DRUGS IN CONTEXT
RIGOROUS • RAPID • RESPONSIVE

A continuous publication, open access, peer-reviewed journal

ACCESS ONLINE

REVIEW

Emollient treatment of atopic dermatitis: latest evidence and clinical considerations

Kam Lun Hon MBBS, MD, FAAP, FCCM, Jeng Sum Charmaine Kung BSc, Wing Gi Gigi Ng BSc, Ting Fan Leung MBChB, MD, MRCP, FRCPCH

Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong

Abstract

Aim: To review current classes of emollients in the market, their clinical efficacy in atopic dermatitis (AD) and considerations for choice of an emollient.

Methods: PubMed Clinical Queries under Clinical Study Categories (with Category limited to Therapy and Scope limited to Narrow) and Systematic Reviews were used as the search engine. Keywords of 'emollient or moisturizer' and 'atopic dermatitis' were used.

Overview of findings: Using the keywords of 'emollient' and 'atopic dermatitis', there were 105 and 36 hits under Clinical Study Categories (with Category limited to Therapy and Scope limited to Narrow) and Systematic Reviews, respectively. Plant-derived products, animal products and special ingredients were discussed. Selected proprietary products were tabulated.

Conclusions: A number of proprietary emollients have undergone trials with clinical data available on PubMed-indexed journals. Most moisturizers showed some beneficial effects, but there was generally no evidence that one moisturizer is superior to another. Choosing an appropriate emollient for AD patients would improve acceptability and adherence for emollient treatment. Physician's recommendation is the primary consideration for patients when selecting a moisturizer/emollient; therefore, doctors should provide evidence-based information about these emollients.

Keywords: atopic dermatitis, emollient.

Citation

Hon KL, Kung JSC, Ng WGG, Leung TF. Emollient treatment of atopic dermatitis: latest evidence and clinical considerations. Drugs in Context 2018; 7: 212530. DOI: 10.7573/dic.212530

Introduction

Atopic dermatitis (AD) is a complex disease with various degrees of skin inflammation, erythema, dryness and staphylococcal infections [1,2]. The cardinal symptoms are pruritus and sleep disturbance, and quality of life is much affected. The mainstay of treatment for AD is regular usage of emollient and topical medications [3]. Emollients provide an occlusive barrier for AD skin, retain moisture and protect it from irritants. Specially formulated emollient products may claim to have antimicrobial, anti-itch and anti-inflammatory actions. They are complex mixtures of chemical agents specially designed to make the epidermis softer and more pliable [4,5]. However, 'emollient' sometimes refers to a specific ingredient that soothes the skin; it is more appropriate to use the term 'moisturizer'. The terms 'emollients' and 'moisturizers' are often used interchangeably. Occlusive agents work by forming a thin hydrophobic film on the surface of the skin to retard transepidermal loss of moisture [4]. They are similar to the intercellular lipid bilayers of ceramide, cholesterol and free fatty acids [4,5]. Examples include lanolin, mineral oils, olive oil, petrolatum ceramide, paraffin and silicone. Humectants attract water vapor to moisturize the skin [4]. They are similar to the natural moisturizing factors in the corneocytes. Examples include glycerin, alpha hydroxyl acids and sorbitol. Emollients fill the cracks between desquamating corneocytes and smoothen the skin [4]. Examples include collagen, elastin, glyceryl stearate and shea butter [6].

Choosing an emollient has been a major concern for patients and physicians. Despite price differences, the major ingredients of an emollient are similar, consisting of petrolatum, paraffin, glycerin, plant-derived butter and oils, and their combinations provide various formulations for the market [7,8]. Recent advances in the understanding of the pathophysiology of AD have led to the production of new moisturizers targeted to replenish ceramides and natural moisturizing factors in the stratum corneum [9]. Many brands of emollients are expensive and claim to contain ingredients targeting AD pathophysiology [5]. A number of these emollients have not been subjected to vigorous scientific evaluations to document their clinical efficacy or relevance. Parents are constantly in search

of an ideal emollient that they will find acceptable for use on their children [7]. We previously tested a number of commercial products and noted patient factors – namely, preference and acceptability – may influence outcomes of topical treatment independent of ingredients in these products [7].

This overview aims to discuss current classes of emollients in the market, clinical evidence and considerations for choice of an emollient.

Methods

PubMed Clinical Queries under Clinical Study Categories (with Category limited to Therapy and Scope limited to Narrow) and Systemic Reviews were used as the search engine to identify relevant publications for this overview. The keywords 'emollient or moisturizer' and 'atopic dermatitis' were used. The reference lists of some of these publications were reviewed to further identify relevant papers.

Overview

Using the keywords 'emollient' and 'atopic dermatitis', there were 105 and 36 hits under Clinical Study Categories (with Category limited to Therapy and Scope limited to Narrow) and Systematic Reviews, respectively. Relevant publications are cited in Table 1 and in other sections accordingly.

Selecting an appropriate emollient for a patient is critical, as it is the fundamental treatment for AD. In one survey, aqueous cream was the most commonly used emollient, with petroleum-derived products the next. When comparing aqueous cream with other emollients, aqueous cream users had lower product acceptability and measurably lower skin hydration [8]. Aqueous cream has been known to contain sodium lauryl sulfate (SLS) that can cause skin irritation. Tsang and colleagues reported that chronic use of aqueous cream can cause reduction in stratum corneum thickness and an increase in transepidermal water loss (TEWL) measurements [10]. Treatment with aqueous cream is associated with increased desquamatory and inflammatory protease activity [11]. Aqueous cream BP should not be used as a leave-on emollient in patients with AD [12]. Other than aqueous cream, commercial products available in the market may contain allergens. Common allergens in emollients include fragrances and tocopherol [13]. Eczematous skin may be prone to secondary sensitization and further damage with frequent application of some of the emollients.

Essential oils have recently shown potential therapeutic effects in treating dermatitis or other health conditions. The North American Contact Dermatitis Group tested three fragrance markers and six types of common essential oils, including tea-tree oil, which is often claimed to have anti-inflammatory effects for AD patients. In the study, tea-tree oil was identified to be accounted for 45% of positive reactions among the subjects who were sensitized to essential oils. More than half of the reactions were strong and with definite/probable clinical relevance [14].

Currently, most skin-care products are commonly labeled as 'dermatologically tested'. Such labeling may be misleading to users. A group conducted a small survey on companies that label their products as 'dermatologically tested' and requested testing information from these companies. Of the 25 companies responded, only 4 disclosed the number of subjects tested; 5 said their products had been tested on human skin, but the nature of the tests were not clarified. Thirteen of the companies said a dermatologist was involved in the testing at some point [15]. The investigators also noted that products claiming to be 'fragrance free' may also contain a fragrance cross-reactor or botanical ingredient [13].

The advertised prices for emollients for AD can vary. Xu and colleagues showed that best-selling moisturizer products ranged from $0.10 to $9.51 per ounce in the USA. Of the 174 products studied, only 12% were allergen free as described by the North American Contact Dermatitis Group. In addition, products with the claim of 'dermatologist recommended' or 'phthalate free' had a higher median price per ounce than products without the claim [13].

Various emollient products have been marketed to treat eczema with claim of therapeutic effect. Common ingredients in emollients include petroleum products, glycerin, fatty acids and plant oils. An ideal emollient should contain a combination of occlusive agents to slow down water loss, humectants to increase capacity to withhold moisture and lubricants to reduce friction against skin. As well as the general moisturizing/water-trapping ingredients, it is common to find other herbal/animal-derived active ingredients added into commercial emollients for supposed advanced beneficial effects.
We previously tabulated published data on a number of moisturizers/emollients [6]. Selected proprietary moisturizers/emollients and their claimed ingredients are described in the present paper for comparison (Table 1).

Plant-derived products

Aloe vera

Aloe vera is a stemless, succulent plant with juicy flesh commonly used in the skin-care industry [16]. Other than its moisturizing property, its extracts possess antibacterial and antifungal actions that may aid in preventing secondary infection for AD patients [17,18]. Though this plant has a list of claimed healing properties, to the authors' best knowledge, there are no control-based trials on AD patients. Most of the clinical trials with aloe vera were done in the field of diabetes and gastrointestinal conditions. The most relevant studies relating aloe vera in AD are two animal studies that were published in 2010 and 2015 [19,20]. Both studies investigated the effect of aloe vera on the immunoglobulin E levels in their AD animal models, though with contrasting results. The group that applied aloe vera extract topically on AD-induced Balb/c mice for 10 days measured a significant reduction in serum IgE levels compared with the placebo control [19]. On the other hand, the group that

Table 1. Selected proprietary moisturizers/emollients and their claimed ingredients.

Moisturizer	Include			List of ingredients		Clinical efficacy	Biophysical effects	References
	P"	A^	S*	Claimed active ingredients	Other ingredients/excipients			
1. Aqueous cream BP				-Not specified	-Emulsifying ointment, white soft paraffin, liquid paraffin, sodium lauryl sulfate, cetostearyl alcohol, phenoxyethanol, purified water	-Not evaluated	-Disrupted maturation process of corneocytes -Thinning of stratum corneum -Increased TEWL -Increased protease activity for desquamatory enzymes (KLK5 & KLK7) and inflammatory enzyme (plasmin & tryptase)	Mohammed et al. [11]
2. Ceradan Cream (Hyphens Pharma Pte Ltd, Singapore)			√	-Hydroxypropyl bispalmitamide MEA (ceramide)	-Water, hydrogenated polydecene, butylene glycol, cyclopentasiloxane, behenyl alcohol, cetyl alcohol, glycerin, *Simmondsia chinensis* (jojoba) seed oil, PEG-60 glyceryl isostearate, glyceryl stearate, linoleic acid, cholesterol, pentylene glycol, beeswax, squalane, trideceth-12, sodium lauroyl lactylate, sorbitan stearate, dimethicone, PEG-6, PEG-32, phenoxyethanol, carbomer, xanthan gum, ethylhexylglycerin, tocopherol, sodium hydroxide	-A statistically significant mean change of SCORAD and PEST scores be –11.46 and –1.33 respectively over 12 weeks	-Not evaluated	Koh et al. [42]
3. Cetaphil Moisturizing Cream (Laboratoires Galderma, Alby-sur-Chéran, France)				-Not specified	-Water, glycerin, petrolatum, dicaprylyl ether, dimethicone, glyceryl stearate, cetyl alcohol, *Prunus amygdalus dulcis* (sweet almond) oil, PEG-30 stearate, tocopheryl acetate, acrylates/C10-30 alkyl acrylate crosspolymer, dimethiconol, benzyl alcohol, phenoxyethanol, glyceryl acrylate copolymer, propylene glycol, disodium EDTA, sodium hydroxide	-No significant improvement in SCORAD after 2 weeks of application	-Significant improvement was found in skin hydration but not for transepidermal water loss	Hon et al. [61]

(Continued)

Table 1. (*Continued*)

Moisturizer	Include			List of ingredients		Clinical efficacy	Biophysical effects	References
	P"	A^	S*	Claimed active ingredients	Other ingredients/excipients			
4. Cetaphil RESTORADERM Skin Restoring Lotion(Galderma Canada Inc., Thronhill, ON, Canada)			√	-Hydroxypalmitoyl sphinganine (ceramide precursor) -Arginine (natural moisturizing factors) -Sodium PCA (natural moisturizing factors)	-Water, glycerin, caprylic triglyceride, *Helianthus annuus* (sunflower) seed oil, pentylene glycol, *Butyrospermum parkii* (shea butter), sorbitol, cyclopentasiloxane, cetearyl alcohol, behenyl alcohol, glyceryl stearate, tocopheryl acetate, niacinamide, allantoin, panthenol, disodium ethylene dicocamide PEG-15 disulfate, glyceryl stearate citrate, ceteareth-20, sodium polyacrylate, caprylyl glycol, citric acid, dimethiconol, disodium EDTA, sodium hyaluronate, cetyl alcohol	-A statistically significant decrease in objective SCORAD from 31.5 to 25.7 among the two-thirds of the subjects who reported very good/good product acceptability over 14 days	-A statistically significant increase in skin hydration from 30.7 (a.u.) to 36.0 (a.u.) among the two-thirds of the subjects who reported very good/ good product acceptability over 14 days	Hon et al. [41]
5. Canoderm cream 5% (ACO Hud, Upplands Väsby, Sweden)			√	-Urea	-Fractionated coconut oil, emulsifying wax, hydrogenated canola oil, propylene glycol, carbomer, dimethicone, hard paraffin, glycerol polymetacrylate, propyl parahydroxybenzoate (E 216), methyl parahydroxybenzoate (E 218), sodium lactate solution, lactic acid, glyceryl stearate, polyoxyethylene stearate and purified water	-Statistically significant delayed mean time of AD relapse on previous eczematous area to >180 days (duration of study) compared with 30 days for the no treatment group	-Not evaluated	Wirén et al. [62]
6. Curel Moisture cream (Kao Corporation, Tokyo, Japan)	√		√	-Cetyl-propyleneglycol-hydroxyethyl-palmitamide (synthetic pseudoceramide) -*Eucalyptus globulus* leaf extract	-Allantoin, bis-methoxypropylamido isodocosane, butylene glycol, cetyl dimethicone, cyclopentasiloxane, dextrin palmitate, dimethicone, dipentaerythrityl hexahydroxystearate, glycerin, isostearyl glyceryl ether, magnesium sulfate, methyl paraben, neopentyl glycol dicaprate, PEG-5 hydrogenated castor oil, PEG-12 dimethicone, polyglyceryl-2 diisostearate, sodium hydroxide, squalene, succinic acid, tocopherol, trisiloxane, water	-No deterioration in eczema severity or quality of life as measured by SCORAD and CDLQI.	-Skin hydration improved significantly after 4 weeks, with no deterioration in TEWL loss.	Hon et al. [45]

(Continued)

Table 1. (*Continued*)

Moisturizer	Include			List of ingredients		Clinical efficacy	Biophysical effects	References
	P"	A^	S*	Claimed active ingredients	Other ingredients/excipients			
7. Curel Moisture cream (Kao Corporation, Tokyo, Japan)	√		√	-Cetyl-propyleneglycol-hydroxyethyl-palmitamide (synthetic pseudoceramide) -*Eucalyptus globulus* leaf extract	-Allantoin, bis-methoxypropylamido isodocosane, butylene glycol, cetyl dimethicone, cyclopentasiloxane, dextrin palmitate, dimethicone, dipentaerythrityl hexahydroxystearate, glycerin, isostearyl glyceryl ether, magnesium sulfate, methyl paraben, neopentyl glycol dicaprate, PEG-5 hydrogenated castor oil, PEG-12 dimethicone, polyglyceryl-2 diisostearate, sodium hydroxide, squalene, succinic acid, tocopherol, trisiloxane, water	-A statistically significant decrease in objective SCORAD from 29.1 to 22.0 over 4 weeks -DLQI and POEM showed significant improvements as well -Adverse events reported: Five patients reported pruritus and one with warmth sensation at week 2; 2 patients reported pruritus after usage at week 4L; one patient developed worsen rashes and acneiform papules on face and discontinued the product at week 3	-Stratum corneum hydration significantly increased from 39.7 to 49.2 -No significant difference in TEWL	Seghers et al. [63]
8. Decubal® original clinic cream (Actavis Pharma, Inc, Parsippany, New Jersey, USA)		√	√	-Anhydrous lanolin -Glycerin	-Isopropyl myristate, cetyl alcohol, sorbitan monosterate, polysorbate, dimethicone, sorbic acid	-Not evaluated	-Hydration of stratum corneum increased most significantly using Decubal® (compared with the other 2 moisturizers) and reached a plateau after 2–3 days within the 7-day study -TEWL not affected by treatment	Moss [64]

(Continued)

Table 1. (*Continued*)

Moisturizer	Include			List of ingredients		Clinical efficacy	Biophysical effects	References
	P"	A^	S*	Claimed active ingredients	Other ingredients/excipients			
9. Ectoin® Dermatitis Cream 7% (Bitop AG, Witten, Germany)			√	-Ectoin	-Aqua, hydrogenated lecithin, ceramide-3, squalene, *Olea europaea* fruit oil, caprylic triglyceride, *Butyrospermum parkii* butter, *Oryza sativa* (rice) bran cera, carbomer, xanthan gum, sodium carbomer, *Cardiospermum halicacabum* flower/leaf/vine extract, glycine, alanine, pentylene glycol, butylene glycol, hydroxyethyl cellulose, glycerin, hydroxyphenyl propamidobenzoic acid	-Significant reduction in AD. Clinical severity measured by SCORAD, IGA or self-assessment over 28 days	-Not evaluated	Marini et al. [58]
10. EpiCeram Skin barrier Emulsion (PuraCap pharmacedutical, Plainfield, NJ, USA)			√	-Bispalmitamide MEA (Ceramide) -Conjugated Linoleic Acid (CLA) -Cholesterol -Palmitic acid	- Purified water, MultiSalTM Neolipids (a proprietary microencapsulation system), Glyceryl stearate, squalene, glycerin, PEG-100 stearate, hydroxypropyl, petrolatum, dimethicone, phenoxyethanol, citric acid, xanthan gum, potassium hydroxide, disodium EDTA, sorbic acid, Capric acid.	-Significant reduction in SCORAD, with improvements in pruritus and sleeping habits, both after 14 and 28 days of treatment, though with no significant difference from the fluticasone propionate cream treated group by 28 days	-Not evaluated	Sugarman et al. [65]
11. Eucerin eczema Relief Body Crème (Beiersdorf Inc, Wilton, Connecticut, United States)	√			-Colloidal oatmeal	-Aqua, glycerin, *Ricinus communis* (castor) seed oil, mineral oil, cetyl alcohol, glyceryl stearate, caprylic triglyceride, octyldodecanol, cetyl palmitate, PEG-40 stearate, *Glycyrrhiza inflata* root extract, ceramide 1,2-hexanediol, phenoxyethanol, piroctone, olamine, caprylyl glycol, ethylhexylglycerin, benzyl alcohol, citric acid	-Significantly lower incidence of flare; shorter median time to flare and reduced risk of flare compared with control group after 6 months -78.9% of flares improved or cleared at week 4 -No AE reported in treatment group	-Not evaluated	Weber et al. [66]

(Continued)

Table 1. (*Continued*)

Moisturizer	Include			List of ingredients		Clinical efficacy	Biophysical effects	References
	P"	A^	S*	Claimed active ingredients	Other ingredients/excipients			
12. Ezerra cream (Hoe Pharma, Petaling Jaya, Malaysia)	√			-Stimu-tex AS (spent grain wax, *Butyrospermum parkii* extract and *Argania spinosa* kemel oil) -Saccharide isomerate	-Water, oleic/linoleic triglyceride, hydrogenated polydecene, pentaerythrityl distearate, glycerin, cetearyl alcohol, dimethicone phenoxyethanol, sodium stearyl glutamate, acrylates/ C10-C30 alkyl acrylate crosspolymer, ethylhexylglycerin, octadecyl di-t-butyl-4-hydroxyhydrocinnamate, disodium EDTA	-Statistically significant decrease of mean pruritus score in SCORAD from 6.7 to 6.0, and CDLQI quality of life score from 10.0 to 8.0	-No statistically significant change in skin hydration, transepidermal water loss, and *Staphylococcus aureus* infection status.	Hon et al. [6]
13. Intense Hydration & Repair Treatment (Receutics, New York City. NY, USA)	√		√	-dimethicone -shear butter oil -glycerin -vitamin B -sodium PCA -sodium hyaluronate -ceramide 3 -cholesterol -phytosphingosine -ceramide 6 II -ceramide 1 -allantoin (botanical anti-inflammatories) -bisabolol (botanical anti-inflammatories)	-Anhydroxylitol, arginine, betaine, *Borago officinalis* seed oil, butylene glycol, capric triglyceride, carbomer, *Cardiospermum halicacabum* extract, cetearyl alcohol, ceteth-10 phosphate, *Chlorella vulgaris* extract, chlorphenesin, pumpkin seed oil, *Cymbopogon schoenanthus* extract, *Cymbopogon schoenanthus* oil, carrot seed oil, dicetyl phosphate, disodium EDTA, *Echium plantagineum* seed oil, ethylhexlyglycerin, glyceryl stearate, sunflower seed oil, unsaponifiables, hydrolyzed align, hydrolyzed sclerotium gum, hydroxyphenyl propamidobenzoic acid, isosorbide dicaprylate, *Laminaria ochroleuca* extract, niacinamide, *Nigella sativa* seed oil, octyldodecanol, *Ormenis multicaulis* oil, panthenol, peg-100 stearate, pentylene glycol, phenoxyethanol, polyglutamic acid, polyquaternium-51, polysorbate 60, potassium lactate, potassium sorbate, sea salt, sodium benzoate, sodium lauroyl lactylate, tomato seed oil, squalene, stevioside, *Tamarindus indica* seed gum, tocopherol, tocopheryl acetate, trehalose, triacetin., urea, *Vaccinium*	-Claimed statistically significant improvement in investigator-assessed scores including irritation, erythema, desquamation, roughness, dryness, lichenification, itching, and overall skin appearance after 2 weeks (but no numerical data on these were provided in this pilot study)	-Skin hydration significantly increased by 44% (from 121.12 to 181.84) after 2 weeks	Draelos et al. [67]

(Continued)

Table 1. (*Continued*)

Moisturizer	Include			List of ingredients		Clinical efficacy	Biophysical effects	References
	P"	A^	S*	Claimed active ingredients	Other ingredients/excipients			
					cranberry seed oil, grape-seed oil, xanthan gum, xylitol, xylitylglucoside, corn starch modified, zinc citrate			
14. Physiogel A.I. Cream (Stiefel Laboratories Inc, Research Triangle Park, NC, USA)			√	-Palmitamide MEA (PEA) -Acetamide MEA	-Aqua, *Olea europaea* fruit oil, glycerin, pentylene glycol, Olus oil, *Elaeis guineensis* oil, hydrogenated lecithin, squalene, betaine, sarcosine, hydroxyethyl cellulose, carbomer, sodium carbomer, xanthan gum	-Intensity of erythema, pruritus, excoriation, scaling, lichenification, and dryness, significantly reduced, assessed by physicians' 4-point scale and patients' self-assessments after both 6 and 38 days -Sleep quality improved significantly according to patients' self- assessing questionnaires after both 6 and 38 days	-Not evaluated	Eberlein et al. [68]
15. Suvex Soothe emollient cream (Naturalife Ltd, Rathnew, Ireland)	√			-*Aloe vera* leaf juice powder -*Ascophyllum nodosum* (Norwegian kelp) plant extract -Capuacu butter -Rice bran oil -Rose hip seed oil, -Shea butter	-Water, octyldodecanol, glycerin, , sorbitan olivate, cetearyl olivate, gluconolactone, sodium polyacrylate, zinc PCA, Tocopherol, sodium benzoate, *Cyamopsis tetragonoloba* gum, *Plantago lanceolata* (lamb's tongue) leaf extract, phenoxyethanol, *Echium plantagineum* (purple viper's bugloss) seed oil, *Cardiospermum halicacabum* (balloon) plant extract, *Helianthus annuus* (sunflower) seed oil, unsaponifiables, potassium sorbate.	-Not evaluated	-TEWL, hydration, skin elasticity and firmness, erythema, skin roughness and smoothness statistically improved over 14 days	Wakeman et al. [69]

"Plant derived claimed-active ingredient.
^Animal derived claimed-active ingredient.
*Special/synthetic claimed-active ingredients.

CDLQI, children's dermatology life quality index; DLQI, Dermatology Life Quality Index; IGA, investigator global assessment; POEM, Patient-Oriented Eczema Measure; SCORAD, scoring atopic dermatitis; TEWL, transepidermal water loss.

fed AD-induced NC/Nga mice with aloe vera gel extracts for 6 weeks resulted in significantly lowered serum IL-5 and IL-10 concentration but increased serum IgE levels [20]. Medicinal properties of the aloe plant may vary due to conditional changes. For example, a study has demonstrated freshly prepared aloe vera is more desirable because the gel is sensitive to enzymatic, oxidative and microbial degradation [16]. Also, the percentage of the plant used in the processed emollient may cause variations in its antimicrobial activities [21]. These may all contribute to the non-unifying results among the limited studies.

Coconut oil

Coconut oil is another natural plant-derived product commonly added into emollient formulations [22]. To be accurate, it is necessary to indicate whether it is coconut oil or virgin coconut oil (VCO) that is tested as they have significant differences in properties [23]. By cold-press method, VCO is claimed to be more superior than coconut oil as the active components (such as fatty acids) are not lost during the harsh process [23]. Nonetheless, only a few clinical trials have been reported. Using PubMed search (last retrieval date 23/1/2018), there were only two clinical trials done in the Philippines that investigated the effect of topical VCO on AD patients [24,25]. Both studies showed VCO significantly reduced eczema severity. Some antibacterial results have also been found with VCO in the smaller study involving 26 patients [24]. Further, a microbiological study on agar-diffusion plate confirmed the antibacterial effect of VCO on *Staphylococcus aureus*. The activity is contributed by the combined effect of medium-chain fatty acids (MCFAs) and monoglycerides, which disrupt the plasma membrane of bacteria [26]. However, another study demonstrated VCO and HVCO did not show their antibacterial activity against several tested bacteria, including *Staphylococcus aureus* [27]. Further clinical trials are needed before any confirmation on VCO efficacy can be made.

Animal products

Lanolin

Lanolin, also known as wool grease/wool wax, is produced from the sebaceous glands of sheep [28–30]. There are different lanolin derivatives in the market, depending on the method of extraction and modification. Though it is often added into emollients for its occlusion effect, there have been very few studies on its efficacy toward AD patients. Most studies investigated its healing effects toward sore nipples of breast-feeding women [31–33] or problems of allergic contact dermatitis caused by the topical application of lanolin [34,35]. Studies have shown a positive association between atopic dermatitis and lanolin contact allergy [36]. Among the limited emollient trials involving lanolin, a randomized controlled trial with 173 preterm infants showed that a daily treatment with an olive oil/lanolin emollient (30% olive oil, 70% lanolin) showed improved skin condition compared with the vehicle (a water-in-oil emollient cream) [37]. However, this study only investigated its effect toward healthy infants without skin disease. Besides, it was also unsure if the effect of better skin hydration and integrity was contributed by the effect of olive oil or lanolin. In summary, there seems to be substantial evidence that AD patients should avoid daily application of lanolin.

Horse oil

Horse oil is a popular folk ingredient used in the cosmetic industry among Asian countries. It is claimed that horse oil has antibacterial, anti-inflammatory and antipruritic actions on the skin [38]. A Korean study (with English abstract) demonstrated the anti-inflammatory effect of horse oil in reducing erythema and IgE level of DNCB-induced contact hypersensitivity in Balb/c mice [38]. Nonetheless, most studies related to the effects of horse oil are only available in Japanese or Korean with no English translations provided, posing difficulties for dermatologists in the field to evaluate and share the results. It is uncertain if horse oil genuinely contains ingredients from the horse, but many products contain urea.

Special ingredients

Ceramides

Ceramides are lipid molecules found naturally in high concentrations within cell membranes of cells in stratum corneum [9]. Their major function is to maintain the integrity of skin barrier which helps to prevent water loss [39]. Studies have found that the skin of AD patients tend to have lower levels of ceramides [40]. Therefore, the need to restore ceramide levels in AD patients gave rise to the development of ceramide/ceramide-precursor containing emollients [9,41,42]. In fact, ceramide-containing creams have become the attention of dermatological investigators. A review from different clinical studies using emollient-containing ceramide/pseudoceramide found mostly positive feedback though the results may not be exactly coherent. For example, a group reported improved SCORAD (SCORing Atopic Dermatitis) and a significant decrease in TEWL [43], another reported a decrease in TEWL together with an increase in skin hydration [44], and two reported improvements in skin dryness and hydration but no significant improvement in SCORAD or TEWL [41,45]. Pseudoceramides refer to commercially synthesized ingredients that are added in newer moisturizers. They are claimed to possess anti-inflammatory property, improve skin permeability and antimicrobial barrier function [9,45,46].

Natural moisturizing factors

Natural moisturizing factors (NMF) are small molecules which absorb water into the corneocytes thereby hydrating the skin. They are water-soluble filaggrin degradation compound, which are responsible for aggregating keratin filaments to form keratin bundles that maintain the rigid structure of the cells in stratum corneum [5,47,48]. Urea, pyrrolidone carboxylic acid [1,2], glutamic acid and other amino acids are filaggrin-

degradation products, collectively referred to as the NMF [49]. These components absorb water from the atmosphere to ensure that the superficial layers of the stratum corneum stay hydrated [50]. The intercellular lipid layer helps prevent the loss of NMF by sealing the outside of each corneocyte [49]. In a small cohort, a test emollient-containing NMF (5% urea), ceramide NP and lactate hydrated the skin to a significantly greater extent and for a longer period of time compared to the control emollient [51]. The results of this small open-label study need to be further confirmed with randomized control trials.

Antimicrobial peptides

Antimicrobial peptides (AMPs), also called host defense peptides, are part of the innate immune response found among all classes of life. These peptides are potent, broad-spectrum antibiotics which demonstrate potential as novel therapeutic agents. AMPs have been demonstrated to kill Gram-negative and Gram-positive bacteria, enveloped viruses, fungi and even transformed cancerous cells [52]. AMPs may also enhance immunity by functioning as immunomodulators. The modes of action by which antimicrobial peptides kill microbes may differ for different bacterial species [53]. Hon et al. investigated an emollient-containing antimicrobial peptide-like activities with claimed multi-actions on barrier repair, antihistaminergic and antimicrobial effects [54]. The investigators found patients who accept the moisturizer have less area affected, disease intensity and severity than the non-accepting counterpart following its usage. However, significant antimicrobial effects are not demonstrated due to the small sample size. Further randomized trials are needed to evaluate the efficacy of the emollient.

Ectoin

Ectoin is an organic osmolyte that has received recent attention. This molecule can be isolated from a wide range of halophilic and halotolerant bacteria that live in extreme conditions [55]. Its function is to provide resistance to the bacteria toward external stresses, mainly dehydration [56] As an osmoprotectant, this molecule is now being studied on human skin with the aim of preventing water loss in dry AD skin through the application of emollient. *In vitro* studies demonstrated water-retaining ability of ectoin [57]. Clinical trials have also been conducted to test the efficacy of this molecule on patients with AD [58,59].

Review of studies and patient preferences

As reported by van Zuuren and colleagues in 2017, the mean duration of clinical studies on emollients (n=77) was 6.7 weeks and mean age of patients 18.6 years [3,60]. The clinical studies ranged from comparing studied product with vehicle or no treatment. Study participants considered the studied product to be more effective in reducing eczema and symptoms of itch compared to control. In addition, participants applying the studied product reported reduced disease severity and flares compared to placebo, vehicle or no moisturizer as assessed by the investigator. Most moisturizers showed some beneficial effects, namely prolonging time to flare, and reducing the number of flares and amount of topical corticosteroids needed to achieve similar reductions in eczema severity. However, the authors found no evidence that one moisturizer is better than the other [3]. Moisturizers themselves were found to have beneficial effects, and combining moisturizers with active topical treatment produced better results when compared to active topical treatment alone [60].

Hon and colleagues studied the practices and preferences of emollient usage in eczema patients and had the following conclusions: doctors remain the most important source of recommendation. The majority of parents and patients think an ideal moisturizer is a nonfragrant, nonherbal, white or transparent cream that needs only to be used 2 to 3 times per day. Compliance may be enhanced if the recommended moisturizer conforms to the parent's/patient's preference [7].

Conclusion

A number of proprietary emollients have undergone trials with clinical data reported in PubMed-indexed journals. Most moisturizers showed some beneficial effects, but there was generally no evidence that one moisturizer is better than the other [3,60]. Choosing an appropriate emollient for AD patients would improve acceptability and adherence for emollient treatment. Physician's recommendation is the primary consideration for patients when selecting a moisturizer/emollient; therefore, doctors should provide evidence-based information about these emollients.

Disclosure and potential conflicts of interest: The authors declare no conflicts of interest. The International Committee of Medical Journal Editors (ICMJE) Potential Conflicts of Interests form for the authors are available for download at: http://www.drugsincontext.com/wp-content/uploads/2018/03/dic.212530-COI.pdf

Article URL: http://www.drugsincontext.com/emollient-treatment-of-atopic-dermatitis-latest-evidence-and-clinical-considerations

Correspondence: Kam Lun Hon, Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong. ehon@cuhk.edu.hk

Provenance: invited; externally peer reviewed.

Submitted: 26 January 2018; **Peer review comments to author:** 16 February 2018; **Revised manuscript received:** 11 March 2018; **Accepted:** 14 March 2018; **Publication date:** 17 April 2018.

Drugs in Context is published by BioExcel Publishing Ltd. Registered office: Plaza Building, Lee High Road, London, England, SE13 5PT.

BioExcel Publishing Limited is registered in England Number 10038393. VAT GB 252772009.

For all manuscript and submissions enquiries, contact the Editorial office dic.editorial@bioexcelpublishing.com

For all permissions, rights and reprints, contact David Hughes david.hughes@bioexcelpublishing.com

References

1. Leung AK, Hon KL, Robson WL. Atopic dermatitis. Adv Pediatr. 2007;54:241–73. http://dx.doi.org/10.1016/j.yapd.2007.03.013
2. Leung TN, Hon KL. Eczema therapeutics in children: what do the clinical trials say? Hong Kong Med J. 2015;10. http://dx.doi.org/10.12809/hkmj144474
3. van Zuuren EJ, Fedorowicz Z, Christensen R, Lavrijsen A, Arents BWM. Emollients and moisturisers for eczema. Cochrane Database Syst Rev. 2017;2:CD012119. http://dx.doi.org/10.1002/14651858.CD012119.pub2
4. Giam YC, Hebert AA, Dizon MV, Van BH, Tiongco-Recto M, Kim KH, Soebono H,Munasir Z, Diana IA, Luk DCK. A review on the role of moisturizers for atopic dermatitis. Asia Pac Allergy. 2016;6:120–8. http://dx.doi.org/10.5415/apallergy.2016.6.2.120
5. Hon KL, Leung AK, Barankin B. Barrier repair therapy in atopic dermatitis: an overview. Am J Clin Dermatol. 2013;14:389–99. http://dx.doi.org/10.1007/s40257-013-0033-9
6. Hon KL, Tsang YC, Pong NH, Lee VW, Luk NM, Chow CM, Leung TF. Patient acceptability, efficacy, and skin biophysiology of a cream and cleanser containing lipid complex with shea butter extract versus a ceramide product for eczema. Hong Kong Med J. 2015;21:417–25. http://dx.doi.org/10.12809/hkmj144472
7. Hon KL, Wang SS, Pong NH, Leung TF. The ideal moisturizer: a survey of parental expectations and practice in childhood-onset eczema. J Dermatolog Treat. 2013;24:7–12. http://dx.doi.org/10.3109/09546634.2012.672713
8. Hon KL, Kung JSC, Tsang KYC, Yu JWS, Lee VW, Leung TF. Emollient acceptability in childhood atopic dermatitis: not all emollients are equal? Curr Pediatr Rev. 2017;CPR-83872. http://dx.doi.org/10.2174/1573396313666170605080034
9. Hon KL, Leung AK. Use of ceramides and related products for childhood-onset eczema. Recent Pat Inflamm Allergy Drug Discov. 2013;7:12–9. http://dx.doi.org/10.2174/1872213X11307010012
10. Tsang M, Guy RH. Effect of aqueous cream BP on human stratum corneum invivo. Br J Dermatol. 2010;163:954–8. http://dx.doi.org/10.1111/j.1365-2133.2010.09954.x
11. Mohammed D, Matts PJ, Hadgraft J, Lane ME. Influence of aqueous cream BP on corneocyte size, maturity, skin protease activity, protein content and transepidermal water loss. Brit J Dermatol. 2011;164:1304–10. http://dx.doi.org/10.1111/j.1365-2133.2011.10338.x
12. Danby SG, Al-Enezi T, Sultan A, Chittock J, Kennedy K, Cork MJ. The effect of aqueous cream BP on the skin barrier in volunteers with a previous history of atopic dermatitis. Br J Dermatol. 2011;165:329–34. http://dx.doi.org/10.1111/j.1365-2133.2011.10395.x
13. Xu S, Kwa M, Lohman ME, Evers-Meltzer R, Silverberg JI. Consumer preferences, product characteristics, and potentially allergenic ingredients in best-selling moisturizers. JAMA Dermatol. 2017;153:1099–105. http://dx.doi.org/10.1001/jamadermatol.2017.3046
14. Warshaw EM, Zug KA, Belsito DV, Fowler JF, Jr., DeKoven JG, Sasseville D, Maibach HI, Mathias CGT, DeLeo VA, Taylor JS, Fransway AF, Marks JG Jr, Pratt MD, Zirwas MJ, Geier J, Uter W. Positive patch-test reactions to essential oils in consecutive patients from North America and Central Europe. Dermatitis. 2017;28:246–52. http://dx.doi.org/10.1097/DER.0000000000000293
15. Dinani N, Patel M, George M. 'Dermatologically tested': what does it really mean? Br J Dermatol. 2017;177:61.
16. Zari S, Zari T. A review of four common medicinal plants used to treat eczema. J Med Plants Res. 2015;9:702–11. http://dx.doi.org/10.5897/JMPR2015.5831
17. Lawrence R, Tripathi P, Jeyakumar E. Isolation, purification and evaluation of antibacterial agents from aloe vera. Braz J Microbiol. 2009;40:906–15.
18. de Rodriguez D, Hernández-Castilloa D, Rodríguez-Garcíaa R, Angulo-Sánchezb JL. Antifungal activity in vitro of. aloe vera pulp and liquid fraction against plant pathogenic fungi. Ind Crops Prod. 2005;21:81–7. http://dx.doi.org/10.1016/j.indcrop.2004.01.002
19. Kim J, Lee I, Park S, Choue R. Effects of Scutellariae radix and aloe vera gel extracts on immunoglobulin E and cytokine levels in atopic dermatitis NC/Nga mice. J Ethnopharmacol. 2010;132:529–32. http://dx.doi.org/10.1016/j.jep.2010.08.049

20. Finberg MJ, Muntingh GL, van Rensburg CE. A comparison of the leaf gel extracts of Aloe ferox and Aloe vera in the topical treatment of atopic dermatitis in Balb/c mice. Inflammopharmacology. 2015;23:337–41. http://dx.doi.org/10.1007/s10787-015-0251-2
21. Dal'Belo SE, Gaspar LR, Maia Campos PM. Moisturizing effect of cosmetic formulations containing Aloe vera extract in different concentrations assessed by skin bioengineering techniques. Skin Res Technol. 2006;12:241–6. http://dx.doi.org/10.1111/j.0909-752X.2006.00155.x
22. Desai AS. Coconut oil: the future of atopic dermatitis treatment? Dermatol Ther. 2017;30:10. http://dx.doi.org/10.1111/dth.12472
23. Marina AM, Man YB, Nazimah SA, Amin I. Antioxidant capacity and phenolic acids of virgin coconut oil. Int J Food Sci Nutr. 2009;60 Suppl 2:114–23. http://dx.doi.org/10.1080/09637480802549127
24. Verallo-Rowell VM, Dillague KM, Syah-Tjundawan BS. Novel antibacterial and emollient effects of coconut and virgin olive oils in adult atopic dermatitis. Dermatitis. 2008;19:308–15. https://www.ncbi.nlm.nih.gov/pubmed/19134433
25. Evangelista MT, Abad-Casintahan F, Lopez-Villafuerte L. The effect of topical virgin coconut oil on SCORAD index, transepidermal water loss, and skin capacitance in mild to moderate pediatric atopic dermatitis: a randomized, double-blind, clinical trial. Int J Dermatol. 2014;53:100–8. http://dx.doi.org/10.1111/ijd.12339
26. Silalahi J, Permata YM, De lux Putra E. Antibacterial activity of hydrolyzed virgin coconut oil. Asian J Pharm Clin Res. 2014;7:90–4. Available at http://innovareacademics.in/journals/index.php/ajpcr/article/viewFile/1042/9913
27. Nguyen VTA, Le TD, Phan HN, Tran LB. Antibacterial activity of free fatty acids from hydrolyzed virgin coconut oil using lipase from Candida rugosa. J Lipids. 2017;2017:7170162. http://dx.doi.org/10.1155/2017/7170162
28. Zesch A, Bauer E. [Quantitative aspects of the percutaneous uptake of wool wax alcohols (cetyl alcohol) and paraffins (octadecane) from different ointment bases]. Derm Beruf Umwelt. 1985;33:15–20. PubMed PMID: 3987517
29. Admani S, Jacob SE. Allergic contact dermatitis in children: review of the past decade. Curr Allergy Asthma Rep. 2014;14:421. http://dx.doi.org/10.1007/s11882-014-0421-0
30. Jacob SE. The lanolin-wool wax alcohol update. Dermatologist. 2014;22:20–2.
31. Jackson KT, Dennis CL. Lanolin for the treatment of nipple pain in breastfeeding women: a randomized controlled trial. Matern Child Nutr. 2017;13:10. http://dx.doi.org/10.1111/mcn.12357
32. Saeidi R, Tafazofi M, Gholami M, Mazloom R. New treatment for nipple soreness in breastfeeding mothers: a clinical trial study. Iran J Neonatol. 2015;6:48–51. http://dx.doi.org/10.22038/IJN.2015.4495
33. Dennis CL, Schottle N, Hodnett E, McQueen K. An all-purpose nipple ointment versus lanolin in treating painful damaged nipples in breastfeeding women: a randomized controlled trial. Breastfeed Med. 2012;7:473–9. http://dx.doi.org/10.1089/bfm.2011.0121
34. Wakelin SH, Smith H, White IR, Rycroft RJ, McFadden JP. A retrospective analysis of contact allergy to lanolin. Br J Dermatol. 2001;145:28–31. PubMed PMID: 11453903
35. Miest RY, Yiannias JA, Chang YH, Singh N. Diagnosis and prevalence of lanolin allergy. Dermatitis. 2013;24:119–23. http://dx.doi.org/10.1097/DER.0b013e3182937aa4
36. Fransen M, Overgaard LEK, Johansen JD, Thyssen JP. Contact allergy to lanolin: temporal changes in prevalence and association with atopic dermatitis. Contact Dermatitis. 2018;78:70–5. http://dx.doi.org/10.1111/cod.12872
37. Kiechl-Kohlendorfer U, Berger C, Inzinger R. The effect of daily treatment with an olive oil/lanolin emollient on skin integrity in preterm infants: a randomized controlled trial. Pediatr Dermatol. 2008;25:174–8. http://dx.doi.org/10.1111/j.1525-1470.2008.00627.x
38. Lee YS, Yoon J-H, Kim B-A, Park CI, Yoo WK, Cho JW, Kim MR. Effects of horse oil on the DNCB-induced contact hypersensitivity in Balb/c mice. Korea J Herbol. 2013;28:77–81. http://dx.doi.org/10.6116/kjh.2013.28.4.77
39. Tessema EN, Gebre-Mariam T, Neubert RHH, Wohlrab J. Potential applications of phyto-derived ceramides in improving epidermal barrier function. Skin Pharmacol Physiol. 2017;30:115–38. http://dx.doi.org/10.1159/000464337
40. Agrawal R, Woodfolk JA. Skin barrier defects in atopic dermatitis. Curr Allergy Asthma Rep. 2014;14:433. http://dx.doi.org/10.1007/s11882-014-0433-9
41. Hon KL, Pong NH, Wang SS, Lee VW, Luk NM, Leung TF. Acceptability and efficacy of an emollient containing ceramide-precursor lipids and moisturizing factors for atopic dermatitis in pediatric patients. Drugs R D. 2013;13:37–42. http://dx.doi.org/10.1007/s40268-013-0004-x
42. Koh MJ, Giam YC, Liew HM, Foong AY, Chong JH, Wong SMY, Tang MBY, Ho MSL, Tan LS, Mason JM, Cork MJ. Comparison of the simple patient-centric atopic dermatitis scoring system PEST with SCORAD in young children using a ceramide dominant therapeutic moisturizer. Dermatol Ther (Heidelb). 2017;7:383–93. http://dx.doi.org/10.1007/s13555-017-0186-1
43. Koppes SA, Charles F, Lammers L, Frings-Dresen M, Kezic S, Rustemeyer T. Efficacy of a cream containing ceramides and magnesium in the treatment of mild to moderate atopic dermatitis: a randomized, double-blind, emollient- and hydrocortisone-controlled trial. Acta Derm Venereol. 2016;96:948–53. http://dx.doi.org/10.2340/00015555-2395

44. Simpson E, Bohling A, Bielfeldt S, Bosc C, Kerrouche N. Improvement of skin barrier function in atopic dermatitis patients with a new moisturizer containing a ceramide precursor. J Dermatolog Treat. 2013;24:122–5. http://dx.doi.org/10.3109/09546634.2012.713461
45. Hon KL, Wang SS, Lau Z, Lee HC, Lee KK, Leung TF, Luk NM. Pseudoceramide for childhood eczema: does it work? Hong Kong Med J. 2011;17:132–6. PubMed PMID: 21471593
46. Lee SE, Jung MK, Oh SJ, Jeong SK, Lee SH. Pseudoceramide stimulates peroxisome proliferator-activated receptor-alpha expression in a murine model of atopic dermatitis: molecular basis underlying the anti-inflammatory effect and the preventive effect against steroid-induced barrier impairment. Arch Dermatol Res. 2015;307:781–92. http://dx.doi.org/10.1007/s00403-015-1584-9
47. Chandar P, Nole G, Johnson AW. Understanding natural moisturizing mechanisms: implications for moisturizer technology. Cutis. 2009;84(1 Suppl):2–15. PubMed PMID: 19702109
48. Steinert PM, Cantieri JS, Teller DC, Lonsdale-Eccles JD, Dale BA. Characterization of a class of cationic proteins that specifically interact with intermediate filaments. Proc Natl Acad Sci USA. 1981;78:4097–101. PMCID: PMC319733
49. Robinson M, Visscher M, Laruffa A, Wickett R. Natural moisturizing factors (NMF) in the stratum corneum (SC). I. Effects of lipid extraction and soaking. J Cosmet Sci. 2010;61:13–22. PubMed PMID: 20211113
50. Warner RR, Boissy YL, Lilly NA, Spears MJ, McKillop K, Marshall JL, Stone KJ. Water disrupts stratum corneum lipid lamellae: damage is similar to surfactants. J Invest Dermatol. 1999;113:960–6. http://dx.doi.org/10.1046/j.1523-1747.1999.00774.x
51. Danby SG, Brown K, Higgs-Bayliss T, Chittock J, Albenali L, Cork MJ. The effect of an emollient containing urea, ceramide NP, and lactate on skin barrier structure and function in older people with dry skin. Skin Pharmacol Physiol. 2016;29:135–47. http://dx.doi.org/10.1159/000445955
52. Reddy KV, Yedery RD, Aranha C. Antimicrobial peptides: premises and promises. Int J Antimicrob Agents. 2004;24:536–47. http://dx.doi.org/10.1016/j.ijantimicag.2004.09.005
53. O'Driscoll NH, Labovitiadi O, Cushnie TP, Matthews KH, Mercer DK, Lamb AJ. Production and evaluation of an antimicrobial peptide-containing wafer formulation for topical application. Curr Microbiol. 2013;66:271–8. http://dx.doi.org/10.1007/s00284-012-0268-3
54. Hon KL, Kung JSC, Tsang KYC, Yu JWS, Lee VW, Leung TF. Testing the actions of a multi-action emollient: patient acceptability determines product efficacy. Curr Pediatr Rev. 2017;CPR-86940.
55. Wang D, Beck LA. Immunologic targets in atopic dermatitis and emerging therapies: an update. Am J Clin Dermatol. 2016;17:425–43. http://dx.doi.org/10.1007/s40257-016-0205-5
56. Bownik A, Stepniewska Z. Ectoine as a promising protective agent in humans and animals. Arh Hig Rada Toksikol. 2016;67:260–5. http://dx.doi.org/10.1515/aiht-2016-67-2837
57. Graf R, Anzali S, Buenger J, Pfluecker F, Driller H. The multifunctional role of ectoine as a natural cell protectant. Clin Dermatol. 2008;26:326–33. http://dx.doi.org/10.1016/j.clindermatol.2008.01.002
58. Marini A, Reinelt K, Krutmann J, Bilstein A. Ectoine-containing cream in the treatment of mild to moderate atopic dermatitis: a randomised, comparator-controlled, intra-individual double-blind, multi-center trial. Skin Pharmacol Physiol. 2014;27:57–65. http://dx.doi.org/10.1159/000351381
59. Wilkowska A, Grubska-Suchanek E, Nowicki R. Evaluation of safety and efficacy of Dermaveel in treatment of atopic dermatitis. Alergol Polska. 2015;2:128–33. http://dx.doi.org/10.1016/j.alergo.2015.09.001
60. van Zuuren EJ, Fedorowicz Z, Arents BWM. Performance and tolerability of the moisturizers cetaphil((R)) and excipial((R)) in atopic dermatitis: what is the evidence based on randomized trials? Dermatol Ther (Heidelb). 2017;7:331–47. http://dx.doi.org/10.1007/s13555-017-0184-3
61. Hon KL, Ching GK, Leung TF, Choi CY, Lee KK, Ng PC. Estimating emollient usage in patients with eczema. Clin Exp Dermatol. 2010;35:22–6. http://dx.doi.org/10.1111/j.1365-2230.2009.03341.x
62. Wiren K, Nohlgard C, Nyberg F, Holm L, Svensson M, Johannesson A, Wallberg P, Berne B, Edlund F, Lodén M. Treatment with a barrier-strengthening moisturizing cream delays relapse of atopic dermatitis: a prospective and randomized controlled clinical trial. J Eur Acad Dermatol Venereol. 2009;23:1267–72. http://dx.doi.org/10.1111/j.1468-3083.2009.03303.x
63. Seghers AC, Cai SC, Ho MS, Giam YC, Tan L, Gronhagen CM, Tang MBY. Evaluation of a pseudoceramide moisturizer in patients with mild-to-moderate atopic dermatitis. Dermatol Ther (Heidelb). 2014;4:83–92. http://dx.doi.org/10.1007/s13555-014-0048-z
64. Moss J. The effect of 3 moisturisers on skin surface hydration: electrical conductance (Skicon-200), capacitance (Corneometer CM420), and transepidermal water loss (TEWL). Skin Res Technol. 1996;2:32–6. http://dx.doi.org/10.1111/j.1600-0846.1996.tb00052.x
65. Sugarman JL, Parish LC. Efficacy of a lipid-based barrier repair formulation in moderate-to-severe pediatric atopic dermatitis. J Drugs Dermatol. 2009;8:1106–11. PubMed PMID: 20027938

66. Weber TM, Samarin F, Babcock MJ, Filbry A, Rippke F. Steroid-Free over-the-counter eczema skin care formulations reduce risk of flare, prolong time to flare, and reduce eczema symptoms in pediatric subjects with atopic dermatitis. J Drugs Dermatol. 2015;14:478–85. PubMed PMID: 25942666
67. Draelos ZD. A pilot study investigating the efficacy of botanical anti-inflammatory agents in an OTC eczema therapy. J Cosmet Dermatol. 2016;15:117–9. http://dx.doi.org/10.1111/jocd.12199
68. Eberlein B, Eicke C, Reinhardt HW, Ring J. Adjuvant treatment of atopic eczema: assessment of an emollient containing N-palmitoylethanolamine (ATOPA study). J Eur Acad Dermatol Venereol. 2008;22:73–82. http://dx.doi.org/10.1111/j.1468-3083.2007.02351.x
69. Wakeman MP. An open-label forearm-controlled pilot study to assess the effect of a proprietary emollient formulation on objective parameters of skin function of eczema-prone individuals over 14 days. Clin Cosmet Investig Dermatol. 2017;10:275–283. http://dx.doi.org/10.2147/CCID.S135841