doi:10.36849/JDD.2020.5536

 ORIGINAL ARTICLE Journal of Drugs in Dermatology

Choosing the Right Partner: Complementing Prescription Acne Medication With Over-the-Counter Cleansers and Moisturizers

Edward Lain MD FAAD,[a] Anneke E. Andriessen PhD[b]
[a]Sanova Dermatology, Austin TX; Austin Institute for Clinical Research, Austin, TX
[b]Radboud UMC Nijmegen, Andriessen Consultants, Malden, NL

ABSTRACT

Background: Acne is the most common dermatological disorder. An impaired barrier function in acne vulgaris has been reported, as well as decreased amounts of epidermal ceramides. Also, many of the systemic and topical medications prescribed for the treatment of acne exacerbate these skin barrier disruptions and can lead to irritation and dry skin conditions.
Aim: The review explored the importance of maximizing adjunctive skincare, such as over-the-counter products for managing acne and avoiding adverse effects.
Methods: A literature review was conducted and included clinical acne guidelines, clinical studies, and review articles on acne prevention, treatment, and maintenance. Searches were made in PubMed and Google Scholar for English-language literature published between Jan 1, 2010, and Apr 1, 2020. Two clinicians manually reviewed selected publications.
Results: Seventy-four articles were included in the analyses. A variety of specialized cleansers and moisturizers are available as suitable adjunctive therapies for acne-prone skin. Lipid-free cleansers were found to be the most appropriate type of cleanser for acne-prone skin as they were associated with a low risk of skin irritation, and a near-physiological stratum corneum pH. Moisturizers typically included ingredients such as humectants, emollients, oil absorbers, and those with anti-inflammatory and/or barrier replenishing properties. Given the various adjunctive products available, decision frameworks were created for clinicians to use when selecting over-the-counter cleansers and moisturizers for acne-prone patients.
Conclusion: Informing clinicians about skin barrier dysfunction in acne and the benefits of adjunctive skincare may help them to choose the right product(s) to complement prescription therapy.

J Drugs Dermatol. 2020;19(11):1069-1075. doi:10.36849/JDD.2020.5536

BACKGROUND

Acne is the most common dermatological disorder.[1] Psychological and emotional distress due to acne, including poor self-esteem, social anxiety, depression, and suicidal ideation have been reported in various studies.[2,3,4] Acne is a complex, multifactorial disease, and its pathophysiology is incompletely elucidated. An impaired barrier function in acne vulgaris has been reported, as well as decreased amounts of ceramides.[5]The structural and functional integrity of the stratum corneum is highly dependent on adequate hydration in the skin barrier. However, in acne-prone skin, barrier integrity is compromised both functionally (sebum excretion is higher, sebaceous glands are larger and subclinical inflammation is present) and via ultrastructural properties (filaggrin expression is enhanced, free fatty acids are reduced, linoleic acid, free sphingosine, and total ceramides are altered).[6]

Many of the systemic and topical medications prescribed for the treatment of acne, such as retinoids, antibiotics, and benzoyl peroxide, are associated with skin barrier alteration.[7] This, in turn, can cause irritation and dry skin conditions.[8] These unwanted effects can reduce adherence to treatment, and therapeutic outcomes.[8,9] Over-the-counter (OTC) non-comedogenic cleansers and moisturizers have been used successfully to reduce skin irritation.[9] However, some of these products, such as those with a high pH, have been shown to interfere with the efficacy of topical treatments for acne.[8] Managing the irritation potential of topical acne medications through the selective use of adjunctive, OTC skincare is an important strategy for improving treatment adherence and outcomes.

Aim of review

A literature review was conducted to explore clinical insights into skin barrier dysfunction in acne and the role of cleansing and moisturizers as adjunctive to prescription acne treatment. Informing health care providers about skin barrier dysfunction in acne and the benefits of adjunctive skincare may help them to choose the right OTC product(s) when complementing prescription therapy.

METHODS

The present literature review includes clinical acne guidelines, clinical studies, and review articles on acne prevention, treatment, and maintenance. Manuscripts focused on dermocosmetic regimens for acne were targeted. For this purpose, searches were made during two phases using PubMed and Google Scholar. The first phase was performed between July 10th and 12th, 2019, using search dates of Jan 1, 2010, to Jul 1, 2019; and the second phase occurred between April 6th and 8th 2020, using the search dates of Jul 2, 2019, to Apr 1, 2020. Searches were made for English-language literature using the following terms: *"Acne vulgaris, acne pathogenesis, skin microbiome and acne, acne exposome, acne therapy with OTC regimens, dermo-cosmetics, active cosmetics, sebostatics, keratinization, acne guidelines, algorithms for adult females with acne."* Exclusion criteria included: No original data (unless a review article was deemed relevant) and not dealing with the management of acne. Two clinicians manually reviewed the selected publications for additional resources.

RESULTS

After the exclusion of duplicates, the review yielded seventy-four papers deemed clinically relevant to adult female acne and the use of OTC regimens.[1-74] These seventy-four articles were used to formulate the below discussion.

DISCUSSION

Acne And Skin Barrier

Increased trans-epidermal-water-loss (TEWL) and inconsistent ceramide content in the stratum corneum are well characterized in acne patients, even in non-lesional skin.[5] Topical treatments for acne, including benzoyl peroxide, tazarotene, and tretinoin, have been proven to disrupt the skin barrier even further.[7] Improving skin barrier function is important for increasing tolerability, leading to enhanced adherence to treatment and, therefore, efficacy.[7] The primary goal of adjunctive skincare focuses on repairing the epidermal barrier in order to reduce TEWL, improve epidermal hydration, and ensure emollience. By sealing in water through occlusion, moisturizers may employ a hydrophobic barrier to water loss. Common ingredients capable of displaying this characteristic include petrolatum, lanolin, cetyl alcohol, ceramides, oils, and silicone/dimethicone. These ingredients have been proven to reduce TEWL by 20 to 98%.[75] Humectants, once incorrectly thought to attract water from the environment, draw hydration from the deeper dermis and epidermis into the stratum corneum. Examples of humectants used in moisturizers include glycerine, hyaluronic acid, vitamin E, sorbitol, sodium lactate, and urea. Ingredients such as cholesterol, squalene, fatty acids, and glycol stearate, fill the gaps between dead corneocytes and thereby smooth the skin surface. This provides an immediate effect of improved skin touch and texture, also known as emollience.

Ceramides are composed of a sphingosine base and a fatty acid and act synergistically on skin hydration and TEWL.[76] In the epidermis, ceramides constitute approximately 50% of the lipid composition of the stratum corneum. Cholesterol, fatty acids, and other lipids constitute approximately 25, 10, and 15%, respectively. Alterations in these ratios within the stratum corneum have been linked to several skin diseases, such as atopic dermatitis, acne, and rosacea, with the common them of impaired barrier function amongst them. Moisturizers can effectively repair barrier function by replacing the physiologic ratio of ceramides, cholesterol, and fatty acids. Particular ceramides used in topical skincare products include types 1, 3, 5, and 6-II. Ceramide 1 participates in cell signaling and thus orchestrates the ratio of the lipid composition of the stratum corneum. Ceramides 3, 5, and 6-II are in high concentration in the lipid bilayer, indicating their relative importance in maintaining the structural component of the stratum corneum as well as imparting essential barrier properties to the outer layer of the epidermis.[77]

Skincare Regimen in Acne Patients

Despite an increase in the sebum secretion rate associated with acne, Yamamoto et al, (1995) showed a reduction in sphingolipids (ceramides) in the stratum corneum.[5] Barrier dysfunction correlates with hyperkeratinization and comedone formation.[22] Therefore, an effective adjuvant skincare regimen must focus on the removal of excess sebum and debris on the skin surface (cleansing) and improving skin barrier (moisturizing). Attributes of effective moisturizers include occlusion, to seal in the water; humectant, to draw water into the stratum corneum; emollient, to improve the softness and smoothness of the skin; and barrier repair, to decrease TEWL through replacement and/or regeneration of the lipid bilayer.[24]

Specialized Cleansers for Acne

Whereas moisturizers seek to introduce natural ingredients back into the skin (eg, water, ceramides), cleansers are used to remove both natural and chemical substances. This makes cleansers more difficult for manufacturers to formulate and patients to use. The optimal cleanser removes sebum and debris while preserving intercellular lipids and moisturizing skin. Types of cleansers are presented in Table 1. Of all categories of cleansers, lipid-free cleansers have the lowest irritancy potential and do not influence the pH of the skin.[8] This makes lipid-free cleansers particularly well suited as being adjunctive therapies for patients experiencing adverse effects associated with the use of prescription acne therapies. Investigations have shown greater lipid-barrier preservation when using lipid-free cleansers, in comparison to a leading sensitive skin cleanser, 1% sodium lauryl sulfate solution, and even when washing with water only. Available lipid-free cleansers suitable for use in acne-prone skin are depicted in Table 2, and a decision framework for clinicians to use when selecting between these products is presented in Figure 1.

TABLE 1.

Types of Cleansers					
Type	**Ingredient**	**Irritancy Potential**	**pH**	**Cleansing Ability**	**Examples**
Lipid-free cleanser	Water, glycerin, cetyl-alcohol, stearyl-alcohol	Extremely low	--	Low	Cerave®, Aquanil®, Cetaphil®, La Roche Posay®Toleriane™
Soap	Fatty acid salt	High	9-10	High	Ivory®
Combar	Fatty acid salt, synthetic detergent	Medium	7-9	medium	Dial®, Coast®
Syndet	Synthetic detergent	Low	5.5-7	Low	Dove®, Olay®

TABLE 2.

Specialized Lipid-free Cleansers for Acne-prone Skin and Their Therapeutic Ingredients		
Product	**Property**	**Ingredients**
Cerave® Hydrating Cleanser	Foaming	Cetearyl alcohol, sodium lauroyl lactylate
	Humectant	Glycerin, hyaluronic acid
	Barrier repair	Ceramide 1, 3, 6-II, cholesterol, phytosphingosine, MVE®Technology
	Surfactant	Polyoxyl 40 stearate, polysorbate 20, sodium lauroyl lactylate
Cerave® Foaming Cleanser	Surfactant	Cocamidopropyl hydrosultaine, sodium lauroyl sarcosinate, sodium methyl cocoyl taurate, sodium lauroyl lactylate
	Moisturizer	Caprylic/capric glycerides, Ceramide 1, 3 and 6-II, cholesterol
	Anti-inflammatory	Niacinamide
Neutrogena® Ultra Gentle Daily Cleanser	Humectant	Glycerin, caprylyl glycol
	Surfactant	Cocamidopropyl betaine, lauryl glucoside, sodium cocoyl sarcosinate, disodium lauroamphodiacetate
Cetaphil® PRO Oil Removing Foaming Face Wash	Surfactant, antibacterial, foaming	Zinc coceth sulfate
	Humectant	Glycerin
	Anti-inflammatory	Dipotassium glycyrrhizate, zinc gluconate

FIGURE 1. A decision framework for clinicians to use when selecting between adjunctive over-the-counter cleansers for acne-prone patients.

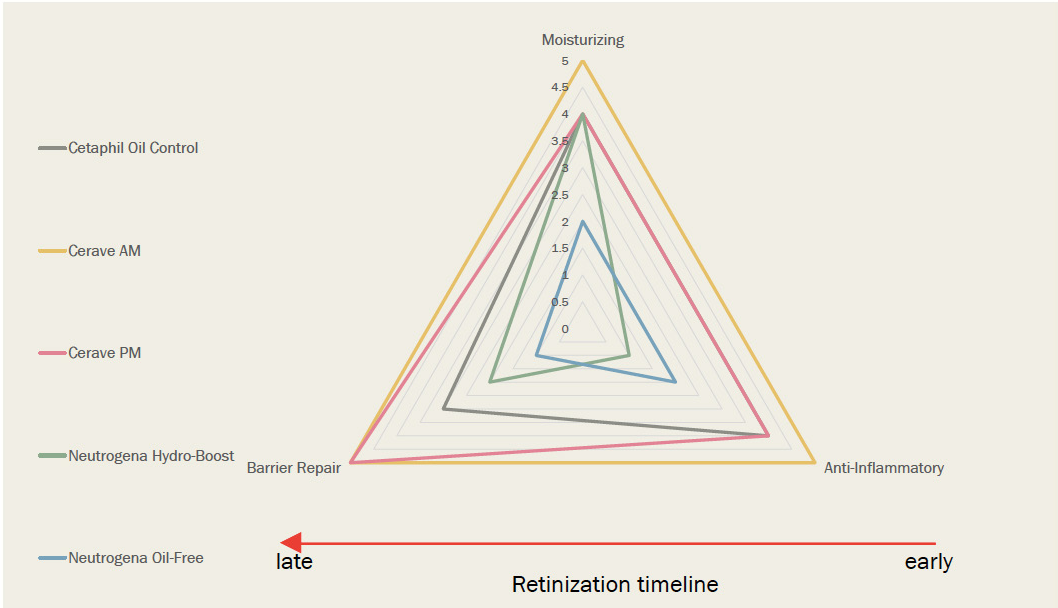


TABLE 3.

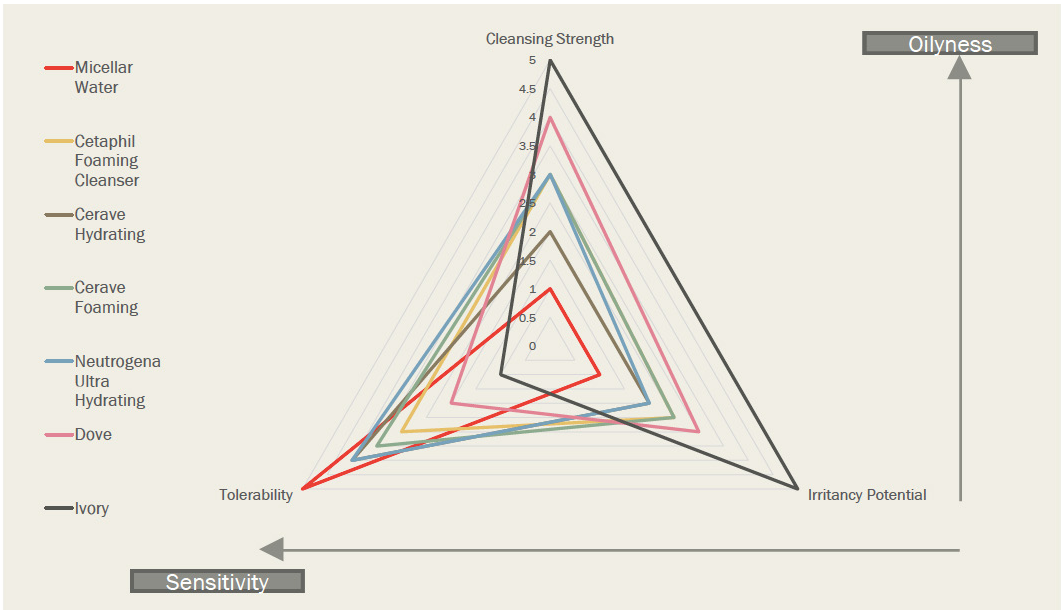
Specialized Moisturizers for Acne-prone Skin and Their Therapeutic Ingredients		
Product	**Property**	**Ingredients**
CeraVe® AM and PM Facial Moisturizing Lotions with SPF 30	Humectant	Glycerin, hyaluronic acid
	Emollient	Dimethicone
	Anti-inflammatory	Niacinamide
	Barrier replenishing	Ceramide 1, 3, 6-II, cholesterol, phytosphingosine in Multivesicular Emulsion (MVE®) Technology.
Neutrogena® Hydro Boost Water Gel	Humectant	Glycerin, sodium hyaluronate
	Emollient	Dimethicone, synthetic beeswax
Neutrogena® Oil-Free Moisture Broad Spectrum SPF 15	Humectant	Glycerin
	Anti-inflammatory	Glycerin soja
Cetaphil® PRO	Humectant	Glycerin
	Emollient	Dimethicone, isopropyl lauroyl sarcosinate, diisopropyl sebacate
	Oil absorber	Silica, polymethyl methacrylate, aluminum starch octenylsuccinate
	Anti-inflammatory	Tocopheryl acetate, glycyrrhetinic acid, zinc gluconate
	Barrier replenishing	Hydroxypalmitoyl sphinganine (Ceramide Technology™), pseudoceramide mimics, ceramide 5

Specialized Moisturizers for Acne

Moisturizers have the potential to offset the negative dermatological effects of prescription acne treatments (eg, erythema, irritation, inflammation, xerosis). They can also be important adjunctive therapies for acne patients if they are non-comedogenic, devoid of skin irritants, and compatible with treatment regimens.[53] A consensus statement from eleven Canadian dermatologists with expertise in treating acne stated that "ceramide-containing moisturizers may enhance adherence and complement existing acne therapies. The panel, therefore, proposes that adjunctive therapy with moisturizers and ceramide-containing moisturizers should be considered in acne-treated patients".[24] Although there are a plethora of skincare moisturizers available on the market, few studies have evaluated their efficacy and compatibility for patients with acne-prone skin.[54]

CeraVe® AM and PM Facial Moisturizing Lotions with SPF 30 (L'Oréal S.A., Clichy, France) contain ceramides, niacinamide, and hyaluronic acid. These creams have been shown to significantly improve the appearance of dry skin conditions and patient's subjective assessments of the quality of their professional life, self-image, and social life.[78] These creams are formulated using new technologies for delivering ceramides,

FIGURE 2. A decision framework for clinicians to use when selecting between adjunctive over-the-counter moisturizers for acne-prone patients.



including multivesicular emulsions, which deposit ceramides in a time-release manner for a continuous effect.[79] Cetaphil® PRO (Galderma Laboratories, L.P., Fort Worth, TX) is an oil-absorbing moisturizer that has been specially formulated for the enhanced treatment of acne-prone skin. Numerous trials have demonstrated its non-comedogenicity, non-acnegenic, and potential for photoprotection and reducing cutaneous irritation.[53,56] Through the incorporation of sebosuppressive and sebum-absorbent ingredients (Table 3) and Ceramide Technology™, Cetaphil® PRO reduces oil (sebum), simultaneously prevents TEWL while enhancing skin hydration and inducing increased endogenous production of ceramides.[53] Neutrogena® Hydro Boost Water Gel and Oil-Free Moisture Broad Spectrum SPF 15 creams alone and in combination have been investigated. A 12-week evaluator-blinded, randomized trial in males and females with mild-to-moderate acne vulgaris revealed that the concomitant use of these creams with an acne treatment resulted in improvements with overall inflammatory lesion redness, inflammatory lesion size, tactile surface roughness, uneven skin tone, skin blotchiness and a lack of skin clarity. These beneficial effects appeared across a wide range of subject ages, races, and Fitzpatrick skin types.[60] This study exemplified the suitability of these creams as adjuncts to acne treatments. A decision framework for clinicians to use when selecting between these products for acne-prone patients is presented in Figure 2.

Limitations

As only English-language publications were considered, a possible selection bias may have been present. In addition, many of the clinical trials included a short duration of follow up (eg, 28 days) and, as such, may have reduced the likelihood of documenting long-term improvements.

CONCLUSION

Acne is associated with a disruption to the skin's barrier function. This may present as a reduction in water-binding capacity and ceramide concentration, which can lead to dry skin and irritation. Systemic and topical treatments for acne can exacerbate these adverse effects. Informing clinicians about skin barrier dysfunction in acne and the benefits of adjunctive skincare may help them to choose the right product(s) to complement prescription therapy.

DISCLOSURES

The authors have no conflicts of interest to declare.

ACKNOWLEDGMENT

The research performed for this review was supported by an unrestricted educational grant from CeraVe LLC, New York, NY, USA.

REFERENCES

1. Bhate K, Williams HC. Epidemiology of acne vulgaris. *Brit J Dermatol.* 2013;168(3):474-85.
2. Vos T, Flaxman AD, Naghavi M et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease study 2010. *Lancet.* 2012;380:2163–96.
3. Halvorsen JA, Stern RS, Dalgard F, Thoresen M, Bjertness E, Lien L. Suicidal ideation, mental health problems, and social impairment are increased in adolescents with acne: a population-based study. *J Investig Dermatol.* 2011;131(2):363-70.
4. Sundström A, Alfredsson L, Sjölin-Forsberg G, Gerdén B, Bergman U, Jokinen J. Association of suicide attempts with acne and treatment with isotretinoin: a retrospective Swedish cohort study. *Br Med J.* 2010;341:c5812.
5. Yamamoto A, Takenouchi K, Ito M. Impaired water barrier function in acne vulgaris. *Arch Dermatol.* 1995;287(2):214-218.
6. Tan JK, Bhate K. A global perspective on the epidemiology of acne. *Br J Dermatol.* 2015;172(Suppl 1):3–12.
7. Del Rosso JQ. Clinical relevance of skin barrier changes associated with the use of oral isotretinoin: the importance of barrier repair therapy in patient management. *J Drugs Dermatol.* 2013 Jun 1;12(6):626-31.
8. Rocha MA, Bagatin E. Adult-onset acne: prevalence, impact, and management challenges. *Clin Cosmet Investig Dermatol.* 2018;11:59-69.
9. Hay RJ, Johns NE, Williams HC, Bolliger IW, Dellavalle RP, Margolis DJ, et al. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. *J Investig Dermatol.* 2014;134(6):1527-34.
10. Auffret N, Claudel JP, Leccia MT, Poli F, Farhi D, Dreno B. AFAST – adult female scoring tool: an easy-to-use tool for scoring acne in adult females. *J Eur Acad Dermatol Venereol.* 2016;(5)30:824–828.
11. Bhargava S, Cunha PR, Lee J, Kroumpouzos G. Acne scarring management: systematic review and evaluation of the evidence. *Am J Clin Dermatol.* 2018;19(4):459-477.
12. Connolly D, Hi V, Mariwalla K, Saedi N. Acne scarring-pathogenisis, evaluation and treatment options. *J Clin Aesthet Dermatol.* 2017;10(9):12-23.
13. Abad-Casintahan F, Chow SK, Goh CL, Kubba R, Hayashi N, Noppakun N, et al. Frequency and characteristics of acne-related post-inflammatory hyperpigmentation. *J Dermatol.* 2016 Jul;43(7):826-8.
14. Abanmi A, Al-Enezi M, Al Hammadi A, Galadari I, Kibbi AG, Zimmo S. Survey of acne-related post-inflammatory hyperpigmentation in the Middle East. *J Dermatolog Treat.* 2019 Sep;30(6):578-581.
15. Gollnick HPM. From new findings in acne pathogenesis to new approaches in treatment. *J Eur Acad Dermatol Venereol.* 2015; 29(Suppl. 5): 1–7.
16. Dreno B, Pecastaings S, Corvec S, Veraldi S, Khammari A, Roques C. Cutibacterium acnes (Propionibacterium acnes) and acne vulgaris: a brief look at the latest updates. *J Eur Acad Dermatol Venereol.* 2018;32 Suppl 2:5-14.
17. Dréno B, Bettoli V, Araviiskaia E, Sanchez Viera M, Boulouc A. The influence of the exposome on acne. *J Eur Acad Dermatol Venereol.* 2018;30: 1–8.
18. Dreno B, Shourick J, Kerob D, Bouloc A, Taieb C. The role of the exposome in acne : results from an international patient survey. *J Eur Acad Dermatol Venereol.* 2020;34(5):1057-1064.
19. Dreno B. What is new in the pathophysiology of acne, an overview. *J Eur Acad Dermatol Venereol.* 2017;31(Suppl 5): 8–12.
20. Thiboutot DM, Dreno B, Abanmi A, Alexis AF, Araviiskaia E, Barona Cabal MI, et al. Practical management of acne for clinicians: An international consensus from the Global Alliance to Improve Outcomes in Acne. *J Am AC Dermatol.* 2018;78(2 Suppl 1)S1-S23.e.
21. Nast A, Dreno B, Bettoli V, Bukvic Mokos Z, Degitz K, Dressler C, et al. European evidence-based (S3) guideline for the treatment of acne - update 2016 - short version. *J Eur Acad Dermatol Venereol.* 2016;30(8):1261-8.
22. 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.
23. Araviiskaia E, Dreno B. The role of dermocosmetics in acne vulgaris. *J Eur Acad Dermatol Venereol.* 2016, 30, 926–935.
24. Lynde CW, Andriessen A, Barankin B, Gannes GD, Gulliver W, Haber R, et al. Moisturizers and ceramide-containing moisturizers may offer concomitant therapy with benefits. *JCAD.* 2014;7(3):18-26.
25. Kwon HH, Suh DH. Recent progress in the research about Propionibacterium acnes strain diversity and acne: pathogen or bystander? *Int J Dermatol.* 2016;55(11):1196-204.
26. Qidwai A, Pandey M, Pathak S, Kumar R, Dikshit A. The emerging principles for acne biogenesis: A dermatological problem of puberty. *Human Microbiome Journal.* 2017;4:7-13.

27. Norstedt S, Lindberg M. Dietary regimes for treatment of acne vulgaris: a critical review of published clinical trials. *Acta Derm Venereol.* 2016; 96:283–284.
28. Agamia NF, Abdallah DM, Sorour O, Mourad B, Younan DN. Skin expression of mammalian target of rapamycin and forkhead box transcription factor O1, and serum insulin-like growth factor-1 in patients with acne vulgaris and their relationship with diet. *Br J Dermatol.* 2016;174:1299–1307.
29. Cengiz FP, Cevirgen Cemil B, Emiroglu N, Gulsel Bahali A, Onsun N. Acne located on the trunk, whey protein supplementation: is there any association? *Health Promot Perspect.* 2017;7:106–108.
30. Lefebvre MA, Pham DM, Boussouira B, Bernard D, Camus C, Nguyen QL. Evaluation of the impact of urban pollution on the quality of skin: a multicentre study in Mexico. *Int J Cosmet Sci.* 2015; 37: 329–338.
31. Lefebvre MA, Pham DM, Boussouira B, Qiu H, Ye C, Long X, et al. Consequences of urban pollution upon skin status. A controlled study in Shanghai area. *Int J Cosmet Sci.* 2016; 38: 217–223.
32. Perkins AC, Maglione J, Hillebrand GG, Miyamoto K, Kimball AB. Acne vulgaris in women: prevalence across the life span. *J Womens Health.* 2012;21(2):223–230.
33. Tyler KH, Zirwas MJ. Contraception and the dermatologist. *J Am Acad Dermatol.* 2013;68:1022–1029.
34. Rocha M, Sanudo A, Bagatin E. The effect on acne quality of life of topical azelaic acid 15% gel versus a combined oral contraceptive in adult female acne: a randomized trial. *Dermatoendocrinol.* 2017;9(1):e1361572.
35. Cardinali G, Kovacs D, Picardo MI. Mechanisms underlying post-inflammatory hyperpigmentation. *Ann Dermatol Venereol.* 2012;139 Suppl 4:S148-52.
36. Woolery-Lloyd HC, Kerri J, Doig S. Retinoids and azelaic acid to treat acne and hyperpigmentation in skin of color. *J Drugs Dermatol.* 2013;12(4):434-7.
37. Nestor MS, Bucay VW, Callender VD, Cohen JL, Sadick N, Waldorf H. Polypodium leucotomos as an adjunct treatment of pigmentary disorders. *J Clin Aesthet Dermatol.* 2014;7(3):13-17.
38. Tan J, Bissonnette R, Gratton D, Kerrouche N, Canosa JM.The safety and efficacy of four different fixed combination regimens of adapalene 0.1%/benzoyl peroxide 2.5% gel for the treatment of acne vulgaris: results from a randomised controlled study. *Eur J Dermatol.* 2018;28(4):502-508.
39. Fabbrocini G, Rossi AB, Thouvenin MD, Peraud C, Mengeaud V, Bacquey A, et al. Fragility of epidermis: acne and post-procedure lesional skin. *J Eur Acad Dermatol Venereol.* 2017;31 Suppl 6:3-18.
40. Zeichner JA. Inflammatory Acne Treatment: Review of Current and New Topical Therapeutic Options. *J Drugs Dermatol.* 2016;15(1 Suppl 1):s11-6.
41. Schorr ES, Sidou F, Kerrouche N. Adjunctive use of a facial moisturizer SPF 30 containing ceramide precursor improves the tolerability of topical tretinoin 0.05%: A randomized, investigator-blinded, split-face study. *J Drugs Dermatol.* 2012;11(9):1104-1107.
42. E. Araviiskaia, B. Dreno. The role of dermocosmetics in acne vulgaris. *J Eur Acad Dermatol Venereol.* 2016;30:926–935.
43. Kar BR, Tripathy S, Panda M. Comparative study of oral isotretinoin versus oral isotretinoin + 20% salicylic acid peel in the treatment of active acne. *J Cutan Aesthetic Surg.* 2013;6:204–208.
44. Baumann LS, Oresajo C, Yatskayer M et al. Comparison of clindamycin 1% and benzoyl peroxide 5% gel to a novel composition containing salicylic acid, capryloyl salicylic acid, HEPES, glycolic acid, citric acid, and dioic acid in the treatment of acne vulgaris. *J Drugs Dermatol.* 2013; 12: 266–269.
45. de Lucas R, Moreno-Arias G, Perez-Lopez M, Vera-Casano A, Aladren S, Milani M. Adherence to drug treatments and adjuvant barrier repair therapies are key factors for clinical improvement in mild to moderate acne: the ACTUO observational prospective multicenter cohort trial in 643 patients. *Br Med Clin Dermatol.* 2015;15:17.
46. Isoda K, Seki T, Inoue Y, Umeda K, Nishizaka T, Tanabe H, et al. Efficacy of the combined use of a facial cleanser and moisturizers for the care of mild acne patients with sensitive skin. *J Dermatol.* 2015;42(2):181-8.
47. Decker A, Graber EM. Over-the-counter acne treatments: a review. *J Clin Aesth Dermatol.* 2012; 5: 32–40
48. Isoda K, Seki T, Inoue Y et al. Efficacy of the combined use of a facial cleanser and moisturizers for the care of mild acne patients with sensitive skin. *J Dermatol.* 2015; 42: 181–188.
49. Fabbrocini G, Rossi AB, Thouvenin MD, Peraud C, Mengeaud V, Bacquey A, et al. Fragility of epidermis: acne and post-procedure lesional skin. *J Eur Acad Dermatol Venereol.* 2017;31 Suppl 6:3-18.
50. Zeichner JA. Inflammatory Acne Treatment: Review of Current and New Topical Therapeutic Options. *J Drugs Dermatol.* 2016;15(1 Suppl 1):s11-6.
51. Schorr ES, Sidou F, Kerrouche N. Adjunctive use of a facial moisturizer SPF 30 containing ceramide precursor improves the tolerability of topical tretinoin 0.05%: A randomized, investigator-blinded, split-face study. *J Drugs Dermatol.* 2012,11(9):1104-1107.
52. Claudel JP, Auffret N, Leccia MT, Poli F, Corvec S, Dreno B. Staphylococcus epidermidis: A potential new player in the physiopathology of acne. *Dermatol.* 2019;235:287–294.
53. Kar BR, Tripathy S, Panda M. Comparative study of oral isotretinoin versus oral isotretinoin + 20% salicylic Acid peel in the treatment of active acne. *J Cutan Aesthetic Surg.* 2013; 6: 204–208.
54. Bowe WP, Kircik LH. The importance of photoprotection and moisturization in treating acne vulgaris. *J Drugs Dermatol.* 2014 Aug;13(8):s89-94.
55. 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.
56. Nestor MS, Swenson N, Macri A, Manway M, Paparone P. Efficacy and tolerability of a combined 445nm and 630nm over-the-counter light therapy mask with and without topical salicylic acid versus topical benzoyl peroxide for the treatment of mild-to-moderate acne vulgaris. *J Clin Aesth Dermatol.* 2016;9(3):25-35.
57. St Surin-Lord S, Miller J. Topical Treatment of Truncal Acne with Tretinoin Lotion 0.05% and Azelaic Acid Foam. *Case Rep Dermatol Med.* 2020:5217567.
58. Batra R, Sadhasivam S, Saini S, Gupta S, Bisen RKS, Sinha M, Ghosh S, Jain S. Efficacy and safety of VB-1953 topical gel in non-responder acne patients with clindamycin-resistant cutibacterium acnes. *Drugs R D.* 2020.
59. Hoffmann J1, Gendrisch F1, Schempp CM1, Wölfle. New herbal biomedicines for the topical treatment of dermatological disorders. *Biomed.* 2020;8(2). pii: E27.
60. Dogra S, Sumathy TK, Nayak C, Ravichandran G, Vaidya PP, Mehta S, Mittal R, Mane A, Charugulla SN. Efficacy and safety comparison of combination of 0.04% tretinoin microspheres plus 1% clindamycin versus their monotherapy in patients with acne vulgaris: a phase 3, randomized, double-blind study. *J Dermatolog Treat.* 2020:1-9.
61. Tanghetti EA, Werschler WP, Lain T, Guenin E, Martin G, Pillai R. Tazarotene 0.045% lotion for once-daily treatment of moderate-to-severe acne vulgaris: results from two phase 3 trials. *J Drugs Dermatol.* 2020;19(1):70-77.
62. Woodburn KW, Jaynes J, Clemens LE. Designed antimicrobial peptides for topical treatment of antibiotic resistant acne vulgaris. *Antibiotics (Basel).* 2020;9(1).
63. Jain S, Yadav V, Bhatia N. Clinical pharmacokinetics, safety and exploratory efficacy study of a topical bactericidal VB-1953: analysis of single and multiple doses in a Phase I trial in acne vulgaris subjects. *Clin Drug Investig.* 2020;40(3):259-268.
64. Zdrada J, Odrzywołek W, Deda A, Wilczyski S. A split-face comparative study to evaluate the efficacy of 50% pyruvic acid against a mixture of glycolic and salicylic acids in the treatment of acne vulgaris. *J Cosmet Dermatol.* 2020 Jan 10. doi: 10.1111/jocd.13288.
65. Shen WT, Wu Y, He HQ, Yu Y, Qin HH, Fei JB, Wang GJ Efficacy and safety of artemether emulsion for the treatment of mild-to-moderate acne vulgaris: a randomized pilot study. *J Dermatolog Treat.* 2020:1-4.
66. Dayal S, Kalra KD, Sahu P. Comparative study of efficacy and safety of 45% mandelic acid versus 30% salicylic acid peels in mild-to-moderate acne vulgaris. *J Cosmet Dermatol.* 2020;19(2):393-399.
67. Zhang J, Zhang X, He Y, Wu X, Huang J, Huang H, Lu C. Photodynamic therapy for severe facial acne vulgaris with 5% 5-aminolevulinic acid vs 10% 5-aminolevulinic acid: A split-face randomized controlled study. *J Cosmet Dermatol.* 2020;19(2):368-374.
68. Raoof TJ, Hooper D, Moore A, Zaiac M, Sullivan T, Kircik L, Lain E, Jankicevic J, Stuart I. Efficacy and safety of a novel topical minocycline foam for the treatment of moderate to severe acne vulgaris: A phase 3 study. *J Am Acad Dermatol.* 2020;82(4):832-837.
69. Harper JC, Roberts WE, Zeichner JA, Guenin E, Bhatt V, Pillai R. Novel tretinoin 0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris: assessment of safety and tolerability in subgroups. *J Dermatolog Treat.* 2020;31(2):160-167.
70. Green L, Kircik LH, Gwazdauskas J. Randomized, controlled, evaluator-blinded studies conducted to compare the efficacy and tolerability of 3 over-the-counter acne regimens in subjects with mild or moderate acne. *J Drugs Dermatol.* 2013;12(2):180-5.
71. Draelos ZD, Shalita AR, Thiboutot D, Oresajo C, Yatskayer M, Raab S. A multicenter, double-blind study to evaluate the efficacy and safety of 2 treatments in participants with mild to moderate acne vulgaris. *Cutis.* 2012;89(6):287-93.
72. Bowe WP, Shalita AR. Effective over-the-counter acne treatments. *Semin Cutan Med Surg.* 2008;27(3):170-6.
73. James Q. Del Rosso, Michael Gold, Maria José Rueda, Staci Brandt, Warren J. Winkelman. Efficacy, safety, and subject satisfaction of a specified skin care regimen to cleanse, medicate, moisturize, and protect the skin of patients under treatment for acne vulgaris. *J Clin Aesthet Dermatol.* 2015;8(1):22–30.
74. Oon HH, Wong SN, Aw DCW, Cheong WK, Goh CL, Tan HH. Acne Management Guidelines by the Dermatological Society of Singapore. *J Clin Aesthet Dermatol.* 2019;12(7):34–50.
75. Bhavana Tetali, Fatima M. Fahs, Darius Mehregan. Popular over-the-counter

cosmeceutical ingredients and their clinical efficacy. *J Dermatol.* 2020; 59(4): 393-405.
76. Spruit D. The interference of some substances with the water vapour loss of human skin. *Dermatologica.* 1971;142(2):89-92.
77. Huang HC, Chang TM. Ceramide 1 and ceramide 3 act synergistically on skin hydration and the transepidermal water loss of sodium lauryl sulfate-irritated skin. *J Dermatol.* 2008;47(8):812-819.
78. Zhang Q, Flach CR, Mendelsohn R, et al. Topically applied ceramide accumulates in skin glyphs. *Clin Cosmet Investig Dermatol.* 2015;8:329-337.
79. Vender RB, Andriessen A, Barankin B, Freiman A, Kyritsis D, Mistos LM, Salsberg J, Amar L. Cohort using a ceramides containing cleanser and cream with salicylic acid for dry, flaking, and scaling skin conditions. *J Drugs Dermatol.* 2019;18(1):80-85.
80. Zeichner JA, Del Rosso JQ. Multivesicular emulsion ceramide-containing moisturizers: an evaluation of their role in the management of common skin disorders. *J Clin Aesthet Dermatol.* 2016;9(12):26-32.

AUTHOR CORRESPONDENCE

Anneke E. Andriessen PhD
E-mail:.....anneke.a@tiscali.nl