



CUSTOM DERMATOLOGY SEARCH:

Skin Therapy Letter Articles

[Volume 17 - 2012 Articles](#)

[Volume 16 - 2011 Articles](#)

[Volume 15 - 2010 Articles](#)

[Volume 14 - 2009 Articles](#)

[Volume 13 - 2008 Articles](#)

[Volume 12 - 2007 Articles](#)

[Volume 11 - 2006 Articles](#)

[Volume 10 - 2005 Articles](#)

[Volume 9 - 2004 Articles](#)

[Volume 8 - 2003 Articles](#)

[Volume 7 - 2002 Articles](#)

[Volume 6 - 2001 Articles](#)

[Volume 5 - 2000 Articles](#)

[Volume 4 - 1999 Articles](#)

[Volume 3 - 1998 Articles](#)

[Volume 2 - 1996-97 Articles](#)

[STL Family Practice Edition](#)

[Volume 7 - 2011 Articles](#)

[Volume 6 - 2010 Articles](#)

[Volume 5 - 2009 Articles](#)

[Volume 4 - 2008 Articles](#)

[Volume 3 - 2007 Articles](#)

[Volume 2 - 2006 Articles](#)

[US Volume 1 - 2006 Articles](#)

[Volume 1 - 2005 Articles](#)

[Medical Treatments](#)

[Acne Treatment](#)

A Look at Epidermal Barrier Function in Atopic Dermatitis: Physiologic Lipid Replacement and the Role of Ceramides

Dušan Sajić, MD, PhD; Rachel Asiniwasis, MD; Sandy Skotnicki-Grant, MD, FRCPC

*Division of Dermatology, University of Toronto Dermatology, Toronto, ON
Bay Dermatology Centre, Toronto, ON*

Conflicts of interest: The authors have no conflicts of interest to declare.

ABSTRACT

This review summarizes and discusses the role and efficacy of moisturizers, particularly the more recently introduced ceramide-based formulations, in the skin care regimen of patients with both active and quiescent atopic dermatitis (AD). It is now well established that a complex interplay of environmental and genetic factors are responsible for disease onset and chronicity. Indeed, several novel genetic mechanisms have been recently discovered to be associated with AD pathogenesis. Moreover, it is increasingly recognized that the epidermal barrier plays a critical role in the initiation, perpetuation, and exacerbation of AD. The skin of patients with AD harbors several defects in epidermal barrier function, including filaggrin and ceramides. An improved understanding of these etiopathogenic factors has led to the development of topical ceramide-dominant moisturizers to replace the deficient molecules and re-establish the integrity of barrier defenses. Some of these products have demonstrated efficacy in the treatment of adult and childhood AD that are similar to mid-potency topical steroids. More importantly, they have been shown to be safe with very few associated side-effects. We recommend the addition of such new agents as both the first step of treatment and in the maintenance of clinically quiescent skin of patients with AD.

Key Words: atopic dermatitis, ceramides, eczema, emollients, epidermal barrier, lipids, transepidermal water loss

Introduction

Atopic dermatitis (AD) is a chronic, inflammatory, pruritic skin disease of increasing prevalence (affecting 15-30% of children and 2-10% of adults).¹ AD is considered by many to be the first step in the "atopic march" that can progress to include asthma and allergic rhinitis, as well as be a precursor to, rather than a consequence of, food allergies.¹ The precise sequence of biochemical events leading to the development of AD has still not been fully elucidated, but most

[Cold Sores Treatment](#)[Eczema Treatment](#)[Fungal Treatment](#)[Psoriasis Treatment](#)[Psoriatic Arthritis Treatment](#)[Rosacea Treatment](#)[Skin Cancer Treatment](#)[Skin Care Treatments](#)[Bacterial Infection Treatment](#)[Lice Treatment](#)[Herpes Treatment](#)[Lupus Treatment](#)[Wart Treatment](#)[Doctor's Toolbox](#)[A-Details](#)[Dermatology Review](#)[Meetings and Proceedings](#)[CME / CHE](#)[Derm News Archives](#)[Dermatology News 2007](#)[Dermatology News 2006](#)

experts agree that it involves a complex interplay of environmental and genetic factors that induce derangements in the structure and function of the epidermal barrier and immune system. Diagnosis can be challenging, as the variability of clinical presentation can be confounding. Morphology alone cannot reliably confirm the diagnosis and the spectrum of features associated with AD must be considered. While several sets of diagnostic criteria for AD have been proposed and validated, the traditionally used being that of Hanifin and Rajka, full agreement amongst clinicians and uniformity of criteria are still lacking.²

Epidermal Barrier Dysfunction

Traditionally, it was thought that the primary pathogenic mechanism of atopic dermatitis was initiated by immune dysfunction leading to a Th2 cytokine imbalance, increased inflammation, and secondary disruption of the epidermal barrier.^{1,3} However, accumulating evidence suggests that rather than merely having a bystander effect, a primary defect in the stratum corneum plays a major role in driving the pathogenesis of atopic dermatitis that leads to sustained cytokine release, recruitment of pro-inflammatory molecules, and stimulation of a Th2 response.^{3,4} Moreover, further barrier disruption in the chronic stages of AD, through mechanical scratching, not only perpetuates but alters the response to a mostly Th1 type.⁵ In addition, while several other cytokines and T cell subsets like IL-31 and Th2,⁶ respectively, have recently been identified within the skin of patients with AD, the role of the skin barrier influencing their expression remains unclear.⁷

AD has been separated into two different subtypes, i.e., intrinsic and extrinsic, which were derived on the basis of the extrinsic subtype stemming from allergic sensitization to an external antigen with subsequent allergen specific IgE production, and the intrinsic variant describes patients with all clinical features of AD, but no detectable allergen specific IgE. However, these subtypes may actually represent different stages of evolution based on the relative degree of sensitization. Under this view, AD in infancy is thought to begin as "intrinsic" or non-atopic dermatitis, and over time it progresses to "true" atopy in the majority of cases via allergen exposure through what is now being more widely recognized as a primarily defective epidermal barrier function.^{1,2}

It is well established that the first line of defense within the epidermal barrier is the stratum corneum, which serves several fundamental roles in maintaining protection from the environment as well as preventing water loss. This "outside-in" theory views a primary defect in the stratum corneum as a key condition that drives the inflammatory cascade of AD, predisposing to increased transepidermal water loss (TEWL), penetration of irritants, allergens, secondary infection, and increased inflammation.⁸ Several lines of evidence demonstrate the capacity of the cutaneous barrier to initiate and perpetuate AD including observations that:

1. the defects in the barrier result in elevated pH that activates proteases capable of directly inducing a Th2 inflammatory response,⁹
2. the severity of the barrier defect parallels AD severity,^{10,11}
3. the barrier defect persists longer than both the clinical lesions and the underlying inflammation,¹¹
4. several genetic disorders with skin lesions similar to AD implicate abnormal gene coding that affect the epidermal barrier, and lastly,¹²
5. therapeutic strategies aimed at repairing the epidermal barrier, as further discussed below, also ameliorates both the inflammation and the clinically

involved skin.¹³

Morphological Changes in Epidermal Lipids in AD

The stratum corneum represents a multicellular vertically stacked layer of cells embedded within a hydrophobic extracellular matrix. This matrix is derived from the secretion of lipid precursors and lipid hydrolases, both of which are secreted from lamellar bodies in the stratum granulosum. These hydrolases cleave the precursors to form essential and non-essential fatty acids, cholesterol, and at least 10 different ceramides, which self-organize into multilayered lamellar bilayers between the corneocytes ("bricks"), resulting in the formation of watertight "mortar", thus, maintaining skin hydration.¹² In physiological balance, the approximate proportions of the lipid component are predominantly composed of 50% ceramides, 25% cholesterol, and 10-20% free fatty acids.⁸ In atopic dermatitis, there is a decrease in all three key lipids, especially ceramides, which are found in both lesional and non-lesional skin.¹ A lipid imbalance and inadequate amounts of ceramides contribute to defective formation of the corneocyte lipid envelope and lipid mortar, which correlates with increased TEWL and enhanced barrier permeability.

Filaggrin Mutations and Exogenous Factors in AD Contribute to Epidermal Barrier Dysfunction

There has been a large focus on the role of genetic abnormalities leading to defects in key structural components of the epidermal barrier. Perhaps the best example of this is a loss of function mutation in the filaggrin gene, which encodes for the filament aggregating protein (FLG), found in up to 60% of AD patients.¹² While there are various other candidate genes that lead to increased susceptibility, including KLK7, SPINK5, and CSTA, FLG remains by far the most prominent.¹⁴ Although filaggrin is certainly one of the most important single genes involved in AD susceptibility, inherent redundancy in the epidermal differentiation complex with several other similar genes may mitigate the negative effect of filaggrin mutations and explain the incomplete penetrance in AD. As such, patients carrying a mutation in the FLG gene display a wide spectrum of disease, ranging from mildly dry skin to more severe manifestations of ichthyosis vulgaris.¹⁵ Moreover, since only 44% of AD patients carry the heterozygous mutation and 76% of homozygous or compound heterozygous FLG mutation carrying patients suffer from AD,¹⁶ this further implicates the role of other genes and the environment in disease pathogenesis. Nevertheless, complete absence of FLG, either as a homozygous mutation or a compound heterozygote mutation, clearly disrupts the epidermal barrier, as all of these patients to date have been shown to present with a clinical picture of ichthyosis vulgaris.^{17,18}

Filaggrin normally assists in cytoskeletal aggregation and formation of the cornified cell envelope (CCE), providing additional strength and structure. It is required for normal lamellar body formation and content secretion. Furthermore, as corneocytes mature and start losing water, FLG dissociates from the CCE and is processed into acidic metabolites acting as osmolytes that help to retain hydration and keep the pH below the threshold required for the activation of Th2-inducing endogenous serine proteases.⁹ Therefore, a FLG mutation contributes to a disrupted epidermal barrier, increased water loss, and inflammation. There are also many exogenous factors that can exacerbate barrier dysfunction, specifically soaps and surfactants in detergents that accelerate corneocyte and lipid degradation. Several antigens, including those

from cockroaches, *Staphylococcus aureus*, dust mites, and scabies induce endogenous proteolytic activity, cleaving corneodesmosomal proteins and filaggrin, thus contributing further to the cycle of inflammation and pruritus.¹

Lipid Replacement Therapy in AD

Traditionally viewed as an immunological disorder, therapies for AD have included topical steroids and immunomodulators, and sometimes more aggressive immunosuppressives that do not target the underlying structural barrier abnormalities.^{4,19} As well, most conventional moisturizers do not address this underlying lipid deficiency. With an improved understanding of AD etiopathogenesis, a new nonpharmacologic approach has emerged aimed at barrier repair involving the delivery of balanced proportions of stratum corneum specific lipids to assist in correcting this epidermal barrier dysfunction.

With accumulating evidence supporting barrier defect-initiated disease pathogenesis and its effects on both triggering and perpetuating AD, it is not surprising that emollients, ointments and oils thought to prevent epidermal water loss and inhibit sensitizing exogenous peptides from traversing the compromised barrier, have become the first-line/adjunctive therapy in patients with AD. While the use of sophisticated moisturizers has been shown to confer protective effects on the skin barrier by delaying onset and decreasing AD severity and flares,¹ it is not appropriate to generalize this benefit to all moisturizers, as they not only differ widely in their compositions, but are classified into subcategories based on the therapeutic properties of their key ingredients, e.g., occlusives, humectants, emollients (e.g., intercellular lipids), or some combination of the three. Within the intercellular lipids category, moisturizers contain a variable mix of ceramides, cholesterol, and free fatty acids.

One of the most promising barrier repair methods have been ceramide-dominant physiological lipid-based barrier repair topical emulsions. In contrast to traditional moisturizers, these formulations focus on physiologic lipid replacement therapy, particularly ceramides, to restore normal balance of the epidermal barrier. In comparison with other emollients (e.g., petrolatum) that form a more superficial occlusive barrier, ceramide-dominant moisturizers are thought to permeate the stratum corneum and are synthesized in the keratinocytes, processed in lamellar bodies, and secreted back into the stratum corneum to become a part of the dermal matrix.^{8,20}

Interestingly, while cholesterol, ceramides, and fatty acids are all required for repair, individually they encumber rather than facilitate barrier recovery.²¹ Moreover, incomplete mixtures can also result in suboptimal recovery,²² underlining the importance of proper physiological ratios of individual components to achieve maximal efficacy. Ceramide-based emulsions, such as EpiCeram® and TriCeram®, contain the physiological 3:1:1 molar ratio of ceramides, cholesterol, and free fatty acids, which emulates the endogenous composition of the stratum corneum and has been shown to repair its integrity and function.²¹ While several reports have shown that the 3:1:1 ratio seems to be important in barrier repair,²¹⁻²⁴ it appears that the "3" does not necessarily need to be a ceramide, as both three-fold higher ratios of a fatty acid or cholesterol rather than a ceramide can significantly improve barrier function when compared to vehicle alone.²³ Moreover, while both TriCeram® and EpiCeram® contain 2.1% of ceramides, one study showed that a dilution of 1:9

also has significant effects on barrier repair.²¹ In addition to assisting in restoration of the lipid defect in AD, these products also help to normalize the pH of the skin, which itself is separately associated with a decrease in epidermal barrier integrity, increased inflammation, and reduced antimicrobial defenses.^{25,26}

Although most of the early studies compared the efficacy of the three component mixtures to vehicle alone, several recent reports have shown that some ceramide-dominant formulations can, on their own, induce improvements comparable to topical steroids in the treatment of mild to moderate disease.^{19,27} Therefore, avoiding associated adverse effects from corticosteroid treatment and certain dosing restrictions, as therapy is suitable for patients of all ages and may be used on sensitive skin sites (e.g., face and intertriginous areas), which are prone to steroid-induced atrophy

Another ceramide-based barrier repair cream is CeraVe™, the first over-the-counter (OTC) product featuring multilamellar vesicular emulsions (MVEs), which are similar to liposomes, but facilitate a slow 24-hour controlled, time-released delivery of the contents. This delivery advance offers once-daily application, thereby encouraging adherence to a simplified regimen of moisturizer use. While no standalone trials have been conducted with MVEs, the combination of MVEs with topical fluocinonide 0.05% has recently been shown to reduce disease duration and time to clearance when compared with the same corticosteroid alone, resulting in accelerated skin barrier recovery.²⁸

Natural vs. Synthetic Ceramides

As previously discussed, ceramides are the main components of the multilayered lamellar bilayers between the corneocytes and, thus, a key factor in water retention and overall integrity of the barrier. Chemically, they are amide-linked free fatty acids with long-chain amino alcohol sphingoid bases, which are amidelinked to hydroxylated, x-hydroxylated or nonhydroxylated fatty acids, and shown to also have functions in apoptosis, cell growth, senescence, and cell cycle control.²⁹ Clinically, while many other moisturizers are important in providing short-term relief from dryness in AD, long-term benefits can only be derived through restoring adequate ceramide levels. While replacement with natural ceramides seems to represent the most logical step in the correction of the barrier, there are three important considerations connected with the use of "natural" ceramides. Firstly, there is a high cost associated with nature-identical, synthetic ceramides (e.g., \$2,000-\$10,000/kg).³⁰ Secondly, inexpensive naturally occurring ceramides are typically extracted from bovine central nervous system, which raises concerns about bovine spongiform encephalopathy ('mad cow disease'). Thirdly, excess intracellular ceramides can be linked with significant toxicity and lead to cell growth retardation and apoptosis.^{20,30} Synthetic ceramides are capable of overcoming most of these obstacles and are currently being explored as potential alternatives to natural ceramides.

Kang et al. showed that application of 1% K6PC-9p (a synthetic ceramide derivative of PC-9S) resulted in similar improvement of tetradecanoylphorbol acetate (TPA)-induced skin inflammation, when compared to 0.1% hydrocortisone.³¹ Moreover, application of a ceramide complex (pseudoceramides and eucalyptus leaf extract) resulted in not only improved TEWL and erythema gradings of treated AD patients when compared to vehicle control, but also increased levels of endogenous stratum corneum ceramides.³² Another study investigated a synthetic pseudoceramide and eucalyptus leaf

extract formulation in patients with mild to severe AD.³³ This double-blind, within subject vehicle-controlled study of patients with AD lesions on the arms and legs assessed TEWL, global assessment, and erythema. A significant differential benefit for the ceramide complex over vehicle was shown. Additionally, the findings demonstrated that this ceramide complex of pseudoceramides appears to work similar to the endogenous ceramides found in the skin.

Other Non-steroidal Barrier Repair Products

While ceramide-based moisturizers clearly appear to be superior to most non-ceramide OTC moisturizers, it should be noted that a recent trial showed the use of a glycyrrhetic acid-containing barrier repair cream (Atopiclair®) resulted in improvement of mild to moderate AD in children that was equivalent to EpiCeram®.³⁴ Similar findings were seen in another recent study that demonstrated non-superiority of topical pimecrolimus when compared to a number of different OTC creams (collectively regarded as one group),²⁵ suggesting that correction of numerous epidermal barrier derangements may be an effective way of controlling AD. As well, a multicenter, observational, uncontrolled study of 2456 AD patients aged 2-70 years showed that regular use of a barrier cream containing lipids and N-palmitoylethanolamine (MimyX®) significantly reduced AD skin symptoms (e.g., erythema, pruritus, excoriation, scaling, lichenification, and dryness), sleep disturbance, and topical steroid use.³⁵ Eletone® is another FDA-cleared 510(k) prescription medical device moisturizer that helps to improve stratum corneum impairment and restore barrier integrity. The product contains 70% oil dispersed in 30% water, but it uses a proprietary reverse emulsion technology that produces a formulary consistency of a cream with occlusive properties of an ointment, resulting in enhanced cosmetic acceptability. In a study assessing the use of twice-daily Eletone® in 133 pediatric patients with mild to moderate AD, at 4 weeks 54% of patients experienced improvement in pruritus and average body surface area involvement decreased by 43.6%.³⁶ Whether such treatments lead to an indirect restoration of ceramide levels remains unknown and warrants further investigation.

Conclusion

AD follows a chronic relapsing course, as such, in addition to pharmacologic intervention, it is essential to maintain hydration and barrier function of the skin with daily regimented moisturizer use. Ceramide-based moisturizers have been shown to be beneficial in reducing TEWL, improving barrier function, and maintaining hydration of the stratum corneum, and thus, can be a useful component in AD management. Adequate moisturization reduces the need for drug treatments, as well as limits the severity and frequency of eczematous flares. Indeed, more studies are showing that correction of the skin barrier defects through emollient therapy inhibits downstream drivers of the inflammatory response, thereby providing the rationale for prophylactic and continuous use. Furthermore, the ceramide-based barrier repair emulsions have an excellent safety profile, without significant adverse events other than occasional transient tingling upon application, and thus, can be safely used in patients of all ages and on sensitive skin regions, including the face and intertriginous areas. Additional research is warranted and will lead to a better understanding of the optimal formulary compositions as well as development of a better treatment ladder for varying severities of AD. Also, long-term studies would be helpful in establishing whether lipid barrier replacement therapy

reduces bacterial colonization or prevents progression of the atopic march.

References

1. Danby S, Cork MJ. A new understanding of atopic dermatitis: the role of epidermal barrier dysfunction and subclinical inflammation. *J Clin Dermatol*. 2010;1:33-46.
2. Bos JD, Brenninkmeijer EE, Schram ME, et al. Atopic eczema or atopiform dermatitis. *Exp Dermatol*. 2010 Apr;19(4):325-31.
3. Elias PM, Schmuth M. Abnormal skin barrier in the etiopathogenesis of atopic dermatitis. *Curr Allergy Asthma Rep*. 2009 Jul;9(4):265-72.
4. Elias PM. An Appropriate response to the black-box warning: corrective, barrier repair therapy in atopic dermatitis. *Clin Med Dermatol*. 2009 Feb 9;2:1-3.
5. Matsushima H, Hayashi S, Shimada S. Skin scratching switches immune responses from Th2 to Th1 type in epicutaneously immunized mice. *J Dermatol Sci*. 2003 Sep;32(3):223-30.
6. Jin H, He R, Oyoshi M, et al. Animal models of atopic dermatitis. *J Invest Dermatol*. 2009 Jan;129(1):31-40.
7. Szegedi K, Kremer AE, Kezic S, et al. Increased frequencies of IL-31 producing T cells are found in chronic atopic dermatitis skin. *Exper Dermatol*. 2012 Jun; 21(6):431-6.
8. Sugarman JL. The epidermal barrier in atopic dermatitis. *Semin Cutan Med Surg*. 2008 Jun;27(2):108-14.
9. Briot A, Deraison C, Lacroix M, et al. Kallikrein 5 induces atopic dermatitis-like lesions through PAR2-mediated thymic stromal lymphopoietin expression in Netherton syndrome. *J Exp Med*. 2009 May 11;206(5):1135-47.
10. Sugarman JL, Fluhr JW, Fowler AJ, et al. The objective severity assessment of atopic dermatitis score: an objective measure using permeability barrier function and stratum corneum hydration with computer-assisted estimates for extent of disease. *Arch Dermatol*. 2003 Nov;139(11):1417-22.
11. Seidenari S, Giusti G. Objective assessment of the skin of children affected by atopic dermatitis: a study of pH, capacitance and TEWL in eczematous and clinically uninvolved skin. *Acta Derm Venereol*. 1995 Nov;75(6):429-33.
12. Elias PM, Wakefield JS. Therapeutic implications of a barrier-based pathogenesis of atopic dermatitis. *Clin Rev Allergy Immunol*. 2011 Dec; 41(3):282-95.
13. Elias PM, Wood LC, Feingold KR. Epidermal pathogenesis of inflammatory dermatoses. *Am J Contact Dermat*. 1999 Sep;10(3):119-26.
14. Cork MJ, Danby SG, Vasilopoulos Y, et al. Epidermal barrier dysfunction in atopic dermatitis. *J Invest Dermatol*. 2009 Aug;129(8):1892-908.
15. Heimall J, Spengel JM. Filaggrin mutations and atopy: consequences for future therapeutics. *Expert Rev Clin Immunol*. 2012 Feb;8(2):189-97.
16. Palmer CN, Irvine AD, Terron-Kwiatkowski A, et al. Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. *Nat Genet*. 2006 Apr;38(4):441-6.
17. Smith FJ, Irvine AD, Terron-Kwiatkowski A, et al. Loss-of-function mutations in the gene encoding filaggrin cause ichthyosis vulgaris. *Nat Genet*. 2006 Mar;38(3):337-42.
18. Hu Z, Xiong Z, Xu X, et al. Loss-of-function mutations in filaggrin gene associate with psoriasis vulgaris in Chinese population. *Hum Genet*. 2012

- Jul; 131(7):1269-74.
19. Kircik LH, Del Rosso JQ, Aversa D. Evaluating clinical use of a ceramidedominant, physiologic lipid-based topical emulsion for atopic dermatitis. *J Clin Aesthet Dermatol*. 2011 Mar;4(3):34-40.
 20. Anderson PC, Dinulos JG. Are the new moisturizers more effective? *Curr Opin Pediatr*. 2009 Aug;21(4):486-90.
 21. Man MQ, Feingold KR, Elias PM. Exogenous lipids influence permeability barrier recovery in acetone-treated murine skin. *Arch Dermatol*. 1993 Jun; 129(6):728-38.
 22. Man MQ, Brown BE, Wu-Pong S, et al. Exogenous nonphysiologic vs physiologic lipids. Divergent mechanisms for correction of permeability barrier dysfunction. *Arch Dermatol*. 1995 Jul;131(7):809-16.
 23. Man MM, Feingold KR, Thornfeldt CR, et al. Optimization of physiological lipid mixtures for barrier repair. *J Invest Dermatol*. 1996 May;106(5):1096-101.
 24. Yang L, Mao-Qiang M, Taljebini M, et al. Topical stratum corneum lipids accelerate barrier repair after tape stripping, solvent treatment and some but not all types of detergent treatment. *Br J Dermatol*. 1995 Nov;133(5):679-85.
 25. Emer JJ, Frankel A, Sohn A, et al. A bilateral comparison study of pimecrolimus cream 1% and a topical medical device cream in the treatment of patients with atopic dermatitis. *J Drugs Dermatol*. 2011 Jul;10(7):735-43.
 26. Elias PM, Choi EH. Interactions among stratum corneum defensive functions. *Exp Dermatol*. 2005 Oct;14(10):719-26.
 27. Sugarman JL, Parish LC. Efficacy of a lipid-based barrier repair formulation in moderate-to-severe pediatric atopic dermatitis. *J Drugs Dermatol*. 2009 Dec;8(12):1106-11.
 28. Draelos ZD. The effect of ceramide-containing skin care products on eczema resolution duration. *Cutis*. 2008 Jan;81(1):87-91.
 29. Sawai H, Domae N, Okazaki T. Current status and perspectives in ceramidetargeting molecular medicine. *Curr Pharm Des*. 2005;11(19):2479-87.
 30. Uchida Y, Holleran WM, Elias PM. On the effects of topical synthetic pseudoceramides: comparison of possible keratinocyte toxicities provoked by the pseudoceramides, PC104 and BIO391, and natural ceramides. *J Dermatol Sci*. 2008 Jul;51(1):37-43.
 31. Kang JS, Yoon WK, Youm JK, et al. Inhibition of atopic dermatitis-like skin lesions by topical application of a novel ceramide derivative, K6PC-9p, in NC/ Nga mice. *Exp Dermatol*. 2008 Nov;17(11):958-64.
 32. Ishikawa J, Shimotoyodome Y, Chen S, et al. Eucalyptus increases ceramide levels in keratinocytes and improves stratum corneum function. *Int J Cosmet Sci*. 2012 Feb;34(1):17-22.
 33. Ishida K, Takahashi A, Koutatsu B, et al. The ability of ceramide complex to reduce erythema and enhance barrier function of atopic skin. Poster #5433 presented at: American Academy of Dermatology 70th Annual Meeting. San Diego, CA. March 16-20, 2012.
 34. Miller DW, Koch SB, Yentzer BA, et al. An over-the-counter moisturizer is as clinically effective as, and more cost-effective than, prescription barrier creams in the treatment of children with mild-to-moderate atopic dermatitis: a randomized, controlled trial. *J Drugs Dermatol*. 2011 May;10(5):531-7.
 35. Eberlein B, Eicke C, Reinhardt HW, et al. Adjuvant treatment of atopic eczema: assessment of an emollient containing N-palmitoylethanolamine (ATOPA study). *J Eur Acad Dermatol Venereol*. 2008 Jan;22(1):73-82.

36. Abramovits W, Alvarez-Connelly E, Breneman D, et al. A double-blind, randomized, vehicle-controlled trial to determine the efficacy and safety of hydrocortisone butyrate 0.1% lipocream in the treatment of mild to moderate atopic dermatitis in pediatric subjects. Poster presented at: 25th Anniversary Fall Clinical Dermatology Conference. Las Vegas, NV. October 6-9, 2006.
-

In this issue:

1. [Biofilms in Dermatology](#)
 2. A Look at Epidermal Barrier Function in Atopic Dermatitis: Physiologic Lipid Replacement and the Role of Ceramides
 3. [Update on Drugs and Drug News - July 2012](#)
-