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# Dermocosmetics for Dry Skin: A New Role for Botanical Extracts

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**Key Words**
Filaggrin · Keratinocyte differentiation · Skin hydration · Transepidermal water loss

**Abstract**
Dry skin is associated with a disturbed skin barrier and reduced formation of epidermal proteins and lipids. During recent years, skin-barrier-reinforcing properties of some botanical compounds have been described. Searching the PubMed database revealed 9 botanical extracts that specifically improve skin barrier and/or promote keratinocyte differentiation in vivo after topical application. The topical application of *Aloe vera* (leaf gel), *Betula alba* (birch bark extract), *Helianthus annuus* (sunflower oleodistillate), *Hypericum perforatum* (St. John's wort extract), *Lithospermum erythrorhizon* (root extract), *Piptadenia colubrina* (angico-branco extract) and *Simarouba amara* (bitter wood extract) increased skin hydration, reduced the transepidermal water loss, or promoted keratinocyte differentiation in humans in vivo. The topical application of *Rubia cordifolia* root extract and rose oil obtained from *Rosa* spp. flowers stimulated keratinocyte differentiation in mouse models. The underlying mechanisms of these effects are discussed. It is concluded that some botanical compounds display skin-barrier-reinforcing properties that may be used in dermocosmetics for dry skin. However, more investigations on the mode of action and more vehicle-controlled studies are required.



## Introduction

The outermost layer of the epidermis, the stratum corneum, represents a thin physical, chemical and immunological barrier that protects the organism from the entry of xenobiotics and minimizes water loss from the epidermis [1]. The stratum corneum has also been identified as a powerful first line of antioxidant defense that is mainly mediated by the small proline-rich family of cornified envelope precursor proteins [2]. The proliferation and differentiation of the epidermis is tightly regulated to maintain its physiologic homeostasis. Injury or disturbed function of the epidermal barrier results in increased transepidermal water loss (TEWL) and the development

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of dry skin. The pathophysiology of an impaired epidermal barrier is characterized by disturbed keratinocyte differentiation and proliferation, changes in epidermal protein and lipid content and a decreased amount of natural moisturizing factors. The discovery of common loss-of-function mutations of the epidermal barrier protein filaggrin in atopic dermatitis [3] has improved our knowledge about the role of epidermal proteins in the barrier function of diseased and normal skin [4]. Besides proteins, epidermal lipids also play an important role in the formation and maintenance of the cornified envelope and the barrier function of the stratum corneum. The hydrophobic extracellular lipid network of the stratum corneum is mainly composed of ceramides, cholesterol and free fatty acids that contribute to the physical and antimicrobial barrier [5, 6]. The interaction of epicutaneously applied lipids with the stratum corneum is very complex and depends, inter alia, on the presence and amount of water and emulsifiers [7]. The effect of topically applied lipids on the barrier function may vary, depending on the treated skin condition [8]. Also, the pH of the skin surface plays a great role in both the epidermal barrier formation and cutaneous antimicrobial defense [9]. Only recently has it been shown that enhanced absorption occurs in damaged or diseased skin, which plays an important role in topical drug delivery [10, 11]. To improve the epidermal barrier function, the use of water-in-oil (w/o) emulsions is usually preferred, whereas the topical use of oil-in-water (o/w) emulsions has been shown to result in a transient increase in skin permeability that may facilitate the introduction of actives in the stratum corneum [12]. On the other hand, o/w emulsions may also display barrier-enhancing effects, for example against the penetration of pollen allergens into hair follicles [13].

Dry skin is an increasing problem not only in atopic eczema but also in the aging population, facilitating pruritus and irritant contact dermatitis in the elderly [14]. Glucocorticoids are often used to treat contact dermatitis or asteatotic eczema in elderly patients. However, even short-term glucocorticoid treatment may display adverse effects on epidermal permeability barrier and stratum corneum integrity, which may worsen the dry skin cycle in aged skin [15]. Therefore, besides natural moisturizing factors, such as urea, glycerol or amino acids [16], the use of barrier-reinforcing actives in dermocosmetics for dry skin is highly desirable. During recent years, a variety of botanical extracts have been identified that improve the skin barrier by modulating the metabolism of keratinocytes. A literature search of the PubMed database using the key words 'dry skin', 'skin barrier', 'moisturizer', 'botanical extract', 'plant extract', 'essential oil', 'keratinocyte' and 'differentiation' identified 9 plants that specifically improve the skin barrier or promote keratinocyte differentiation after topical application in vivo.

### *Aloe vera*

Leaf extracts from *Aloe vera* (syn. *A. barbadensis*) rich in polysaccharides are often used in cosmetics and over-the-counter drugs for the treatment of burns, sunburn, wounds and skin inflammation [17]. In a randomized vehicle-controlled study on 20 volunteers, the effect of different concentrations of lyophilized *A. vera* extract on skin hydration and TEWL was assessed. After 2 weeks of application, all tested *A. vera* concentrations (0.1, 0.25 and 0.5%) significantly improved skin hydration as opposed to the vehicle. No significant change in the TEWL was observed [18].

### *Betula alba*

With a recently developed triterpene extract from the outer bark of birch *(Betula alba)*, with over 80% betulin, a cream can be produced without the aid of emulsifiers. It only consists of 4.5% (v/v) birch bark extract, vegetable oil and water. In an artificially damaged skin barrier, a comparable or even superior effect of the birch bark cream with respect to improvement in stratum corneum hydration, reduction of TEWL and skin erythema as opposed to 'hydrophilic cream NRF' (consisting of non-ionic emulsifying alcohols, 2-ethylhexyllauromyristate, glycerol, potassium sorbate, citric acid and water) was seen [19]. In vitro, birch bark extract increased calcium influx into primary keratinocytes and upregulated various differentiation markers including keratin-10 and involucrin [20]. Topical treatment with an oleogel containing 10% (v/v) birch bark extract of actinic keratosis, which represent in situ squamous cell carcinomas with disturbed epithelial differentiation, resulted in upregulation of keratin-10 in situ [20].

### *Helianthus annuus* (Sunflower Oil)

Sunflower oil is obtained by extraction of the fruits of *Helianthus annuus*. In its natural state, sunflower oil contains high levels of essential fatty acids, such as linoleic acid, linolenic acid, oleic acid, palmitic acid and stearic

acid. Sunflower oleodistillate (SOD) contains 90% essential fatty acids, 5% phytosterols and 1% tocopherol. SOD has been shown to activate the peroxisome proliferator-activated receptor (PPAR)-α in vitro. PPAR-α stimulates the expression of involucrin and filaggrin, and enhances the lipid metabolism in keratinocytes with increased synthesis of cholesterol, cholesterol sulfate and ceramides. In vivo, a cream containing 2% SOD increased epidermal lipid synthesis and skin hydration, reduced the TEWL and displayed a corticosteroid-sparing effect in atopic dermatitis [21].

### *Hypericum perforatum*

Hyperforin, the lipophilic main active ingredient of *Hypericum perforatum* (St. John's wort), induced a strong $Ca^{2+}$ influx in proliferating primary keratinocytes by direct activation of the cation channel TRPC6, leading to decreased proliferation and increased expression of differentiation markers like keratin-1, keratin-10 and involucrin [22]. In a randomized placebo-controlled double-blind half-side comparison, the effect of a cream containing 1.5% (v/v) hyperforin was examined on 21 patients with subacute atopic dermatitis. The efficacy of the cream was superior to the vehicle, with excellent skin tolerability and cosmetic acceptance on the part of the users [23]. In a 4-week use trial with 15 adult atopic patients after treatment with hyperforin cream, an increase in hydration as well as a reduction of TEWL and scaliness was observed as opposed to the vehicle control [24].

### *Lithospermum erythrorhizon*

The roots of *Lithospermum erythrorhizon* are used in traditional Chinese medicine for a variety of disorders. Recently, the effect of various concentrations of a standardized root extract of *L. erythrorhizon* was investigated on the skin of 30 healthy Asian females. Emulsions containing 1, 2.5 and 5% (v/v) of the extract were applied twice daily over 28 days. All concentrations improved skin hydration and reduced TEWL as opposed to the vehicle [25].

### *Piptadenia colubrina*

The mimosa-like timber tree *Piptadenia colubrina* is native to South American rain forests. A hydroglycolic extract of *P. colubrina* enhanced the expression of aquaporin-3, involucrin and filaggrin in cultured keratinocytes and human skin explants. Skin capacitance and glycerol index were improved after treatment with a cream containing 5% *P. colubrina* extract in a placebo-controlled half-side comparison with 30 human volunteers [26]. The cream improved skin hydration after 14 days of treatment as opposed to the vehicle [26].

### *Rubia cordifolia*

*Rubia cordifolia* was tested for skin-reinforcing properties in a mouse model. An ethyl acetate extract obtained from *R. cordifolia* roots displayed antiproliferative and apoptosis-inducing effects on HaCaT keratinocytes [27]. In BALB/c mice, the effect of a *R. cordifolia* extract-containing gel was evaluated after 4 weeks of application on the mouse tails. The gel with 5% *R. cordifolia* extract significantly increased the thickness of the granular layer and the epidermis as opposed to the vehicle [27].

### *Rosa* spp. (Rose Absolute Oil)

Rose absolute oil obtained by distillation of *Rosa* spp. flowers inhibited proliferation and induced the expression of involucrin and filaggrin in cultured keratinocytes in vitro. In vivo, 0.1% rose absolute oil reduced the TEWL and increased the expression of filaggrin in tape-stripped skin of hairless mice as opposed to the vehicle [28].

### *Simarouba amara*

An aqueous bark extract from *Simarouba amara* (bitter wood) was investigated on cultured skin equivalents. It increased the formation of involucrin and transglutaminase as well as cholesterol sulfate, cholesterol and ceramides. In a double-blind half-side comparison study, an ointment containing 0.2% *S. amara* extract reduced TEWL and increased skin hydration on the face of 20 healthy volunteers after 4 weeks of epicutaneous application [29].

## Conclusion

Selected botanical compounds display interesting skin-barrier-reinforcing properties (fig. 1). The improvement in skin hydration, reduction of TEWL, stim-

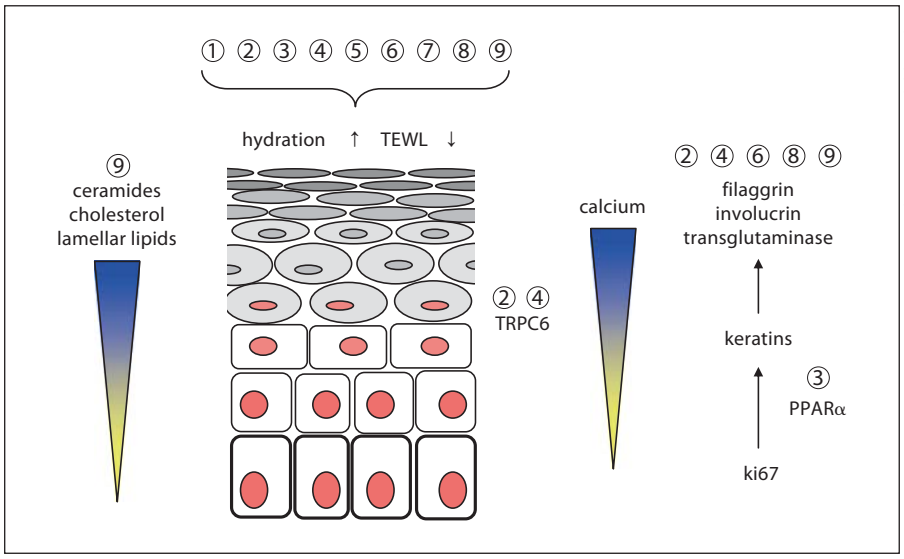


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**Fig. 1.** Skin-barrier-reinforcing properties of botanical extracts. 1 = *Aloe vera*; 2 = *Betula alba*; 3 = *Helianthus annuus*; 4 = *Hypericum perforatum*; 5 = *Lithospermum erythrorhizon*; 6 = *Piptadenia colubrina*; 7 = *Rubia cordifolia*; 8 = *Rosa* spp.; 9 = *Simarouba amara*.

ulation of keratinocyte differentiation, and production of epidermal lipids and proteins predestines these botanicals for roles as new actives in dermocosmetics for dry skin. However, although most of the data discussed here originate from in vivo studies, the molecular targets of the active compounds have only partly been identified. Therefore, much more investigation into their mode of action and more vehicle-controlled studies are required.


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## Disclosure Statement

C.M.S. jointly holds a patent on the dermatological use of hyperforin-rich extracts from St. John's wort. The other authors declare no conflict of interest.

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