

# The Use of Acneceuticals to Improve Acne Care: Introduction of a New Term and Review of the Literature

Hilary Baldwin MD,<sup>a</sup> Helen Bui MD,<sup>b</sup> Valerie Callender MD,<sup>c</sup> Cheri Frey MD,<sup>d</sup> Adelaide Hebert MD,<sup>e</sup> Edward (Ted) Lain MD,<sup>f</sup> Evan Rieder MD,<sup>g</sup> Todd Schlesinger MD<sup>h</sup>

<sup>a</sup>Rutgers Robert Wood Johnson Medical Center, New Brunswick, NJ; The Acne Treatment and Research Center Brooklyn, NY

<sup>b</sup>Howard University College of Medicine, Washington, DC

<sup>c</sup>Howard University College of Medicine, Washington, DC; Callender Dermatology and Cosmetic Center, Glenn Dale, MD

<sup>d</sup>Howard University College of Medicine, Washington, DC

<sup>e</sup>McGovern Medical School, Houston TX; Children's Memorial Hermann Hospital, Houston, TX

<sup>f</sup>Sanova Dermatology, Austin, TX

<sup>g</sup>Private Practice, New York, NY

<sup>h</sup>Clinical Research Center of the Carolinas, Charleston SC;

The George Washington University School of Medicine and Health Sciences, Washington, DC

## ABSTRACT

**Background:** Acne is a multifactorial inflammatory skin condition that commonly presents to the dermatology clinic. Treatment generally involves the use of pharmaceutical agents and procedural techniques. Recently, the importance of over-the-counter skin care in acne has been recognized in many studies. This paper introduces the term acneceuticals to encompass a wide range of FDA monographed, yet non-prescription ingredients proven to alter the structure and function of acneic skin.

**Methods:** A panel of 8 dermatologists with an interest in acne and skin care performed a literature review of active skin care in acne. The role of acneceuticals in the treatment of acne — as monotherapy, adjunctive, and maintenance therapy — was evaluated using a modified Delphi approach. Studies were limited to in vivo human trials involving acne. Individual actives were assessed separately.

**Results:** The quality of evidence was moderate-to-low for many of the ingredients. Most of the actives included in the final assessment had been studied in vehicle-controlled, blinded, often comparative studies but enrolled a small number of subjects. In these studies, the acneceuticals were found to reduce lesion count, reduce sebum production, and improve efficacy of existing pharmacologic therapies.

**Conclusion:** Acneceuticals have demonstrated benefits in treating acne, alone or in conjunction with established pharmaceutical agents. These data allow us to make quality recommendations for our patients that should be a part of every patient encounter. The recommendations also serve as a guide for patients searching the internet for beneficial self-care products.

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## INTRODUCTION

Acne is the most common cutaneous disease worldwide and the most frequent disorder to present to the dermatology practice. Although efficacious treatments exist, clinicians continue to search for better regimens with improved safety for our patients. Our patients search, too — with or without our guidance. Many patients are looking for more “natural” approaches to skin care. Selecting skincare products gives patients a satisfying sense of control that can help attenuate the psychological sequelae of acne. Unfortunately, the media and the internet abound with alternatives to prescription medications; many without efficacy and some with harmful consequences. Since delay in acne therapy is associated with

an increased risk of scarring, uneducated postings can lead to permanent disfigurement. As a result, it is incumbent upon clinicians to be well-versed in routine skin care as well as active ingredients in over the counter (OTC) products that may augment care. Many clinicians fail to discuss skin care, missing an opportunity to enhance patient outcome.

Clinicians in the United States are far behind our European colleagues who have embraced the concept of what they have termed “dermocosmetics.”<sup>1-3</sup> Dermocosmetics are defined as products with both cosmetic and active ingredients that improve cutaneous disorders. The term “acneceuticals” is thus introduced to encompass formulations with active ingredients

that have a potential role in acne therapy, whether as first-line or adjunctive therapy. Like cosmeceuticals for anti-aging, acneceuticals fall short of being drugs; yet they contain FDA-monographed ingredients that alter the structure and function of acneic skin and have many clinical studies to substantiate their efficacy.

The most recent publication on the topic, an international consensus recommendation for the use of dermocosmetics in acne, is a comprehensive review of the topic.<sup>4</sup> After a thorough literature search and endeavoring to review actives with only the highest quality of in vitro and in vivo data, the authors evaluated dermocosmetics by class rather than by individual agents. They noted that studies of individual ingredients often had few, low quality studies, which made their goal of an evidence-based review unattainable.

However, patients often inquire about acneceuticals by ingredient name and a review of existing data for individual actives is worthy of assessment, even if less rigorous. Combination products are not given consideration herein, particularly proprietary formulas that are unobtainable by our patients. This review is limited to in vivo human trials in patients with acne. Benzoyl peroxide (BP) and adapalene are not included given that these are drugs, not acneceuticals. The goal of this compilation is to simplify the OTC acne landscape for prescribers as well as for patients looking to self-treat with effective and safe products.

## MATERIALS AND METHODS

A scoping literature review was conducted in August 2023 on PubMed and Google Scholar and evaluated by 2 reviewers (HB, HB). Search terms were Acne AND adjunctive skincare or cosmeceuticals or dermocosmetics or barrier repair. Once the list of acneceuticals of interest was generated (see Table 1), a search was done for each active AND acne. Included studies were limited to in vitro, human and participants with acne. In September 2023, a panel of 7 dermatologists convened, and using the modified Delphi method, reviewed the data and came to consensus on which acneceuticals had sufficient data for inclusion. The goal was to provide specific evidenced-based skincare recommendations for acne therapy.

The clinician's choice of which active ingredients to review was based on knowledge of acne pathophysiology. Four central factors are thought to be most important: hyperkeratinization, hyperseborrhea and dysseborrhea, *Cutibacterium acnes* (*C. acnes*) colonization, and inflammation.<sup>5,6</sup> Additional studies implicate skin barrier dysfunction as a material contributor to the pathophysiology of acne. In 1995, Yamamoto and co-workers demonstrated that acne should be considered a barrier deficiency disorder alongside atopic dermatitis and psoriasis.<sup>7</sup> The authors found an increase in transepidermal water loss (TEWL) as well as

a statistically significant reduction in ceramides, both hallmarks of barrier deficiency. Barrier dysfunction is known to be accompanied by hyperkeratosis of the follicular epithelium and therefore, Yamamoto et al postulated that barrier dysfunction could be partially responsible for comedone formation.

**TABLE 1.**

### Proposed Mechanism of Action of Acneceuticals in Acne

Mechanism of action	Actives
Keratolytic	Alpha and beta hydroxyacids
	Azelaic acid
	Retinol derivatives
	Bakuchiol
	Silymarin
Antibacterial	Sulfur
	Azelaic acid
	Niacinamide
	Zinc
	Green Tea
	Resveratrol
	Silymarin
	Bakuchiol
	Soy
	Probiotics
	Retinaldehyde
	Sodium hypochlorite
Anti-inflammatory	Tea tree oil
	Niacinamide
	Bakuchiol
	Salicylic acid
	Azelaic acid
	Linoleic acid
	Lactobacillus
	Aloe vera
	Green tea
	Cannabidiol
	Zinc
	Resveratrol
	Silymarin
	Sodium hypochlorite
Sebum reduction	Tea tree oil
	Niacinamide
	Zinc
	Green tea
	Silymarin
	Bakuchiol
	Linoleic acid
	Clay
Barrier repair	Soy
	Resveratrol
	Hyaluronic acid
	Alpha and beta hydroxy acids
	Glycerin
	Colloidal oatmeal
	Niacinamide
	Panthenol
	Ceramides
	Shea butter

Based on these tenets of acne pathophysiology, potential therapeutic targets focus on keratolysis, inhibition of sebum production, and antibacterial and anti-inflammatory agents. More recently, the importance of barrier repair in acne care has gained traction in the literature.

### Mechanism of Action

Active ingredients meeting initial consensus were divided into 5 mechanisms of action: keratolytic, anti-inflammatory, sebum control, antibacterial (preferably specifically *C. acnes*), and skin barrier repair in acne studies (see Table 1). Studies were further divided into those with data supporting use of the active as monotherapy, adjunctive therapy with established prescription agents and maintenance therapy after prescription drug discontinuation (see Tables 2-4).

Many actives had data demonstrating efficacy in acne as standalone treatments. However, it is likely that in clinical practice, combination treatment will be necessary for maximum effectiveness, selecting agents from several categories to approach acne from different directions simultaneously. Studies looking at adjunctive therapy were of 2 types: the addition of an acneceutical to prescription care to augment effectiveness and the addition of a barrier repair acneceutical to improve prescription drug tolerability and therefore adherence and efficacy. Acne medications often need to be discontinued, whether due to achievement of adequate clearance, side effects, cost, or concerns about antibiotic resistance. Maintenance or treatment transition is necessary and several acneceuticals are uniquely suited to this role — continuing improvement attained with the prescription drugs or in some cases improving outcome. Choosing an acneceutical from the list of agents having the same mechanism of action as the drug itself is expected to be the most effective: switching prescription antibiotic to an acneceutical with antibacterial activity, or retinoid to OTC keratolytic.

### Keratolytics

Keratolytics are thought to work in acne by decreasing adhesion of keratinocytes in the stratum corneum, helping to remove the superficial portions of follicular plugging, reducing further occlusion. Additionally, the disruption of the stratum corneum allows other actives to penetrate more effectively, increasing their efficacy.

Acneceuticals with data supporting keratolytic activity included azelaic acid (AzA), Alpha- and Beta-hydroxy acids (AHA, BHA), retinol derivatives, bakuchiol, and sulfur.

### Sebum Control

The inflammatory state of acne may be partly driven by hyperseborrhea and dysseborrhea. Decreased levels of linoleic acid, total ceramides, free sphingosine, and higher levels of inflammatory free fatty acids have been noted. This

dysseborrhea has been clinically correlated with epidermal barrier dysfunction.<sup>8,9</sup>

Acneceuticals with data supporting sebum control include niacinamide, clay, zinc, green tea, resveratrol, silymarin, and bakuchiol. Consideration was purposely limited to those actives with data indicating reduced sebum production (sebumeter, tape stripping) as opposed to those that reduce the appearance of oiliness (eg, mattifying agents such as perlite, kaolin, calcium carbonate, bentonite, methacrylate copolymer).

**TABLE 2.**

Actives With Monotherapy Data	
Active	Reference
Azelaic acid	22-24
Bakuchiol	25
Beta hydroxy acids	16-19
Cannabidiol	27
Clay	28,29
Green Tea	32-34
Niacinamide	37-40
Probiotics	43-37
Resveratrol	48
Retinol derivatives	49-50
Silymarin	51,52
Sodium hypochlorite	55
Soy	56
Tea tree oil	57,58
Zinc	60-62

**TABLE 3.**

Actives as Adjunctive Therapy to Prescription Medications	
Active	Reference
Aloe vera and tretinoin	13
Azelaic acid and erythromycin	23
Azelaic acid and clindamycin	24
Ceramide/niacinamide with BP/clindamycin	42
Lipohydroxy acid and BP	19
Niacinamide and BP	41,42
Salicylic acid and BP	20
Silymarin and Salicylic acid peels	53
Tea tree oil and adapalene	59
Zinc and erythromycin	63,64

**TABLE 4.**

Actives With Maintenance Data	
Active	Reference
Lipohydroxy acid	20
Hydroxy acid complex	21
Retinol derivatives	24
Salicylic acid	20,21

**Antibacterial Agents**

*C. acnes* has an important role in the pathogenesis of acne. Although antibiotics, both topical and oral, are highly effective in the treatment of acne, eventual discontinuation results in rapid bacterial repopulation. Antibiotics also cause collateral damage on the skin and the gut, altering the normal healthy microbiome in both locations. Acneceuticals with antibacterial activity may not only be effective, but preferable to prescription antibiotics, allowing us to be good stewards of antibiotics by reducing the development of resistant microbes.

Acneceuticals with data supporting antibacterial activity include zinc, hypochlorous acid, tea tree oil (TTO), resveratrol, AzA, aloe vera, green tea, *Lactobacillus spp.*, *Enterococcus faecalis*, and cannabidiol.

**Anti-inflammatory Agents**

Acne is a chronic inflammatory condition, and anti-inflammatory agents can reduce lesion number, size, and erythema. Acneceuticals with anti-inflammatory activity and demonstrated efficacy in acne include niacinamide, bakuchiol, salicylic acid (SA), AzA, linoleic acid, zinc, soy, aloe vera, silymarin, *Lactobacillus spp.*, green tea, and cannabidiol.

**Skin Barrier Repair**

Skin barrier repair in acne serves 2 distinct purposes. First is the possibility that improving the inherent barrier dysfunction in acne affects improvement in the disease. Data suggests that good quality skin care alone can result in acne improvement. We frequently see this when faced with unexpectedly good results in the vehicle arms of acne studies. Small studies have demonstrated that daily use of a facial cleanser and moisturizer can reduce acne lesions without aggravating epidermal barrier dysfunction, thereby reducing TEWL, mitigating aberrations of cutaneous pH, and fostering the growth of a diverse microbiome.<sup>8</sup>

Second is the ability of quality skin care to improve pharmaceutical tolerability. The acne management paradigm is built on topical retinoids and BP. In addition to having documented efficacy for acne, these ingredients can also increase cell turnover, induce stratum corneum thinning, and increase TEWL, often leading to xerosis, irritation, and even inflammation.<sup>2,8,10</sup> When combined with acne treatment regimens, the use of gentle cleansers, quality moisturizers, and sunscreen can improve patient comfort and patient-centered goals, including minimizing the adverse effects of dryness, irritation, and photosensitivity. Although there are many factors leading to poor compliance, skin irritation is a prominent factor.<sup>11,12</sup> A double-blinded, randomized study compared the outcome of an acne treatment regimen consisting of a twice-daily skincare routine in addition to a nightly combination topical agent (adapalene 0.3%/BP 2.5%).<sup>13</sup> Use of a ceramide-containing cleanser and moisturiz-

er during the 12-week treatment period resulted in a statistically significant improvement in both primary endpoints: markers of skin barrier function and acne severity.

Acneceuticals that have specifically been shown to improve the ability of patients to tolerate acne pharmaceuticals include hyaluronic acid, alpha hydroxy acids, glycerin, panthenol, niacinamide, colloidal oatmeal, ceramides, shea butter, aloe vera, and petrolatum.

**Acneceutical Data***Aloe Vera*

Aloe vera as an anti-inflammatory and hydrating agent was evaluated as adjunctive therapy in a double blind, randomized, 8-week study of 60 participants with mild and moderate acne. Tretinoin 0.5% cream combined with a 50% aloe vera formulation resulted in better lesion reduction compared to tretinoin 0.5% alone.<sup>14</sup>

*Alpha and Beta Hydroxy Acids*

Hydroxy acids act as keratolytics and hydrating agents in the treatment of acne, reducing follicular obstruction and increasing absorption of coapplied ingredients. Data are most rigorous for the beta hydroxy acids, including SA and lipohydroxy (LHA). The most used alpha hydroxy acid is glycolic acid; although, in topical preparations, it is most often used in combination with other active ingredients.

Zander and Weisman reported that pads containing 0.5% and 2% SA resulted in lesion resolution in 3 small placebo-controlled studies.<sup>15</sup> A comparison study of 2% SA vs 10% BP cleansers in 30 participants showed superiority of the SA cleanser after 4 weeks.<sup>16</sup> A combination of SA-based products was effective in reducing inflammatory acne over 8 weeks without side effects.<sup>17</sup> LHA was as effective as 5% BP in 80 patients with mild-moderate disease.<sup>18</sup> LHA twice daily was also as effective as 2.5% tretinoin cream in 85 mild-moderate patients after 3 months with fewer side effects.<sup>19</sup>

Hydroxy acids have been evaluated extensively as ideal maintenance products after discontinuation of prescription medications. One hundred participants who improved on BP were randomized to receive either a SA/niacinamide combination cream or vehicle. Continued improvement was seen with the SA cream over 12 weeks.<sup>20</sup> Continued improvement was also seen with a tri-acid complex serum (glycolic acid, SA, and LHA) in 30 participants once daily for 2 months after discontinuation of prescription medications.<sup>21</sup>

*Azelaic Acid in OTC Concentrations*

AzA, in its prescription concentration of 15% and 20%, is thought to be effective in acne due to its anti-inflammatory activities, its ability to inhibit growth of *C. acnes*, and its mild keratolytic

effects. This product is available OTC in lower concentrations with limited data supporting its use.

As monotherapy, in a small uncontrolled, 8-week study of patients with mild-to-moderate acne, once-daily application of a 10% AzA gel resulted in significant reduction in inflammatory lesions and non-inflammatory lesions.<sup>22</sup>

As adjunctive therapy, use of AzA 5% with erythromycin 2% was more effective than monotherapy with erythromycin 2% or 20% AzA in a randomized, double-blind, 12-week study of 147 patients with mild-to-moderate acne.<sup>23</sup> The combination product was better tolerated than the 20% AzA. In a similar double-blind, randomized, 12-week trial of 150 patients with mild-to-moderate disease, the combination of azelaic acid 5% and clindamycin 2% was significantly more effective than either monotherapy arm in reducing both inflammatory lesions and non-inflammatory lesions.<sup>24</sup>

#### *Bakuchiol*

Bakuchiol has been touted as a more tolerable retinol alternative. Although it is not structurally similar to retinoids, it does demonstrate retinol-like regulation of gene expression. Its use in acne has been based on in vitro data demonstrating anti-inflammatory, antibacterial and keratolytic activity.

As monotherapy, a small study of 13 patients with mild-to-moderate acne used a 5% formulation twice daily for 12 weeks with a significant reduction of inflammatory lesions.<sup>25</sup>

As adjunctive therapy, a combination dermocosmetic containing bakuchiol was shown to improve the efficacy of adapalene 1% in a 2-month study of 111 patients.<sup>26</sup> An improvement in seborrhea was also noted.

#### *Cannabidiol*

Cannabidiol has been proposed for the treatment of acne due to its anti-inflammatory activity. It has also been shown to inhibit *C. acnes* growth in vitro. A small pilot study of 30 participants showed a decrease in inflammatory lesions.<sup>27</sup>

#### *Clay*

There are limited studies for clay masks in acne. Clay has hydrating and anti-inflammatory activity as well as data demonstrating reduced sebum production. As monotherapy, a mask used twice weekly for 4 weeks resulted in reduced acne lesion counts, decreased sebumeter values, and improved subjective oiliness in 75 adults with oily skin.<sup>28</sup> An open label study of 194 patients with mild acne demonstrated a 54% reduction in total lesion count after utilizing a mask 2 to 3 times/week for 6 weeks.<sup>29</sup>

#### *Green Tea*

Green tea has been evaluated for the treatment of acne due to its antimicrobial and anti-inflammatory activity, as well as evidence that it can reduce sebum production.

In 2 uncontrolled studies, green tea extract was shown to decrease sebum production: a split-face study of 11 men found a 27% reduction in sebumeter values after 60 days of daily use<sup>30</sup>; a 3% extract showed similar results in 10 participants after 8 weeks of use.<sup>31</sup>

As monotherapy, green tea extract was evaluated in several studies. In an uncontrolled study of 20 patients, a 2% extract resulted in a statistically significant reduction in lesion counts after 6 weeks of daily use.<sup>32</sup> A 1% or 5% extract was utilized in a split-face study vs vehicle in 35 patients with acne: at 8 weeks there was a significant decrease in both inflammatory and non-inflammatory lesions.<sup>33</sup> A comparison of 2% extract to vehicle in 60 patients resulted in a statistically significant reduction in inflammatory lesions at 8 weeks and high patient satisfaction.<sup>34</sup>

#### *Linoleic Acid*

A decrease in linoleic acid in surface lipids has been found in patients with acne compared to healthy controls. This is thought to be related to an alteration in the quality of sebum produced by acne patients. Linolenic acid is a potent inhibitor of 5-alpha reductase and is an anti-inflammatory that has been used in combination with many other agents in numerous studies. Recently, it has been reported that a combination cream containing linoleic acid, linolenic, and lecithin was effective in 4 patients in a case series.<sup>35</sup>

#### *Niacinamide/Nicotinamide*

The best studied of the acneceuticals is niacinamide. This anti-inflammatory and antimicrobial (including activity against *C. acnes*) is hydrating and has sebum-reducing activity. Niacinamide/nicotinamide has been extensively studied as monotherapy and as adjunctive therapy.

As monotherapy, Draelos et al evaluated the ability of 2% niacinamide to reduce facial sebum production in 100 participants vs vehicle for 4 weeks and in 30 split-face participants for 6 weeks.<sup>36</sup> In both studies there was a statistically significant reduction in sebum excretion rate by sebumeter. Three studies evaluated niacinamide 4% and 5% in comparison to clindamycin 1% or 2% with similar success at study conclusion.<sup>37,38,39</sup> It was also found to be comparable to 1% green tea extract.<sup>40</sup>

As adjunctive therapy, Kaewsanit et al evaluated the use of niacinamide 5% in a split-face study of 21 participants with mild-to-moderate acne who were treated with 2.5% BP.<sup>41</sup> The entire



face was treated with BP, and niacinamide was applied once daily to 1 side of the face and cream base was applied to the other. The niacinamide-treated side showed superior reduction of non-inflammatory lesions at 12 weeks and a significant decrease in sebum at 6 weeks. Another split-face study evaluated the addition of a niacinamide/ceramide cream to 1 side of the face that had been treated with 5% BP/.1% Clindamycin. The niacinamide/ceramide-treated side showed superior reduction of inflammatory and non-inflammatory lesions and sebum production, as well as superior tolerability.<sup>42</sup>

#### Probiotics

Acne lesions create an environment that facilitates the excess growth of *C. acnes*. In vitro studies have shown the ability of some bacteria to directly inhibit *C. acnes* growth. *Lactobacillus spp*, *Enterococcus faecalis*, and *Nitrosomonas eutropha* have the most data behind them.

*Lactobacillus* was shown in 10 participants with mild-to-moderate acne to reduce *C. acnes* and Staphylococcal taxa after 8 weeks of twice-daily application.<sup>43</sup> In a vehicle-controlled study of 79 patients, there was a 34% decrease of inflammatory lesions (vs control 1.7%).<sup>43</sup> In a randomized controlled trial vs 2.5% BP in 104 participants, reduction of total lesion count was comparable with fewer side effects in the participants treated with *Lactobacillus*.<sup>44</sup> Results were also similar in comparison to salicylic acid 1% in 10 patients.<sup>45</sup>

A lotion containing *Enterococcus faecalis* was shown to be effective in reducing inflammatory lesions in 70 participants with mild-to-moderate disease after 8 weeks.<sup>46</sup>

*Nitrosomonas eutropha* is an ammonium oxidizing bacterium that converts ammonium into nitric oxide, known to be antimicrobial and anti-inflammatory. This probiotic was studied in a phase 2b study of 358 patients with mild-to-moderate acne for 4 weeks resulting in a 2-grade (5-point scale) improvement in investigator global assessment.<sup>47</sup>

#### Resveratrol

Resveratrol has antimicrobial and anti-inflammatory activities and some evidence suggesting it decreases sebum production. In a single-blind, vehicle controlled, split-face pilot study of 20 participants, resveratrol demonstrated a 54% (vs 6% vehicle) reduction in global improvement after 2 months.<sup>48</sup>

#### Retinol Derivatives

Retinoids such as retinol, retinal, and retinaldehyde abound in the OTC space and are used widely for anti-aging indication. Compared to prescription retinoids, OTC retinoids are far less effective in the treatment of acne. However, in their ability to act as keratolytics, they may help mild disease. Retinaldehyde

has been shown to differ from the other OTC retinoids in its significant in vitro antibacterial activity and may be the most effective.<sup>49</sup>

A combination cream of hydrocypinocolone retinoate and retinol glycospheres was evaluated for its ability to prevent disease recurrence post-isotretinoin use. The need for additional acne treatment was only 15.38% at 12 months, but there was no control group.<sup>50</sup>

#### Silymarin

Silymarin has keratolytic, anti-inflammatory, and antioxidant activities and may also reduce sebum production.

As monotherapy, it was evaluated in 56 patients demonstrating a 45% reduction in inflammatory lesions and 43% reduction in non-inflammatory lesions after 12 weeks of use.<sup>51</sup> In a split-face comparison study, 1.4% silymarin cream twice daily was compared to SA 30% peels twice monthly for 3 months.<sup>52</sup> Treatments were equally effective.

Two studies evaluated the addition of silymarin to existing acne therapy of various types. Forty patients noted improvement in existing inflammatory and non-inflammatory lesions, as well as a reduction in sebumeter values.<sup>51</sup> An open label study evaluated 22 patients with mild-to-moderate acne already on therapy, in whom the addition of 0.5% serum twice daily reduced lesion count and sebum secretion after 4 weeks.<sup>53</sup>

#### Sodium Hypochlorite

Sodium hypochlorite has anti-inflammatory activity and is bacteriocidal against *C. acnes*. A study of 40 participants utilized 0.005% 3 times daily for 1 month resulting in a significant resolution of papules without irritation.<sup>54</sup> It was shown to be as effective in the treatment of mild-to-moderate disease as BP 5%.<sup>55</sup>

#### Soy

Soy has anti-inflammatory, antioxidant, and antimicrobial activities as well as hydrating and antiandrogenic activity. However, as monotherapy there are few studies. Ghyczy et al reported on 7 small open-label trials totaling 77 patients in whom split-face use daily for 20 days to 2 months resulted in a reduction in inflammatory lesions.<sup>56</sup>

#### Sulfur

Sulfur has been used for decades in the treatment of acne and is thought to act by keratolytic activity. This topical agent has been extensively studied in combination with resorcinol, zinc, salicylic acid, and sodium sulfacetamide but there are no human studies of sulfur alone in the treatment of acne.

### Tea Tree Oil

TTO has anti-inflammatory and anti-bacterial activity.

Five percent TTO formulations have been studied in single- and double-blind studies in comparison to BP 5%. In a study of 119 and another of 60 participants with mild-to-moderate acne, the 2 arms showed similar improvement with more side effects in the BP 5% arm.<sup>57,58</sup>

As an adjunctive, a randomized comparison trial evaluated the use of 6% TTO in addition to adapalene 0.1%. A total of 100 patients were randomized to be treated with either 6% TTO or adapalene 0.1% plus 6% TTO. After 12 weeks, the patients treated with the combination had a better outcome in both inflammatory and non-inflammatory lesions.<sup>59</sup>

### Zinc

Zinc has anti-inflammatory activities, is bacteriostatic against *C. acnes* and has been shown to decrease sebum production. It has been used both orally and topically in the treatment of acne with mixed results. The following is limited to topical alone.

As monotherapy, it was evaluated in a placebo-controlled trial of 60 patients for 8 weeks with superior outcome compared to vehicle.<sup>60</sup> Compared to BP 5% in 28 patients for 8 weeks, results were comparable.<sup>61</sup> It was found inferior to 2% TTO in an 8-week comparison trial of 40 patients.<sup>62</sup>

As adjunctive therapy, addition of zinc to erythromycin 4% in 60 patients for 12 weeks and erythromycin 2% for 3 weeks resulted in minimal improvement compared to erythromycin alone.<sup>63,64</sup>

## CONCLUSION

There is a strong need for both clinician and patient education regarding skincare selection and ingredients suitable for acne care. Acneceuticals play an important supportive role in acne management. They can be used to increase the efficacy of prescription products, increase the tolerability of prescription products, and maintain or repair the skin barrier. Although beyond the scope of this paper, acne sequelae such as dyschromias may also respond to acneceuticals.

For the dermatologist to optimize outcomes, it is vital to dedicate time during initial and follow-up encounters to patient education regarding the importance of a sound skincare regimen. When combined with prescription therapy, gentle cleansers, quality moisturizers, and acne actives are capable of mitigating irritation, erythema, dryness, pruritus, and other symptoms common during the initiation phase of topical regimens. They may also have additive or synergistic effects in achieving treatment outcomes aside from maximizing adherence.

The symptoms of epidermal barrier dysfunction – erythema, pruritus, peeling, dryness – are common adverse effects of first-line acne treatment options. Without appropriate counseling and management, these symptoms may lead to regimen nonadherence, negative patient experience, and poor outcomes. Patient education regarding acneceuticals may give patients a greater sense of involvement and buy-in to their care. Given the expansive selection of commercial cleansers and moisturizers, dermatologists may be able to combat patient's choice-paralysis by providing specific recommendations as well as instruction on when and in what order to apply their skincare and prescription products.

Current limitations include the lack of robust, long-term clinical trial data especially within diverse populations. Despite the lack of rigor, data exist that support the recommendation of acneceuticals within dermatology practices. Perhaps more importantly, this provides patients with a roadmap for self-treatment and the ability to obtain efficacious and safe acne care regardless of insurance coverage.

While challenging to execute within the confines of a high-volume practice, improving patient knowledge of comprehensive acne treatments may be an effective way to maximize regimen efficacy and provide patients with the necessary tools for personalized and successful acne treatments.

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Dr Rieder is a consultant for Abbvie, L'Oreal, Merz, Procter and Gamble, UCB, and Unilever. Dr Schlesinger serves as a consultant, investigator, speaker, and/or advisor for Abbvie, Almirall, Allergan, ASLAN, Arcutis, Biofrontera, Beiersdorf, Benev, Bristol-Myers Squibb, Castle Biosciences, Galderma, Eli Lilly, ExoCoBio, Incyte, Janssen, LEO, L'Oreal, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, Takeda, UCB, and Verrica.

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## AUTHOR CORRESPONDENCE

### Hilary Baldwin MD

E-mail:..... HBaldwin@acnetrc.com