The Importance of Photoprotection and Moisturization in Treating Acne Vulgaris

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ABSTRACT

Skin care products are recognized by dermatologists as critical adjunctive therapeutic modalities for patients suffering from acne vulgaris (AV). Prescribing an acne medication without reviewing a patient's skin care regimen can lead to poor compliance, intolerable side effects, and resulting patient and physician frustration. Striking that delicate balance between maintaining the skin barrier while controlling oil and shine has always been a challenge when treating this chronic inflammatory condition, and it necessitates a unique set of ingredients and formulation. Cetaphil® DermaControl™ Moisturizer SPF 30 (Galderma Laboratories, L.P., Fort Worth, Texas) is a new generation of skin care specifically designed for acne-prone skin and acne-affected skin. Both Cetaphil® DermaControl™ Foam Wash and Cetaphil DermaControl Moisturizer SPF 30 incorporate pharmacologically tested, state-of-the-art ingredients and technologies that studies have shown impart substantial benefits to AV patients.

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INTRODUCTION

The primary treatment goals for acne vulgaris (AV) are to achieve initial control of the disease, prevent flares, prevent physical scarring, and manage psychosocial morbiditites.[1] Although dermatologists have a number of therapies in their armamentarium that are empirically proven to actualize these goals, therapies such as benzoyl peroxide (BPO) and retinoids (both oral and topical) have the potential to adversely affect epidermal barrier functions and induce skin inflammation.[2] The symptoms and cutaneous effects associated with acne treatment include edema, erythema, irritation, inflammation, photosensitivity, and xerosis.[3] Furthermore, an increasing body of literature has emerged indicating that AV itself causes epidermal skin barrier impairment because it is associated with a deficiency of ceramides and specifically linoleic acid.[2]

Sebum production is clearly increased in AV, but AV patients appear to lack healthy, protective fats on the epidermal surface, whose function is to retain moisture in the skin and prevent transepidermal water loss (TEWL). Although AV patients' skin might have an oily, shiny sheen, we now understand that they are overproducing "bad" fats while under-producing "good" ones—a concept that is both novel and complex.

Not only is nurturing the skin barrier in acne patients and keeping the skin properly hydrated absolutely essential, but the need for photoprotection must also be stressed. Many acne therapies thin the skin and predispose to ultraviolet (UV) damage, and UV damage itself has been shown to generate free radical formation, which has been implicated in acne flares. Many acne patients may not find it intuitive nor consider it necessary to use a moisturizer or photoprotection as part of their skin care regimen, but it is an essential part of restoring a balanced barrier and long-term skin health. Therefore, it is crucial to counsel acne patients regarding both moisturization and sun protection.

Moisturizers and photoprotectants have the potential to offset the negative dermatological effects of BPO and retinoids and to be highly beneficial for AV patients who are receiving AV therapies.[3] They can also be important adjunctive therapeutic modalities for patients with AV if they are noncomedogenic, devoid of skin irritants, and compatible with therapeutic regimens.[3]

Although there are currently numerous skin care moisturizers on the market, there is a paucity of studies that have evaluated their efficacy and compatibility specifically in AV patients and those with acne-prone skin.[4] Consequently, AV patients have a myriad of options with regards to over-the-counter skin care products that have the potential to complement their treatment, but in some cases these products magnify the side effects of prescription therapies or even exacerbate the patient's AV.[4] Therefore, professional direction of patients to skin care products that will complement their prescribed AV therapies is very important in the overall management of AV.[4]

Cetaphil® DermaControl™ Moisturizer SPF 30

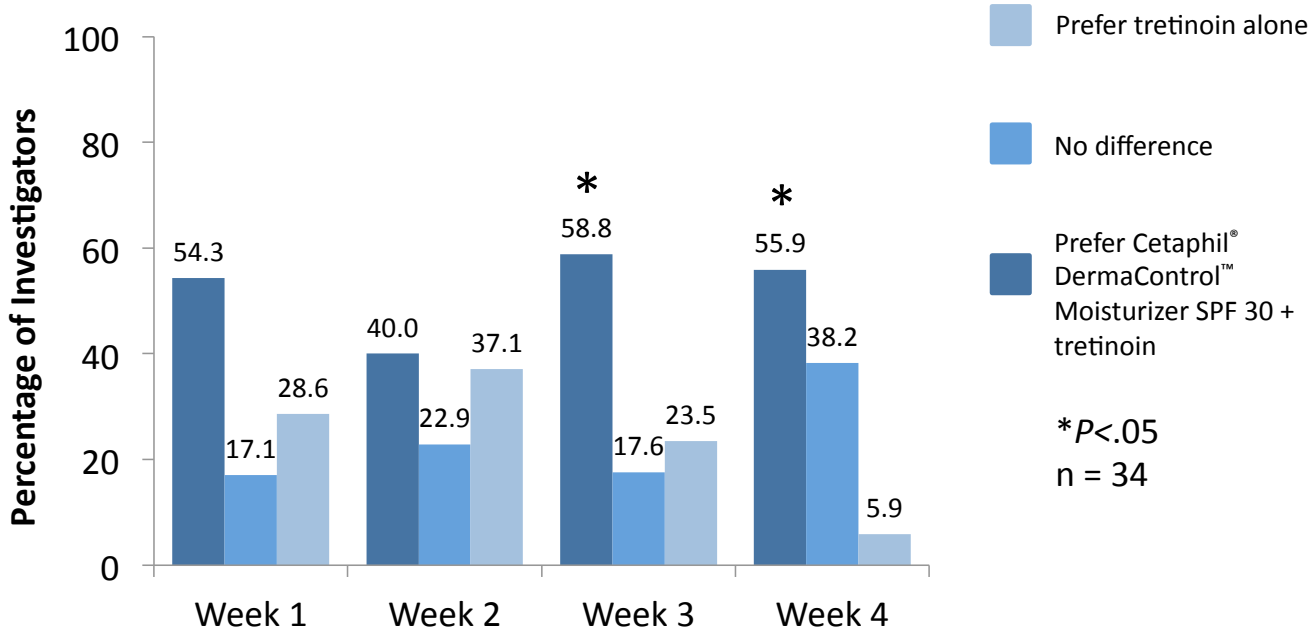
Cetaphil® DermaControl™ Moisturizer SPF 30 (Galderma Laboratories, L.P., Fort Worth, Texas) is a new generation of pho-

TABLE 1.

Cetaphil® DermaControl™ System Clinical Study Overview: 6 Studies (n=316)		
Study Title	**Completed Study**	**Findings**
Cetaphil® DermaControl™ Moisturizer SPF 30	n=316	• No allergic reaction • No sensitization potential • Good skin tolerability • Long-lasting hydration • Significantly more hydration than competitors studied • Decrease in transepidermal water loss • Increase in corneometry • High cosmetic acceptability • Non-comedogenic • Non-acnegenic • Broad spectrum SPF 30
Human Repeat Epicutaneous Patch Testing for Sensitizing Potential	n=108	
Dermatological Use Test for Sensitive Skin	n=32	
24-Hour Moisturization	n=29	
Tolerance and Performance in Acne Subjects Under Acne Treatment	N=82	
Tolerance and Acnegenicity Test and Cosmetic Acceptability	n=55	
SPF Testing	n=10	

Del Rosso JQ. The role of skin care as an integral component in the management of acne vulgaris: Part 1: The importance of cleanser and moisturizer ingredients, design, and product selection. *J Clin Aesthet Dermatol.* 2013;6(12):19-27.

FIGURE 1. Investigator preference assessment.



Schorr ES, Sidou F, Kerrouche N. Adjunctive use of a facial moisturizer SPF 30 containing ceramide precursor improves tolerability of topical tretinoin 0.05%: a randomized, investigator-blinded, split-face study. *J Drugs Dermatol.* 2012;11(9):1104-1107.

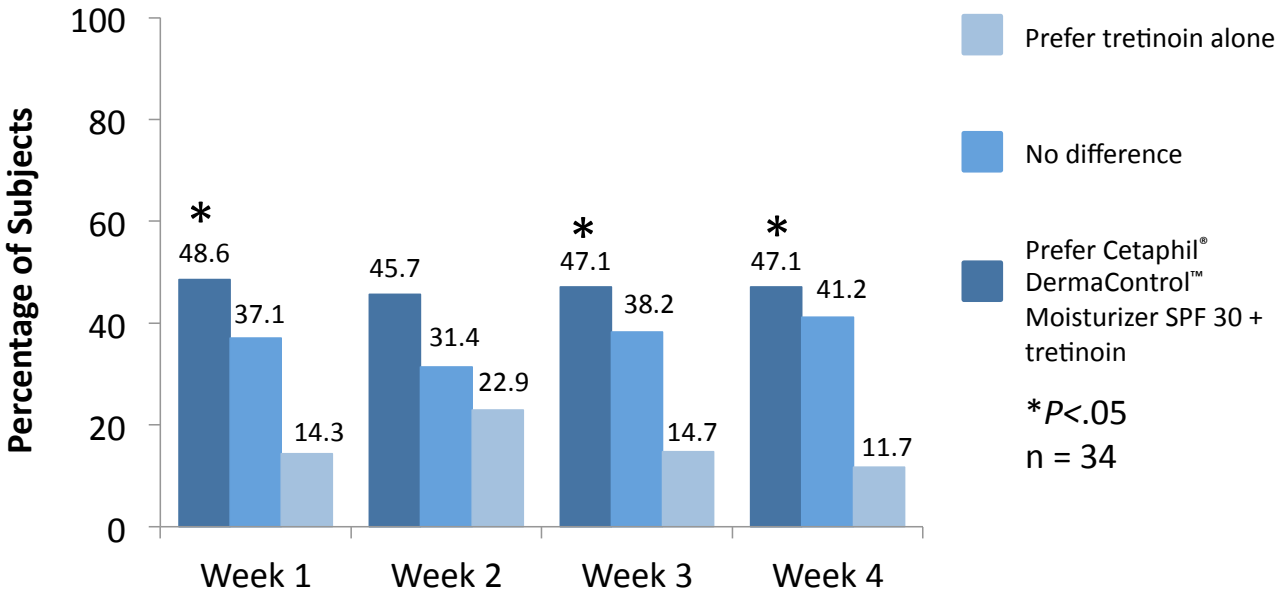
toprotecting moisturizer specifically designed for acne-prone skin and acne-affected skin, and incorporates pharmacologically tested, state-of-the-art ingredients and technologies that are proven to impart substantial benefits to AV patients. The efficacy of Cetaphil DermaControl Moisturizer SPF 30 for the enhanced treatment of AV has been demonstrated by a number of studies evaluating its potential for cutaneous irritation, comedogenicity, acnegenicity, and photoprotection (Table 1).[4]

Schorr and colleagues evaluated the benefit of Cetaphil DermaControl Moisturizer SPF 30 in reducing the side effects associated with topical tretinoin cream.[6] The randomized, investigator/evaluator-blinded, split-face 28-day trial had 174 healthy subjects apply tretinoin cream 0.05% once daily to their whole face and Cetaphil DermaControl Moisturizer SPF 30 to one side of their face.[6] The investigators found that approximately 85% of the study's subjects experienced skin irritation on both sides of their face, but the skin irritation was predominantly milder on the side of the face that was treated by Cetaphil DermaControl Moisturizer SPF 30 (Figure 1).[6] The subjects' tolerability preferences also favored the Cetaphil DermaControl Moisturizer SPF 30–treated skin (Figure 2).[6]

Zinc Gluconate

Cetaphil DermaControl Moisturizer SPF 30 contains zinc gluconate. Zinc plays a crucial role in human physiology, and dietary

FIGURE 2. Subject preference assessment.



Schorr ES, Sidou F, Kerrouche N. Adjunctive use of a facial moisturizer SPF 30 containing ceramide precursor improves tolerability of topical tretinoin 0.05%: a randomized, investigator-blinded, split-face study. *J Drugs Dermatol.* 2012;11(9):1104-1107.

zinc deprivation has been shown to result in moderate to severe dermatitis because zinc-based enzymes and proteins play an integral role in epidermal renewal.[7] Zinc is especially important in wound healing and inflammation reduction, and oral zinc supplements and topical zinc applications have been shown to accelerate the processes of wound healing and inflammation reduction.[7]

In a double-blind trial, Dreno and colleagues randomized 66 AV patients to receive either oral zinc gluconate (200 mg/day) or placebo for 3 months.[8] Inflammatory scores based on the number of lesions—papules, pustules, and nodules—significantly improved in the group that received zinc gluconate compared with the placebo group ($P<.02$).[8] The investigators concluded that the efficacy of zinc gluconate for the treatment of AV could be explained by the action of zinc on inflammatory cells, especially granulocytes.[8]

Sardena and Garg administered oral zinc methionine plus antioxidants to 48 mild to moderate AV patients 3 times a day for 3 months, followed by a 4-week treatment-free period.[9] The subjects had a significant reduction in pustules at 8 weeks ($P<.05$) and 12 weeks ($P<.001$), and papules and closed comedones at 8 weeks ($P<.05$) and 12 weeks ($P<.001$).[9] At the end of the 3-month treatment period, the study's subjects had a statistically significant improvement in their global acne count ($P<.05$), which began after 8 weeks ($P<.05$).[9] Nearly 79% (38/48) of the subjects had 80% to 100% improvement.[9] Sardena and Garg concluded that zinc methionine for mild to moderate facial AV is efficacious and well tolerated.[9]

Topical zinc has also demonstrated a sebosuppressive effect. In a double-blind, randomized trial, 14 volunteers applied a 4% erythromycin plus 1.2% zinc topical formulation on half of their foreheads, and a 4% erythromycin lotion on the other half of their foreheads twice daily for 3 months.

Evaluations of the subjects' casual level of sebum and sebum excretion rate were made with a Sebumeter, and their total area of lipid spots was measured by Sebutape® (Cuderm Corporation, Dallas, Texas) at 3-week intervals. Significant reductions in subjects' casual level of sebum, sebum excretion rates, and total area of lipid spots were observed for the erythromycin-zinc formulation compared with the erythromycin control lotion at 6 and 9 weeks.[10] One of the molecular mechanisms for zinc's reported therapeutic efficacy in the treatment of AV may be its antiandrogen activity through an inhibition of 5α-reductase.[11]

Broad-Spectrum Photoprotection With Oleosome Technology™

Patients with AV are frequently prescribed topical retinoids, oral tetracyclines, BPO–containing formulations, etc, that necessitate photoprotection; and Cetaphil DermaControl Moisturizer SPF 30 incorporates patented Oleosome Technology™, which is an innovative delivery system that provides UV protection with fewer UV filters.[12] Oleosomes are found on oil-bearing plant seeds, and they are between 0.6 µm and 2 µm in diameter.[13] At the core of an olesosome are emollient plant oils and vitamin E, which are surrounded by a phospholipid membrane and stabilized by a protein coat.[12] Olesosomes mimic the cell

TABLE 2.

Cetaphil® DermaControl™ Moisturizer SPF 30 Sunscreen Active Ultraviolet Filters					
Cetaphil® DermaControl™ Moisturizer SPF 30	Aveeno® Active Naturals Positively Radiant Daily Moisturizer SPF 30	Neutrogena® Healthy Defense® Daily Moisturizer SPF 30	Neutrogena® Men® Sensitive Skin Oil-Free Moisture with Helioplex SPF 30	Olay® Complete Defense Daily UV Moisturizer Sensitive Skin SPF 30	CeraVe® Facial Moisturizing Lotion AM with SPF 30
Avobenzone 3%	Avobenzone 3%	Avobenzone 3%	Avobenzone 3%		
Octisalate 5%	Octisalate 5%	Octisalate 5%	Octisalate 5%	Octisalate 2.5%	
Octocrylene 7%	Octocrylene 1.7%	Octocrylene 2.35%	Octocrylene 1.7%	Octocrylene 2.5%	Octocrylene 2%
	Oxybenzone 3%	Oxybenzone 6%	Oxybenzone 3%		
				Octinoxate 7.5%	Octinoxate 7.5%
				Zinc Oxide 6%	Zinc Oxide 3.5%
15%	24.7%	28.4%	24.7%	18.5%	25%

Sambandan DR, Ratner D. Sunscreens: an overview and update. *J Am Acad Dermatol*. 2011;64(4):748-758.

membranes on the stratum corneum (SC), and, upon application, they significantly enhance its barrier function.[14]

Oleosomes can significantly augment the SPF-boosting potential of traditional sunscreen products, especially those containing UVA and UVB sunscreen filters. Because the performance of traditional sunscreen ingredients is augmented via Oleosome Technology, fewer sunscreen filters are needed to provide the same level of broad-spectrum UV protection. Minimizing AV patients' exposure to sun filters is highly desirable as the filters have the potential to exacerbate their AV.[12] Extensive in vivo clinical testing has been completed on several Oleosome Technology™ formulations that have minimal sun filter concentrations of octylmethoxycinnamate and butyl methoxydibenzoylmethane, but yield exceptionally high SPF values that are consistent and stable over time.[12] Cetaphil DermaControl Moisturizer SPF 30 is composed of 15% sunscreen filters, whereas many moisturizers are composed of between 18.5% and 28.4% sunscreen filters (Table 2).[12]

"Not only is nurturing the skin barrier in acne patients and keeping the skin properly hydrated absolutely essential, but the need for photoprotection must also be stressed."

Ceramide Technology™

Cetaphil DermaControl Moisturizer SPF 30 also incorporates patented Ceramide Technology™. The SC is primarily composed of ceramides, free fatty acids, and cholesterol, which play an integral role in the skin barrier function of the upper layer of the SC because their synthesis restricts water movement and penetration.[15] Cetaphil DermaControl Moisturizer SPF 30 contains a pseudo-ceramide—hydroxypalmitoyl sphinganine—that is structurally similar to ceramide 5.[16] When hydroxypalmitoyl sphinganine is grown in a media of cultured human reconstructed skin, the resultant effect is a proliferation of ceramides 1, 2, and 3. Consequently, exogenous hydroxypalmitoyl sphinganine is able to induce the production endogenous ceramides.[16]

Yamamoto and colleagues conducted a study that evaluated the sebum secretion rate, lipid content (including ceramides), and water barrier function of the SC in 36 AV patients and 29 healthy controls.[17] The investigators found that a significantly elevated sebum secretion rate in AV patients was accompanied by impairment in water barrier function and a marked decrease of ceramides.[17] Moreover, linoleic acid has been shown to be an essential structural component of ceramides, and linoleic acid undergoes a rapid oxidation and degradation process in sebaceous cells.[18,19]

Skin barrier dysfunction is commonly associated with conditions such as atopic dermatitis, but studies like the one conducted by Yamamoto and colleagues highlight the emerging evidence that supports the link between skin barrier dysfunction and AV. If the skin barrier is compromised in AV, even in the absence of therapies such as retinoids and BPO, might gentle skin care and moisturization play an even greater role than initially suspected?

Beta-Glycyrrhetinic Acid

Cetaphil DermaControl Moisturizer SPF 30 contains beta-glycyrrhetinic acid, which is derived from the licorice species *Glycyrrhiza glabra* by hydroalcoholic extraction hydrolysis and crystallization methods. The *G glabra* species of licorice has been used for millennia in Western and Eastern medicine.[20] Pharmacological analysis has shown that *G glabra* has a wide spectrum of medicinal applications that are hepato-protective, anti-inflammatory, immunomodulatory, and antiviral.[21-26]

Licorice derivatives are increasingly used in therapeutic and cosmeceutical formulations for their anti-inflammatory effects and skin brightening effects.[27] Acne vulgaris is characteristic of excess sebum production and the induction of inflammatory reactions via the cyclooxygenase-2 (COX-2) and prostaglandin E_2 (PGE_2) pathway.[28] To counteract this inflammatory cascade, licorice derivatives have demonstrated the capacity to suppress the inflammatory responses of the COX-2 and PGE_2 pathway.[26]

The herbal formulations of *G glabra* have also been used to treat a number of dermatologic disorders, including dermatitis, eczema, pruritus, and cysts.[29] Moreover, *G glabra* has demonstrated considerable antibacterial activity against *Propionibacterium acnes* that resulted in a minimal induction of resistance when compared with the marked development of resistance that was induced in *P acnes* treated with erythromycin.[30]

"Cetaphil DermaControl Moisturizer SPF 30 provides broad spectrum photoprotection while improving moisturization, and is designed for patients with acne-prone skin."

Silica Beads and Corn Starch

Cetaphil DermaControl Moisturizer SPF 30 also contains silica beads and corn starch, which are sebum absorbent. Silica beads and corn starch have been shown not only to significantly reduce sebum, but also to reduce "facial shine," an oily sheen of sebum that becomes pronounced on the faces of AV patients.[4]

A study evaluated the potential of Cetaphil DermaControl Moisturizer SPF 30 to mitigate sebum and "facial shine."[4] After application of Cetaphil DermaControl Moisturizer SPF 30 to the faces of AV patients, sebum excretion rates were measured using a Sebumeter, and Sebutape was also used to collect sebum released from infundibular reservoirs.[4] The investigators found that "facial shine" and sebum levels were significantly reduced within hours of Cetaphil DermaControl Moisturizer SPF 30 application, and the effect lasted for up to 8 hours.[4]

The reduction of sebum production and "facial shine" is essential in the management of AV patients' psychosocial morbiditites because "facial shine" can be emotionally disconcerting to AV patients. Moreover, by incorporating sebosuppressive and sebum-absorbent ingredients (ie, zinc gluconate, silica beads, and corn starch), and also Ceramide Technology, Cetaphil DermaControl Moisturizer SPF 30 is a formulation that reduces "oil" or sebum while simultaneously preventing TEWL and enhancing skin hydration.

CONCLUSION

Cetaphil DermaControl Moisturizer SPF 30 provides broad spectrum photoprotection while improving moisturization, and is designed for patients with acne-prone skin. The key ingredients of the photoprotecting moisturizer are unique and specifically designed to balance the effects of acne treatments while not irritating the skin or exacerbating acne.

DISCLOSURES

Dr. Kircik has served as an advisor, investigator, consultant, and speaker for Allergan, Bayer, Galderma, Johnson & Johnson, Promius Pharma, Quinnova, Stiefel/GSK, LeoPharma, Taro, Valeant, and Warner-Chilcott.

Dr. Bowe has served as a consultant, advisory board participant, and/or speaker for Allergan, Bayer, Galderma, Johnson and Johnson, L'Oreal USA, Onset Therapeutics, and Proctor and Gamble.

REFERENCES

1. Goodman G. Cleansing and moisturizing in acne patients. *Am J Clin Dermatol.* 2009;10(suppl 1):s1-s6.
2. Thiboutot D, Del Rosso JQ. Acne vulgaris and the epidermal barrier: is acne vulgaris associated with inherent epidermal abnormalities that cause impairment of barrier functions? Do any topical acne therapies alter the structural and/or functional integrity of the epidermal barrier? *J Clin Aesthet Dermatol.* 2013;6(2):18-24.
3. Bikowski J. The use of therapeutic moisturizers in various dermatologic disorders. *Cutis.* 2001;68(suppl 5):s3-s11.
4. Del Rosso JQ. The role of skin care as an integral component in the management of acne vulgaris: Part 1: The importance of cleanser and moisturizer ingredients, design, and product selection. *J Clin Aesthet Dermatol.* 2013;6(12):19-27.
5. Del Rosso JQ, Brandt S. The role of skin care as an integral component in the management of acne vulgaris. Part 2: Tolerability and performance of a designated skin care regimen using a foam wash and moisturizer SPF 30 in patients with acne vulgaris undergoing active treatment. *J Clin Aesthet Dermatol.* 2013;6(12):28-36.
6. Schorr ES, Sidou F, Kerrouche N. Adjunctive use of a facial moisturizer SPF 30 containing ceramide precursor improves tolerability of topical tretinoin 0.05%: a randomized, investigator-blinded, split-face study. *J Drugs Dermatol.* 2012;11(9):1104-1107.
7. Schwartz JR, Marsh RG, Draelos ZD. Zinc and skin health: overview of physiology and pharmacology. *Dermatol Surg.* 2005;31(7 pt 2):837-847.
8. Dreno B, Amblard P, Agache P, Sirot S, Litoux P. Low doses of zinc gluconate for inflammatory acne. *Acta Derm Venereol.* 1989;69(6):541-543.
9. Sardena K, Garg VK. An observational study of methionine-bound zinc with antioxidants for mild to moderate acne vulgaris. *Dermatol Ther.* 2010;23(4):411-418.
10. Piérard-Franchimont C, Goffin V, Visser JN, Jacoby H, Piérard GE. A double-blind controlled evaluation of the sebosuppressive activity of topical erythromycin-zinc complex. *Eur J Clin Pharmacol.* 1995;49(1-2):57-60.
11. Piérard GE, Piérard-Franchimont C. Effect of a topical erythromycin-zinc formulation on sebum delivery. Evaluation by combined photometric-multi-step samplings with Sebutape. *Clin Exp Dermatol.* 1993;18(5):410-413.
12. Sambandan DR, Ratner D. Sunscreens: an overview and update. *J Am Acad Dermatol.* 2011;64(4):748-758.
13. Parthibane V, Rajakumari S, Venkateshwari V, Iyappan R, Rajasekharan R. Oleosin is bifunctional enzyme that has both monoacylglycerol acyltransferase and phospholipase activities. *J Biol Chem.* 2012;287(3):1946-1954.
14. Hydresia—Oleosomes Technology Overview. Available at http://www.botaneco.ca. Accessed June 24, 2014.
15. Pappas A. Epidermal surface lipids. *Dermatoendocrinol.* 2009;1(2):72-76.
16. Castiel-Higounenc I, Ferraris C, Lavalle A, et al. Exogenous sphinganin derived sphingolipid increases epidermal ceramide content in human reconstructed skin. *Nouv Dermatol.* 1999;18:541-546.

17. Yamamoto A, Takenouchi K, Ito M. Impaired water barrier function in acne vulgaris. *Arch Dermatol Res.* 1995;287(2):214-218.
18. Downing DT, Stewart ME, Wertz PW, Strauss JS. Essential fatty acids and acne. *J Am Acad Dermatol.* 1986;14(2 pt 1):221-225.
19. Pappas A, Anthonavage M, Gordon JS. Metabolic fate and selective utilization of major fatty acids in human sebaceous gland. *J Invest Dermatol.* 2002;118(1):164-171.
20. Baumann L. Botanical ingredients in cosmeceuticals. *J Drugs Dermatol.* 2007;6(11):1084-1088.
21. Armanini D, Karbowiak I, Funder JW. Affinity of liquorice derivatives for mineralocorticoid and glucocorticoid receptors. *Clin Endocrinol.*1983;19(5):609-612.
22. Okimasu E, Moromizato Y, Watanabe S, et al. Inhibition of phospholipase A2 and platelet aggregation by glycyrrhizin, an antiinflammation drug. *Acta Med Okayama.* 1983;37(5):385-391.
23. Ohuchi K, Kamada Y, Levine L, Tsurufuji S. Glycyrrhizin inhibits prostaglandin E2 production by activated peritoneal macrophages from rats. *Prostaglandins Med.* 1981;7(5):457-463.
24. Kao TC, Shyu MH, Yen GC. Glycyrrhizic acid and 18beta-Glycyrrhetinic acid inhibit inflammation via PI3K/Akt/GSK3beta signaling and glucocorticoid receptor activation. *J Agric Food Chem.* 2010;58(15):8623-8629.
25. Racková L, Jancinová V, Petríková M, et al. Mechanism of anti-inflammatory action of liquorice extract and glycyrrhizin. *Nat Prod Res.* 2007;21(14):1234-1241.
26. Bhattacharjee S, Bhattacharjee A, Majumder S, Majumdar SB, Majumdar S. Glycyrrhizic acid suppresses Cox-2-mediated anti-inflammatory responses during Leishmania donovani infec*J Antimicrob Chemother.* 2012;67(8):1905-1914.
27. Cosmetic Ingredient Review Expert Panel. Final report on the safety assessment of glycyrrhetinic acid, potassium glycyrrhetinate, disodium succinoyl glycyrrhetinate, glyceryl glycyrrhetinate, glycyrrhetinyl stearate, stearyl glycyrrhetinate, glycyrrhizic acid, ammonium glycyrrhizate, dipotassium glycyrrhizate, disodium glycyrrhizate, trisodium glycyrrhizate, methyl glycyrrhizate, and potassium glycyrrhizinate. *Int J Toxicol.* 2007;26(suppl 2):79-112.
28. Sato T1, Shirane T, Noguchi N, Sasatsu M, Ito A. Novel anti-acne actions of nadifloxacin and clindamycin that inhibit the production of sebum, prostaglandin E(2) and promatrix metalloproteinase-2 in hamster sebocytes. *J Dermatol.* 2012;39(9):774-780.
29. Saeedi M, Morteza-Semnani K, Ghoreishi MR. The treatment of atopic dermatitis with licorice gel. *J Dermatolog Treat.* 2003;14(3):153-157.
30. Nam C, Kim S, Sim Y, Chang I. Anti-acne effects of Oriental herb extracts: a novel screening method to select anti-acne agents. *Skin Pharmacol Appl Skin Physiol.* 2003;16(2):84-90.

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