it is tough to circumvent the allergens entangled for the condition, more so in the underprivileged candidate of the disease. Nonetheless, it is valuable to dwell on the therapies available thus far to relieve the symptoms and signs. Although dermal corticosteroids are often used to manage the predominant symptoms of the ailment, the persistency of the situation increases the risk of everlasting unwanted effects. Herbal medicine is as old as civilization. Utilization of traditional herbal medicine is extensive in different province of the world. Herbal remedies are generally distinguished as effective and have fewer side effects. Many herbs are used to treat various dermal diseases including eczema. Among them is *A. vera* which has demonstrated great results in dermal diseases [12].

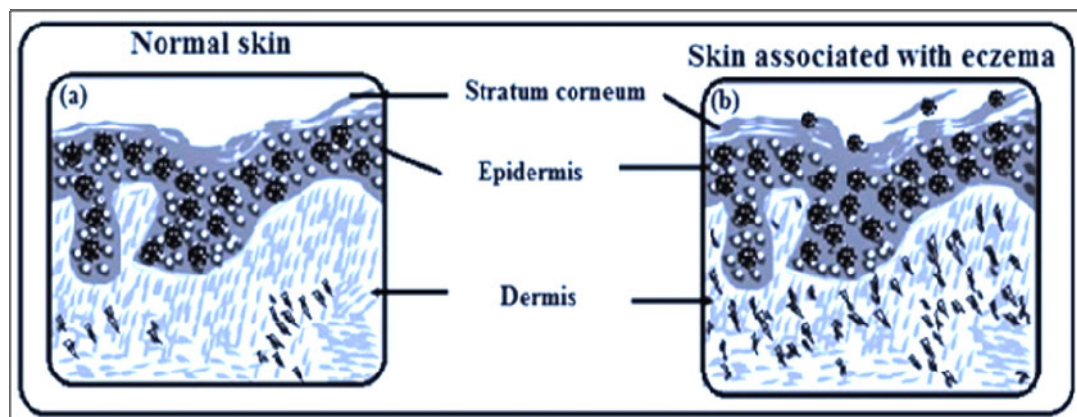


Figure 1. Schematic illustration of eczema. **Figure 1** compares normal skin (a) and skin affected by eczema (b).
Source: Gupta [8]

GLIMPSE ON ALOE VERA

The scientific name of *A. vera* is *Aloe barbadensis miller*. It is a member of *Asphodelaceae (Liliaceae)* family, and is a shrubby or dendriform, perennial, xerophytic, fleshy with serrated edges, green color plant. *A. vera* leaf is comprise of three strata: 1) An inner clear gel; 2) The middle layer of

latex, 3) The outer thick layer of 15-20 cells. *A. vera* has antioxidant, anti-inflammatory, antimicrobial, antineoplastic, hypoglycemic and immune enhancing properties. It is applied traditionally to manage many ailments. It is applied topically for wound healing, soothing inflamed skin and various dermal lesions. Many investigations revealed that *A. vera* decreases the manifestations of eczema such as skin

dehydration, scaling and refined the skin quality. In addition, its antimicrobial properties prevent further infection [13,14].

MEDICINAL PROPERTIES OF *ALOE VERA*

The medicinal properties of *A. vera* are based on mostly by incidental data. Though most of these applications are interesting, systematic trials are essential to measure its effectiveness in all the following diseases.

Properties based on scientific corroboration

These properties have been tested in humans or animals. Safety and efficacy have not always been proven. Medicinal properties based on scientific evidence was observed in the conditions like psoriasis, seborrheic dermatitis, vulgaris, skin burns, genital herpes, Type 2 diabetes, HIV infection, neoplastic lesions, ulcerative colitis, wound healing, mucositis, radiation dermatitis, acne vulgaris, lichen planus, frostbite, constipation, and aphthous stomatitis [15].

Properties based on historical convention or theory

These medicinal properties often have not been thoroughly investigated in humans. Safety and effectiveness have not always been proven in traditional and scientific theories for the conditions like alopecia, bacterial and fungal dermal infections, chronic leg wounds, systemic lupus erythematosus, arthritis and parasitic infections [2].

Aloe vera in Dermal Protection and Disease

A. vera maintains the skin moist and thus it is conventionally used as a moisturizer to cure the dehydrated skin. For example, *A. vera* gel gloves can build up dermal integrity and reduces the appearance of fine lines and erythema [16] and can be used for the treatment of pimples. Among different *A. vera* extracts, aloe mucopolysaccharides aid to combine water with the skin [17], thus providing moisturizing results. The leaf gel materials of *A. vera* was investigated which reveals that it boosts skin entropy, uniformity and energy at 30 and 90 min post application and thus have a greater hydrating effect [18]. *A. vera* also shields the skin from aging and it is thus having lots of scope in cosmeceuticals [17]. In clinical studies of radiation-induced dermatitis, *A. vera* extract can lower the influence of ultraviolet light on the skin, as some of the antioxidants and vitamins found in *A. vera* leaf can counteract the impact of ultraviolet (UV) radiation [19]. *A. vera* gel can alter the release of dermal keratinocytes derived from immunosuppressive cytokines like interleukin-10 (IL-10), thereby minimizing UV-induced delayed hypersensitivity responses [20]. Observations have shown that *A. vera* gel accommodates small molecule immunomodulators, such as G1C2F1, which minimizes epidermal Langerhans cells from UV-induced dermal immune responses [21]. These investigations presumed scientific proof holding up the traditional use of *A. vera* as a topical protective agent. *A. vera* gel has conventionally been considered to be a skin healing flora [22]. *A. vera* gel also exhibited beneficial

consequence on the epidermal keratinocytes during the wound healing activity. *A. vera* gel plays a crucial part in the management of superficial and partial thickness burns. *A. vera* gel also exhibited beneficial consequence on the epidermal keratinocytes during the wound healing activity. *A. vera* gel plays a crucial part in the management of superficial and partial thickness burns.

Several relevant investigations have showed that Aloe and its active components have potent therapeutic effects on several chronic dermal diseases like psoriasis and acne [23], as well as various kinds of dermal inflammations (**Table 1**). Moreover, it has been reported that *A. vera* lotion has a prophylactic action by reducing the impact of radiation-induced dermatitis [19]. Several earlier investigations have revealed that *A. vera* and its active compounds have encouraging potential for the effective management of dermal diseases with lower adverse effects.

QUERCETIN AT A GLANCE

Quercetin is classified as plant derived component, flavanol. It is reported that, quercetin has shown an excellent *in vitro* antioxidant. Within the flavonoid family, quercetin is the most potent scavenger of Reactive oxygen species. Earlier *in vitro* studies have shown that quercetin also possesses anti-microbial, anti-inflammatory, anti-proliferative activities, immuno-suppressive, anti-fibrotic, anti-coagulative, anti-atherogenic and antihypertensive. Quercetin also confines great prospective for dermal application, as it shows strong protective influence against UV-induced lipid peroxidation [32] and proved to be efficacious on human skin with anti-ageing activity and skin rejuvenation potentiality [33].

QUERCETIN IN CUTANEOUS DISORDERS

Quercetin is an encouraging potential compound for dermal diseases as it holds powerful antioxidant [34] and broad anti-inflammatory activities [35]. These activities can be executed in the management of dermal inflammatory diseases like psoriasis and in the favor of skin in response to oxidative stress persuaded by UV irradiation [36]. As the outermost protective organ of the human body, the skin is vulnerable to oxidative stress caused by environmental imbalance, which leads into various skin damage and diseases, such as aging, cancer, and inflammation (**Figure 2**). In the countenance of ultraviolet radiation, air pollution, and other extrinsic factors on the skin, it is of great importance to use substance that can hinder oxidative stress and inflammatory response to treat inflammatory dermal lesions and delay the skin aging. The antioxidant ability of OH on quercetin is playing a crucial role for anti-inflammatory and anti-oxidative responses. It is investigated that quercetin is applicable in treatment of furunculosis, dermatitis, atopic dermatitis, eczema, and other inflammatory dermal diseases.

Table 1. Different formulation of *A. vera* in the management of dermal or topical diseases and results obtained from different studies.

S. No.	Disease	Remedies	Outcome	Reported by
1	Various infections including skin transmitted infections	<i>A. vera</i> extracts	Maximum antibacterial activities and antifungal activity were observed in acetone extracts	Arunkumar [24]
2	Scabies	Crude gel of <i>A. vera</i>	The scabietic lesions virtually disappeared in all patients	Oyelami [25]
3	Burne wound	<i>A. vera</i> gel	Early epithelialization in the treated aloe vera gel area.	Visuthikosol [26]
4	Chronic pruritic skin lesions	<i>A. vera</i> /olive oil combination cream	<i>A. vera</i> /olive oil cream was at least as effective as betamethasone 0.1% in the treatment of sulfur mustard-induced chronic skin complications	Panahi [27]
5	Oral aphthous ulceration	Acemannan, a polysaccharide extracted from <i>A. vera</i>	Acemannan can be used for the treatment of oral aphthous ulceration in patients who wish to avoid the use of steroid medication	Bhalang [28]
6	Atopic dermatitis	Microencapsulation of copper enriched Aloe gel garment	Control of skin disease through medicated textiles.	Krishnaveni [29]
7	Atopic Eczema	<i>A. vera</i> gel	Dose dependent anti-inflammatory activity <i>A. vera</i> gel	Afzal [30]
8	Venous Eczema	Medical Moisture Retention Cream of <i>A. vera</i> (ALHYDRAN®),	Effective, safe, and feasible in the treatment of venous eczema	Rondas [31]

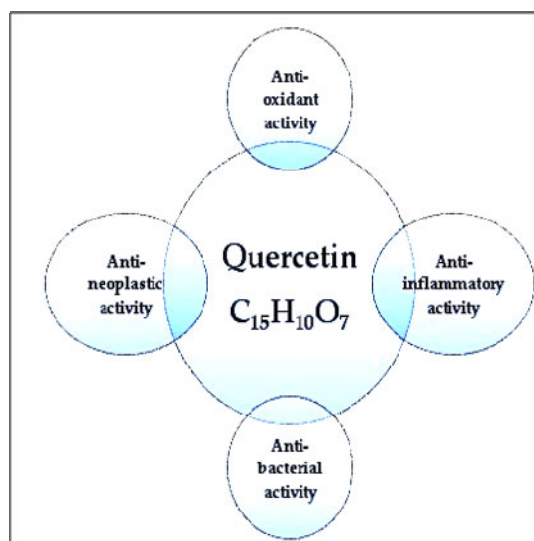


Figure 2. Quercetin: A natural flavanol with multifunctional therapeutic properties.

Source: Gupta [8]

NOVEL TOPICAL FORMULATIONS IN THE MANAGEMENT OF ECZEMA

Therapeutics is applied dermally to the skin especially for their local or site-specific action. Even though, the dermal delivery of the drug can also be applicable for systemic activity. Over the previous years, dermal delivery of drugs has given rise to more and more attention, of which, systemic side effects can be minimized in comparison to parenteral or oral drug delivery. Dermal delivery of the drug circumvents hepatic first-pass metabolism and extensive fluctuations of drug-plasma levels caused by repeated oral administration of rapidly eliminated drugs. Based on the characteristics of the ingredients and on the condition of the skin to be applied, a dispensing medium to provide a stable physicochemical environment that protects the active compound from chemical and enzymatic degradation should be developed, that can be a liquid or semi-solid, monophasic or multiphasic (dispersed systems). Inflammation of hypertrophic scar on the eczematous lesions forms a strong barrier for the skin permeation of medicaments through dermal route. To overcome this challenge, various novel topical formulations such as hydrogels, microemulsions, solid lipid nanoparticles, liposomes, dendrimers, and microsponges, nanogels, organogels etc. [37] have been explored for the penetration enhancement and prolonged release actions. These preparations are depicted to be applied not only as “drug carriers”, but also play a role in “drug depots” for releasing active ingredients over a sustained period of time.

SCOPE OF PHYTO-CHEMICAL IN NOVEL TOPICAL FORMULATION

Dermal applications of drugs, herbal or others are applied with a diversity of desired effects, including the targeting of

local tissues for dermal consequences, to the targeting of deeper strata, to the seeking out of a broader systemic influence. The history of the dermal application of plant-based medicines is over the prolonged period of time with documentations within traditional medicinal systems [38]. Herbal medicines are used in the management of a wide variety of conditions extending from dermatitis and psoriasis to dermal infections to dermal malignancies. However, the skin does provide an alarming barrier and novel drug delivery systems are being revolve to as a means to enhance dermal absorption. It is the incorporation of herbal medicines into such novel drug delivery systems. The key novel formulations that have been more specifically utilized for the dermatological and transdermal applications of herbal medicines are polymeric nanoparticles, liposomes, ethosomes, nano-emulsions, transferosomes, phytosomes and novel gels (Table 2). All these are reserving much interest to aggravate the therapeutic efficacy of phytochemicals [39].

CONCLUSIONS

Eczema is characterized by dry, rough and broken topmost layer of the skin known as stratum corneum. Several medicinal plant species applied to treat dermal ailments was investigated and documented since ancient time. Several investigated species are claimed very useful. However, these medicinal floras demanding a phytochemical screening for active moieties, biological properties and clinical studies are of universal significance. Using natural constituents in different novel topical formulations for skin care are very popular today. Moreover, one such type of natural plant; *A. vera* contain a lot of constituents which can be useful for dermal care. It is reported that *A. vera* possesses anti-aging and wrinkles reducing properties, moisturizing and cooling responses on the skin without allergic reaction, and burned

wound healing effects on the skin. Their potential is still undefined and need more investigations. Indeed, more research trials and clinical evidences are needed. It was shown that using only one natural constituent is not enough for skin care. Maybe, combination of several different

natural components is a right solution. Quercetin along with *A. vera* might be useful in the management of eczema due to its antioxidant and anti-inflammatory activity. Also, it is necessary to find out in which novel formulation the selected combination is stable and showing the best results.

Table 2. Phyto-chemical in different novel topical formulation to manage the various dermal diseases and ailments.

S. No.	Formulation	Merits	Therapeutic properties	Reported by
1	Quercetin liposomes	Enhanced skin permeation	Antioxidant and protective against UV β - radiation	Liu [40]
2	Mixed liposomes of quercetin and curcumin	Enhanced skin penetration	Anti-oxidant	Di Marzio [41]
3	<i>A. vera</i> liposomes	Enhanced bioavailability of AGE	Increased proliferation and synthesis of collagen in human skin cell line	Takahashi [42]
4	Quercetin nanoparticles	Enhanced skin uptake	Antioxidant	Tan [43]
5	Curcumin nanoparticles	Increased cellular uptake, better <i>in vitro</i> and <i>in vivo</i> bioavailability	Wound healing	Krausz [44]
6	Silver nanoparticles of <i>Citrullus colocynthis</i> extract	Enhanced penetration	wound healing	Satyavani [45]
7	Solid lipid nanoparticles of <i>Kaempferia parviflora</i> extract	Enhancement in skin permeability	Anti-inflammatory	Sutthanut [46]
8	Poly-herbal phytocomplex of <i>Trichosanthes curcumerina</i> extract and <i>Abrus precatorius</i> extract	Enhanced hair growth promoting effect	Anti-alopecia	Sandhya [47]
9	Genistein nanoemulsion	Enhancement of skin penetration	Anti-inflammatory	Momenkiaei [48]
10	Curcumin transferosome gel	Improvement in skin penetration	Antipsoriatic	Patel [49]
11	<i>Withania somnifera</i> niosomes	Improved delivery of withaferin A and withanolide A to the epidermis and dermis	Anti-melanoma	Chinembiri [50]

CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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