



Original Research

Safety and efficacy of a novel three-step anti-acne regimen formulated specifically for women



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ABSTRACT

Background: Due to ambient environmental- and lifestyle-associated stressors, the prevalence of acne in adult women has been increasing. Classical anti-acne treatments using benzoyl peroxide technology are associated with dehydration of the skin, which may accelerate aging and further reduce treatment compliance. The addition of bio-functional actives intended to replenish hydration and improve barrier function may hasten the onset of anti-acne benefits while restoring a healthy appearance and counteracting skin aging effects.

Objective: The objective of this study was to test the safety and efficacy of a new three-step topical anti-acne regimen designed specifically to improve the overall condition and appearance of the skin in women with acne.

Methods: Safety and efficacy were tested in an 8-week study of women ages 22 to 44 years with mild to moderate acne. Skin endpoints were monitored at baseline and weeks 1, 4, and 8 by clinical grading, measurement of sebum secretion using a sebumeter, standardized pictures, and self-validation questionnaires.

Results: A total of 31 women completed the study. Acne severity and lesion counts, including comedones and papules, improved gradually starting from week 1 and continued to improve throughout the study period, reaching statistical and clinical relevance at weeks 4 and 8. Moreover, significant improvements in skin roughness, radiance, overall healthy appearance, and oiliness (further confirmed with decreased sebum production) were observed. Compared with baseline responses, participants reported noticeable improvements in acne lesions and overall healthier-looking skin. Participants also noticed overall younger-looking skin at the end of the study period.

Conclusion: This three-step regimen provided efficacious anti-acne benefits to the skin that were also gentle, safe, and well tolerated.

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Introduction

Adult acne is a multifactorial inflammatory disease of the pilosebaceous unit caused by the confluence of several factors that affect the entire person, although the clinical manifestation is predominantly cutaneous (Bhate and Williams, 2013; Roosterman et al., 2006). Adult acne refers to new-onset acne or the persistence of adolescent acne past the mid-twenties (after 25 years of age) and presents mainly as inflammatory lesions and comedones on the neck, jawline, and perioral regions (Addor and Schalka, 2010; Holzmann and Shakery, 2014; Rocha and Bagatin, 2018). The

prevalence of acne in women (12%–41%) has been increasing in recent decades, attributable in part to noxious environmental stimuli, including ultraviolet light and pollution, as well as lifestyle stressors (Albuquerque et al., 2014; Do et al., 2009; Goulden et al., 1999; Knaggs et al., 2004; Krutmann et al., 2017; Rocha and Bagatin, 2018; Skroza et al., 2018).

Regardless of the timing of acne onset, acne lesions are associated with postinflammatory erythema and/or postinflammatory hyperpigmentation (PIH), followed by scarring in the majority of cases (Capitanio et al., 2010; Poli et al., 2001; Zaenglein et al., 2016). These visible aspects are intimately associated with the invisible scars of acne: poor self-image, depression, and anxiety (Do et al., 2009; Gallitano and Berson, 2018; Hassan et al., 2009).

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Benzoyl peroxide (BPO) remains the gold standard of topical acne treatments based on antimicrobial and antiinflammatory activities that result in the aerobic death of *Cutibacterium acnes* (*C. acnes*) without causing bacterial resistance (Ozolins et al., 2005; Webster et al., 2009; Zaenglein et al., 2016). However, a potential limitation of BPO is concentration-dependent dryness and irritation that aggravates visible signs of aging, such as fine lines, wrinkles, and redness, further affecting patient compliance and anti-acne efficacy (Feldman and Chen, 2011). The inclusion of bio-functional actives intended to soothe the skin, improve hydration, and restore barrier function can help alleviate the drying and anti-aging effects attributable to BPO (Ozolins et al., 2005).

In an attempt to overcome the disadvantages of traditional BPO-based regimens, we developed a novel anti-acne regimen that features potent blemish-reducing technologies fortified with carefully selected bio-functional ingredients tailored to aged skin distributed across three products: 1) a gentle exfoliating cleanser containing colloidal sulfur, salicylic acid, and vitamin E; 2) a pore-clarifying toner with glycolic acid, gluconolactone, and panthenol; and 3) an innovative dual-chamber BPO leave-on lotion treatment with niacinamide, allantoin, and a blend of ceramides. All constituents of the regimen were designed specifically to reduce skin sensitivity and improve barrier function with concomitant hydration and firmness for anti-aging benefits (Sacchidanand et al., 2017; Zaenglein et al., 2016).

The aim of this study was to assess the efficacy, safety, and tolerability of this new anti-acne regimen designed specifically for women with acne-associated blemishes.

Methods

Study design

All participants gave written informed consent before enrollment. The study was approved by an independent institutional review board and adhered to Good Clinical Practice and International Conference on Harmonization standards. The efficacy of this three-step adult acne regimen was evaluated in an 8-week, open-label clinical study conducted at a single site over four visits: baseline, week 1, week 4, and week 8. Eligible participants were between the ages of 22 and 45 years, had any Fitzpatrick Skin Type I to VI, and could be from any ethnic group. Additionally, participants were required to have mild to moderate acne as defined by the six-point Investigator's Global Assessment (IGA) scale for acne severity. This inclusion criterion required an IGA score of 2 to 3, where 0 = clear and 5 = very severe. Furthermore, participants had to have a minimum of five inflammatory lesions on the face (jawline to hairline) and mild to moderate crow's feet and wrinkles, as determined by a score of 1 to 6 on a 10-point scale where 0 = none and 9 = severe.

The exclusion criteria were having used topical over-the-counter products that contain BPO, sulfur, or salicylic acid in the past 2 weeks and/or any prescription systemic acne treatment within the past 2 months.

Participants received the three study products at baseline and week 4, as needed, and were instructed to use the products twice daily (morning and evening) in a stepwise manner, washing with the exfoliating cleanser, followed by applying the pore clarifying toner, and lastly administering the innovative dual-chamber BPO leave-on lotion treatment. The BPO lotion used a dual-chamber dispenser designed to keep the BPO-containing fluid separate until the moment of use to retain its activity and deliver a precise dose of 2.5% BPO. Lastly, participants applied a facial sun protection factor (SPF) product as they normally would. A shine-free SPF lotion was provided; however, use of the sponsor-supplied SPF was optional, and participants were permitted to use a product of their choice.

Biophysical instrumentation

Sebum on the face was quantified with a Sebumeter 815 (Courage + Khazaka Electronic GmbH, Cologne, Germany), which uses grease spot photometry to measure oiliness on the skin. Two readings were taken at all four study visits: one on the forehead and one on the left cheek. All postbaseline measurements were compared with the baseline values.

Clinical grading

Fourteen anti-aging parameters were assessed at all four study visits by clinical grading using a 10-point scale (0 = none, 1–3 = mild, 4–6 = moderate, 7–9 = severe) for overall healthy appearance of skin condition, skin roughness (tactile), pore appearance, skin clarity, radiance, oiliness, plumpness/fullness, even skin tone, crow's feet fine lines, crow's feet wrinkles, under-eye fine lines and wrinkles, skin firmness (tactile), and suborbital elasticity/resiliency (pinch recoil). All postbaseline scores were compared with the baseline. Improvements based on clinical grading were indicated by a decreased score for each of the 14 attributes. Acne severity was clinically graded at all four study visits using a six-point IGA scale (0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = severe, 5 = very severe). The number of inflammatory and noninflammatory lesions on the entire surface of the face were also counted at all four study visits. Additionally, all participants completed a self-assessment questionnaire while examining their skin in a mirror at each of the four study visits. Study questionnaires also evaluated participant satisfaction with skin condition and study products.

Standardized pictures were obtained at each of the four study visits with the Visia CR facial imaging system (Gen 2.2, Canfield Scientific, Inc.; Parsippany, NJ). Three angled images were taken, each using five high-resolution lighting modes (regular flash with strobe, regular flash with flat lighting, parallel polarized, cross polarized, and ultraviolet fluorescence) for visual documentation.

Safety and tolerability

To determine safety of the products tested, erythema, edema, dryness, and scaling/peeling skin were assessed at each of the four study visits using a four-point scale (0 = none, 1 = mild, 2 = moderate, and 3 = severe).

Statistical analysis

For continuous variables, descriptive statistics including number of participants and mean and standard deviation values were calculated. For categorical variables, the frequency and percentage of each category were calculated. For the clinical grading and non-image instrumentation values, paired *t* tests were used to compare change from baseline to zero (no change). Paired *t* tests were also used to evaluate the instrumentation measurements, which were analyzed to identify participants who improved, remained the same, or worsened compared with baseline. Binomial tests were used to evaluate participant self-assessment questionnaires. The level of statistical significance was set at $p < .05$ for all analyses.

Results

Demography

A total of 32 women with mild to moderate adult acne were enrolled, and 31 completed the study. Data collected from one participant were not analyzed due to noncompliance (per-protocol

population: $n = 30$). The majority of participants were Caucasian (90%; $n = 28$), and 10% ($n = 3$) were African American. The average age of the participants was 29.5 years.

Efficacy

The overall improvement in acne severity was significant ($p < .001$) as demonstrated by a mean decline in IGA scores by $\Delta > .5$ points (perceivable clinical relevance). In addition, this improvement was observed from week 1 and increased by weeks 4 and 8 compared with the baseline measures (Fig. 1A). Lesion counts represented by total papules (Fig. 1B) and closed comedones (Fig. 1C) also dropped gradually starting from week 1 of treatment, with further improvements observed at weeks 4 and 8, reaching statistical significance ($p \leq .001$) and clinical ($\Delta > 4$ points) relevance. The overall appearance of the skin was improved significantly at week 1 and continued to improve throughout the entire study period (Fig. 1D). Reductions in PIH and pore appearance were also observed; however, these measures did not reach the level of statistical significance (Fig. 1E and F, respectively).

Skin roughness (tactile) was statistically ($p < .001$) and perceptibly ($\Delta = .83$) improved as soon as week 1 (Fig. 1G). A trend in skin radiance/luminosity (visual) improvement was observed from week 1 with further clinical relevance gained at weeks 4 ($\Delta = .68$; $p < .001$) and 8 ($\Delta = .9$; Fig. 1H). Even skin tone, as assessed by the appearance of redness, blotchiness, and hyperpigmented discoloration was first statistically ($p < .001$) and perceptibly ($\Delta > .5$) improved at week 4 and continued through the end of the study period (Fig. 1I). Improvement in the appearance of fine lines was observed as early as week 1 and continued to improve, reaching statistical ($p \leq .005$) significance at the end of the study (Fig. 1J).

The three-step regimen lead to a significant improvement in skin oiliness in 76% of participants starting from week 1, with further reductions observed through the end of the study period (in 97% of participants compared with baseline). These perceivable

improvements were measured with clinical grading ($\Delta = .9$ at week 1; $\Delta = 1.55$ at week 4; and $\Delta = 1.9$ at week 8; Fig. 1K) and with a Sebumeter on the forehead, confirming a significant reduction in sebum excretion rate at each visit compared with the baseline measures (Fig. 1L).

The clinical grading and self-assessed improvements in overall skin qualities were visualized by the standardized pictures taken at baseline and week 8 (Fig. 2A). Participant self-assessments demonstrated significant improvements in most attributes related to acne and healthy- and younger-looking skin at week 8. Depending on the skin attribute, improvements ranged from being perceived in 42% for younger-looking skin up to 77% for skin being less oily (Fig. 2B).

The majority of aging-related skin characteristics self-assessed by the study participants improved gradually and significantly in a large subset of the participants. These included skin tone evenness at week 1 (51.7%; $p = .034$) and week 8 (67.7%; $p < .001$), radiance at week 1 (58.6%; $p = .003$) and week 8 (64.5%; $p < .001$), and smoothness at week 1 (62.1%; $p = .002$), week 4 (67.7%; $p = .005$), and week 8 (51.6%; $p = .005$).

Safety

All three study products were well tolerated and safe in general. There were no reports of erythema or edema and only very slight increases (no statistically significant worsening) in dryness ($\Delta = .05$) and scaling/peeling ($\Delta = .02$), both recorded at week 4. These symptoms self-resolved and did not require any additional treatment or change of study product usage. All safety parameters had returned to baseline scores (0 = none) by week 8.

Six adverse events (conjunctivitis, stomach virus, common cold, corneal abrasion, alopecia, dermatitis) occurred during the study, none of which were serious or considered related to the study products, and none required a change in study product usage. Four adverse events were resolved by the end of the study, and two

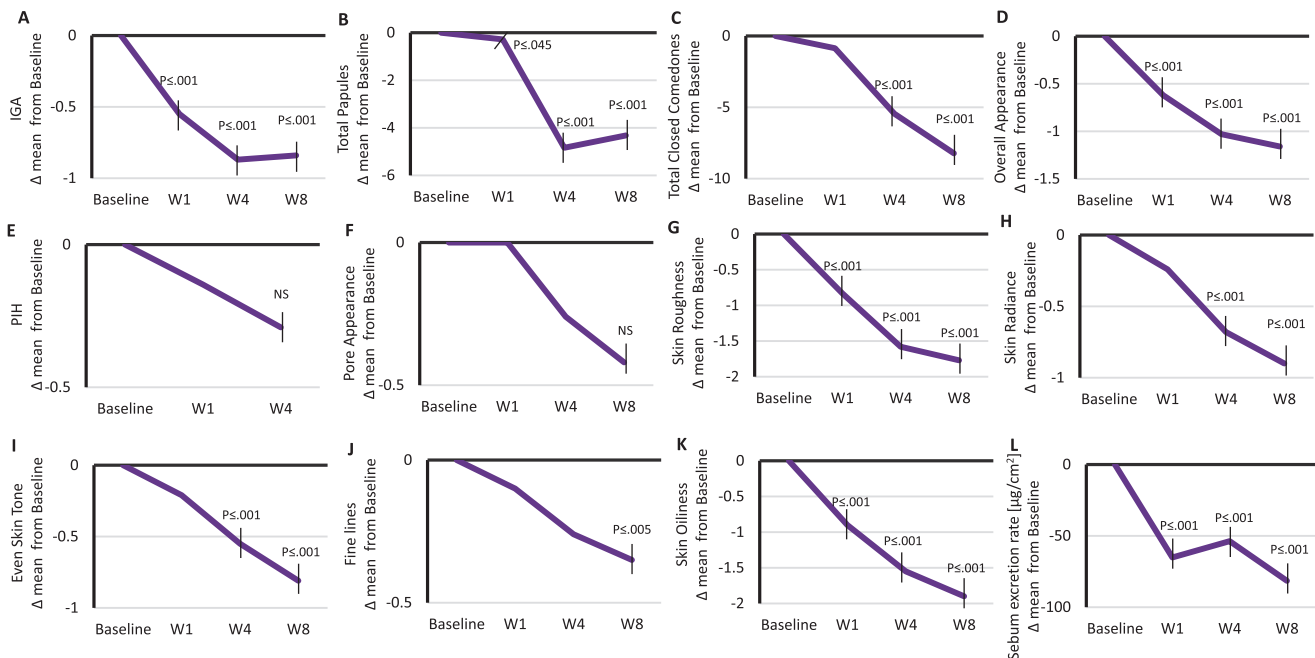


Fig. 1. Gradual and consistent improvements in skin attributes related to acne and aging signs assessed by clinical grading over 8 weeks of topical treatment with three-step regimen. (A) Investigator's Global Acne Assessment; (B) total papules; (C) total close comedones; (D) overall skin appearance; (E) postinflammatory hyperpigmentation; (F) pore appearance; (G) skin roughness (tactile); (H) skin radiance; (I) even skin tone; (J) fine lines; (K) skin oiliness; and (L) sebum production (Sebumeter). $n = 30$.

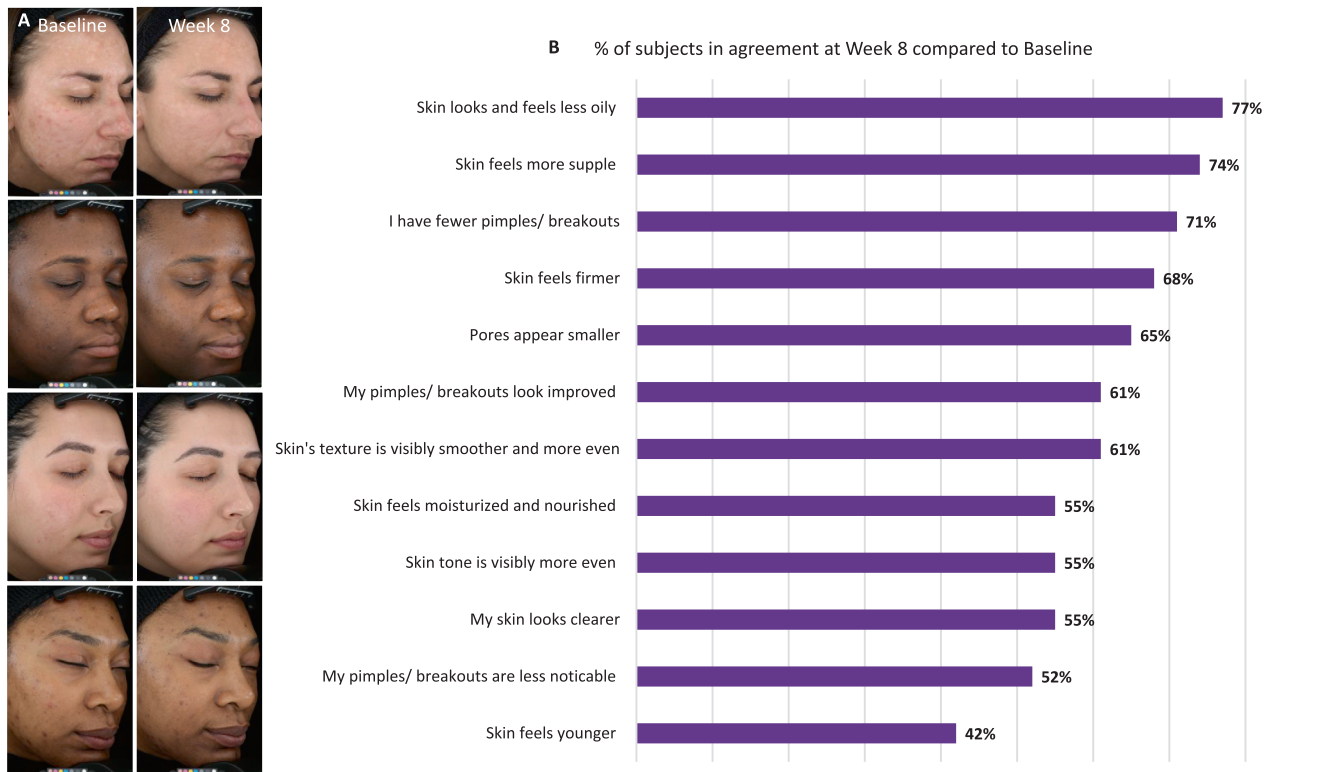


Fig. 2. (A) Visual improvements (regular flash with flat lighting mode) of overall skin quality represented by the decreased acne lesions and improved hydration. Self-assessed improvements in skin attributes expressed as percentage of participants in agreement at week 8 compared with baseline.

events (alopecia and dermatitis) were considered ongoing at the end of the study.

Discussion

This 8-week study demonstrated that the novel three-step regimen designed specifically for women with mild to moderate acne led to a significant improvement in the signs and sequelae of acne, as well as in the overall appearance and condition of the skin. The high compliance (only one dropout) indicates a great safety profile, tolerability, and fast onset of benefits, much higher compared with other studies using similar technology (Webster et al., 2009). The most dramatic improvements involved the reduction of acne lesions and their severity and skin oiliness, the latter being validated by both clinical and biophysical measurements. Additionally, significant improvements in selected lesion counts and trending reductions in redness and PIH demonstrated the effectiveness of the regimen in treating acne.

Furthermore, a majority of the study participants experienced moderate to significant benefits in overall healthy appearance, skin radiance, and clarity, attributes commonly related to healthy- and younger-looking skin. These perceived benefits were likely due to a combination of fewer acne lesions and more homogenous skin tone and texture due to stronger barrier function capable of retaining hydration. Although wrinkle reduction and elasticity enhancement were observed, these measurements did not rise to the level of statistical or clinical relevance.

This regimen uses BPO, an effective agent with a fast onset of action and broad range of benefits against acne (Ozolins et al., 2005; Russell, 2000; Webster et al., 2009). BPO has both bactericidal and comedolytic activities (Rodan et al., 2017), which contribute to a decrease in inflammatory (papules, pustules) and

noninflammatory (comedones) lesions (Russell, 2000). Additionally, the use of BPO does not induce bacterial resistance, unlike other anti-bacterial therapies where resistance may reach up to 90% and contribute to decreased efficacy and compliance (Okamoto et al., 2016; Ozolins et al., 2005; Snyder et al., 2014). However, BPO is known to be poorly solubilized in cosmetic formulations and tends to crystallize, leading to the formation of conglomerates with higher BPO percentages that can result in local irritation (Okamoto et al., 2016; Weber et al., 2009).

The study product features an innovative dual-chamber dispenser that delivers BPO in a precise 2.5% concentration, ensuring anti-acne effectiveness (Weber et al., 2009) while being gentle and nonirritating (Snyder et al., 2014). The highly precise BPO dose, carefully formulated to deliver mild yet effective treatment, contributed to both high levels of efficacy and compliance compared with other regimens using similar technologies, as assessed by the study participants (Kawashima et al., 2017). The clinical grading, sebum excretion rate measured by Sebumeter, and participant self-assessment results confirmed a significant reduction in sebum production at each visit. The improvement in skin oiliness may be attributable not only to BPO, but also to sebum-controlling alpha- and beta-hydroxy acids featured in the exfoliating wash (Dreno et al., 2013; Zaenglein et al., 2016).

Nevertheless, BPO, acting as an oxidizer, tends to have a drying effect with concomitant epidermal barrier disruption. Collectively, these effects may accelerate skin aging, expressed as fine lines, wrinkles, and loss of elasticity (Chularojanamontri et al., 2014; Lodén, 2003; 2009; McCook, 2016; Papakonstantinou et al., 2012). The addition of hydrating (sodium hyaluronate, zinc PCA, gluconolactone) and barrier-improving (niacinamide) bio-functional actives may counteract the dehydration associated with the use of BPO (Majewski et al., 2017; Papakonstantinou et al.,

2012; Raab et al., 2017; Rawlings et al., 1995). Moreover, the high content of vitamin E, panthenol, and phenolic extract of *C. sinensis*, featuring epigallocatechin-3-gallate, contributed to a reduction in inflammation and elastin degradation, improving skin firmness and elasticity (Bucay and Day, 2013; Lodén, 2009). With age, the ceramide composition of the stratum corneum diminishes, jeopardizing barrier function integrity (Tessema et al., 2017; Verdier-Sevrain and Bonte, 2007). The regimen formulas tested in this study replenish the skin with a ceramide blend, cholesterol, and fatty acids to restore barrier function and reduce water loss (Lebwohl and Herrmann, 2005; Verdier-Sevrain and Bonte, 2007). Postinflammatory erythema, PIH, and irritation are some of the most troubling consequences of acne and can reduce quality of life in patients.

A limitation of the study was its open-label design, which did not allow for a comparison with other regimens. Nevertheless, statistically significant improvements in several attributes were corroborated by clinical grading, instrumental measurements, and participant assessments that collectively confirmed the findings.

Conclusion

This study demonstrated the ability of a new anti-acne regimen tailored for adult female skin that has withstood the drying effects of intrinsic/extrinsic aging to improve both the signs of acne and the condition and appearance of the skin. Its efficacy and tolerability likely stem from the use of gentle formulations fortified with actives that replenish lost endogenous compounds, as well as plant extracts possessing a wide spectrum of activities.

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Conflicts of interest

All authors are employees of Rodan & Fields in San Francisco, California.

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Study Approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

References

Addor FA, Schalka S. Acne in adult women: Epidemiological, diagnostic and therapeutic aspects. *An Bras Dermatol* 2010;85(6):789–95.

Albuquerque RG, Rocha MA, Bagatin E, Tufik S, Andersen ML. Could adult female acne be associated with modern life? *Arch Dermatol Res* 2014;306(8):683–8.

Bhate K, Williams HC. Epidemiology of acne vulgaris. *Br J Dermatol* 2013;168(3):474–85.

Bucay VW, Day D. Adjunctive skin care of the brow and periorbital region. *Clin Plast Surg* 2013;40(1):225–36.

Capitanio B, Sinagra JL, Bordignon V, Cordiali Fei P, Picardo M, Zouboulis CC. Underestimated clinical features of postadolescent acne. *J Am Acad Dermatol* 2010;63(5):782–8.

Chularojanamontri L, Tuchinda P, Kulthanan K, Pongparit K. Moisturizers for acne: What are their constituents? *J Clin Aesthet Dermatol* 2014;7(5):36–44.

Do JE, Cho SM, In SI, Lim KY, Lee S, Lee ES. Psychosocial aspects of acne vulgaris: A community-based study with Korean adolescents. *Ann Dermatol* 2009;21(2):125–9.

Dreno B, Layton A, Zouboulis CC, López-Esteban JL, Zalewska-Janowska A, Bagatin E, et al. Adult female acne: A new paradigm. *J Eur Acad Dermatol Venereol* 2013;27(9):1063–70.

Feldman SR, Chen DM. How patients experience and manage dryness and irritation from acne treatment. *J Drugs Dermatol* 2011;10(6):605–8.

Gallitano SM, Berson DS. How acne bumps cause the blues: The influence of acne vulgaris on self-esteem. *Int J Womens Dermatol* 2018;4(1):12–7.

Goulden V, Stables GI, Cunliffe WJ. Prevalence of facial acne in adults. *J Am Acad Dermatol* 1999;41(4):577–80.

Hassan J, Grogan S, Clark-Carter D, Richards H, Yates VM. The individual health burden of acne: Appearance-related distress in male and female adolescents and adults with back, chest and facial acne. *J Health Psychol* 2009;14(8):1105–18.

Holzmann R, Shakery K. Postadolescent acne in females. *Skin Pharmacol Physiol* 2014;27(Suppl 1):3–8.

Kawashima M, Nagare T, Katsuramaki T. Open-label, randomized, multicenter, phase III study to evaluate the safety and efficacy of benzoyl peroxide gel in long-term use in patients with acne vulgaris: A secondary publication. *J Dermatol* 2017;44(6):635–43.

Knaggs HE, Wood EJ, Rizer RL, Mills OH. Post-adolescent acne. *Int J Cosmet Sci* 2004;26(3):129–38.

Krutmann J, Moyal D, Liu W, Kandahari S, Lee GS, Nopadon N, et al. Pollution and acne: Is there a link? *Clin Cosmet Investig Dermatol* 2017;10:199–204.

Lebwohl M, Herrmann LG. Impaired skin barrier function in dermatologic disease and repair with moisturization. *Cutis* 2005;76(6 Suppl):7–12.

Lodén M. Role of topical emollients and moisturizers in the treatment of dry skin barrier disorders. *Am J Clin Dermatol* 2003;4(11):771–88.

Lodén M. Hydrating substances. In: Barel AO, Paye M, Maibach HI, editors. *Handbook of cosmetic science and technology*. 3rd ed. New York, NY: Informa Healthcare; 2009. p. 107–19.

Majewski G, Rodan K, Fields K, Ong D, Falla T. Hydrating the skin with a novel interpenetrating polymer network. *J Clin Exper Cosme Derma* 2017;1(1):1–8.

McCook JP. Topical products for the aging face. *Clin Plast Surg* 2016;43(3):597–604.

Okamoto K, Ikeda F, Kanayama S, Nakajima A, Matsumoto T, Ishii R, et al. In vitro antimicrobial activity of benzoyl peroxide against *Propionibacterium* acnes assessed by a novel susceptibility testing method. *J Infect Chemother* 2016;22(6):426–9.

Ozolins M, Eady EA, Avery A, Cunliffe WJ, O'Neill C, Simpson NB, et al. Randomised controlled multiple treatment comparison to provide a cost-effectiveness rationale for the selection of antimicrobial therapy in acne. *Health Technol Assess* 2005;9(1):iii–212.

Papakonstantinou E, Roth M, Karakiulakis G. Hyaluronic acid: A key molecule in skin aging. *Dermatoendocrinol* 2012;4(3):253–8.

Poli F, Dreno B, Verschoore M. An epidemiological study of acne in female adults: Results of a survey conducted in France. *J Eur Acad Dermatol Venereol* 2001;15(6):541–5.

Raab S, Yatskayer M, Lynch S, Manco M, Oresajo C. Clinical evaluation of a multimodal facial serum that addresses hyaluronic acid levels in skin. *J Drugs Dermatol* 2017;16(9):884–90.

Rawlings A, Harding C, Watkinson A, Banks J, Ackerman C, Sabin R. The effect of glycerol and humidity on desmosome degradation in stratum corneum. *Arch Dermatol Res* 1995;287(5):457–64.

Rocha MA, Bagatin E. Adult-onset acne: Prevalence, impact, and management challenges. *Clin Cosmet Invest Dermatol* 2018;11:59–69.

Rodan K, Fields K, Falla TJ. Efficacy of a twice-daily, 3-step, over-the-counter skincare regimen for the treatment of acne vulgaris. *Clin Cosmet Invest Dermatol* 2017;10:3–9.

Roosterman D, Goerge T, Schneider SW, Bunnett NW, Steinhoff M. Neuronal control of skin function: The skin as a neuroimmunoendocrine organ. *Physiol Rev* 2006;86(4):1309–79.

Russell JJ. Topical therapy for acne. *Am Fam Physician* 2000;61(2):357–66.

Sacchidanand SA, Lahiri K, Godse K, Patwardhan NG, Ganjoo A, Kharkar R, et al. Synchronizing pharmacotherapy in acne with review of clinical care. *Indian J Dermatol* 2017;62(4):341–57.

Skroza N, Tolino E, Mambrin A, Zuber S, Balduzzi V, Marchesiello A, et al. Adult acne versus adolescent acne: A retrospective study of 1167 Patients. *J Clin Aesthet Dermatol* 2018;11(1):21–5.

Snyder S, Crandell I, Davis SA, Feldman SR. Medical adherence to acne therapy: A systematic review. *Am J Clin Dermatol* 2014;15(2):87–94.

Tessema EN, Gebre-Mariam T, Neubert RHH, Wohlrab J. Potential applications of phyto-derived ceramides in improving epidermal barrier function. *Skin Pharmacol Physiol* 2017;30(3):115–38.

Verdier-Sevrain S, Bonte F. Skin hydration: A review on its molecular mechanisms. *J Cosmet Dermatol* 2007;6(2):75–82.

Weber S, Lodge J, Saliou C, Packer L. *Handbook of cosmetic science and technology*. New York, NY: Informa Healthcare; 2009.

Webster G, Rich P, Gold MH, Mraz S, Calvarese B, Chen D. Efficacy and tolerability of a fixed combination of clindamycin phosphate (1.2%) and low concentration benzoyl peroxide (2.5%) aqueous gel in moderate or severe acne subpopulations. *J Drugs Dermatol* 2009;8(8):736–43.

Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, Baldwin HE, Berson DS, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol* 2016;74(5). 945–73.e933.