

## Advancements in Topical Treatments for Acne Vulgaris: A Comprehensive Review of Efficacy, Safety, and Management

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### Abstract

Acne vulgaris remains a challenging dermatological condition, necessitating a nuanced understanding of the evolving landscape of topical treatments. This literature review examines the multifaceted aspects of topical therapies for acne vulgaris, meticulously examining their efficacy, safety profile, and patient satisfaction. Leveraging recent clinical trials, randomized controlled studies, and meta-analyses, this review scrutinizes the mechanisms of action and adverse effects associated with commonly prescribed topical agents, including retinoids, benzoyl peroxide, salicylic acid, and topical antibiotics. Furthermore, emerging trends in combination topical therapies are explored, highlighting the potential for personalized treatment approaches tailored to individual patient needs. By synthesizing current evidence and identifying areas for improvement, this review aims to equip dermatologists with a comprehensive understanding of topical acne treatments, facilitating informed decision-making and enhancing patient-centered care strategies. Our analysis serves as a crucial tool for dermatologists, focusing on a specific understanding of the current landscape of topical treatments for acne vulgaris and empowers clinicians to make informed decisions, thereby enhancing the quality of care and outcomes for patients.

### Introduction

Acne vulgaris is a highly prevalent and multifactorial dermatological condition that presents significant challenges in clinical practice. Affecting virtually all individuals at least once in their lifetime, it can profoundly impact self-esteem, social interactions, and employment opportunities [1]. Acne vulgaris impacts an estimated 9.4% of the global population, making it the eighth most prevalent disease worldwide [2]. The condition predominantly affects adolescents, with a prevalence rate of nearly 85%, but it can persist or even emerge in adulthood, particularly in women [3].

The pathogenesis of acne involves complex interactions, including hormonal changes, follicular hyperkeratinization, increased sebum production, and colonization by *Cutibacterium acnes* (formerly *Propionibacterium acnes*). Genetic predisposition also plays a significant role, with family history being a strong predictor of severity [4]. This condition primarily affects sebaceous follicles, leading to the concentration of acne lesions on the face, chest, and back. The manifestations of acne vulgaris range from comedones and papules to pustules, nodules, and cysts, which can cause significant physical discomfort and psychological distress.

Effective treatment of acne vulgaris is often complicated by the need for long-term management, the potential for antibiotic resistance, and the variability in individual patient responses to therapy. Post-inflammatory hyperpigmentation and scarring can persist long after active lesions have resolved, underscoring the importance of early and effective intervention. Initiating

appropriate therapy in a timely manner is crucial to achieving satisfactory results and reducing the long-term physical and psychosocial effects experienced by patients. While topical therapy is essential for managing non-inflammatory comedones and mild-to-moderate inflammatory acne, the efficacy of topical treatments hinges on a nuanced understanding of their formulations, mechanisms of action, and potential adverse side effects. Topical therapy formulations include retinoids, benzoyl peroxide, salicylic acid, and topical antibiotics.

Due to the intricacy of acne vulgaris management, combination therapy is often employed to enhance efficacy and minimize side effects. Topical treatments are typically applied twice daily, but this schedule can be adjusted according to the patient's experience with the treatment to ensure maximum benefits with minimal irritation. Additionally, the choice of vehicle for a patient's treatment can vary depending on skin type and preference for tactile properties, with most topical treatments available in the form of creams, gels, solutions, and lotions. In this literature review, we delve into the current landscape of topical treatments for acne vulgaris, exploring their diverse formulations and clinical applications. By examining recent research and clinical insights, we aim to provide a comprehensive overview that enhances dermatologists' ability to navigate treatment choices effectively, ultimately improving care and outcomes for patients suffering from acne vulgaris.

## Discussion

### *Personalized Treatment Approaches*

Opportunities for individualized patient care within acne vulgaris treatment are substantial. It is essential to discuss the factors influencing treatment selection and customization by dermatologists. The following key factors will be examined:

1. Acne severity
2. Skin type
3. Medication tolerability
4. Comorbidities

By considering these four factors, dermatologists can tailor their treatment strategies to optimize efficacy and minimize adverse effects. This personalized approach not only improves clinical outcomes but also enhances patient satisfaction and adherence, ultimately leading to better long-term management of acne vulgaris.

#### **1. Acne Severity**

The severity of acne vulgaris determines the need for topical treatments alone or combination therapy. Consistent assessment scales, such as the algorithm published by Reynolds et al. in the *Journal of the American Academy of Dermatology*, facilitate consistent treatment options for adults, adolescents, and preadolescents aged nine and older [5]. Mild acne, characterized by comedones and a few inflammatory lesions, typically responds well to topical treatments such as benzoyl peroxide, salicylic acid, and topical retinoids. Moderate acne, which includes more inflammatory lesions, may require a combination of topical treatments or the addition of oral antibiotics. Severe acne, characterized by numerous inflammatory lesions, nodules, or cysts, often necessitates a combination of oral antibiotics, hormonal therapies, and sometimes isotretinoin [5]. Accurate assessment of acne severity is essential for devising an effective treatment plan that addresses the specific needs of the patient.

#### **2. Skin Type**

Skin type plays a critical role in the selection of acne treatments. Dermatologists must consider whether a patient has oily, dry, combination, or sensitive skin, as this will influence the choice of treatment to minimize adverse effects and maximize efficacy. Patients with oily skin may benefit from treatments that reduce sebum production, such as topical retinoids and benzoyl peroxide, which help prevent clogged pores by controlling excess oil production [6]. Alternatively, patients with dry or sensitive skin may require gentler formulations to avoid irritation, such as topical treatments with added moisturizers or anti-inflammatory agents [6]. Combination skin types may require a tailored approach, where different treatments are applied to different areas of the face [7]. Understanding the patient's skin type allows dermatologists to select the most appropriate formulations and concentrations, thereby improving treatment outcomes and minimizing side effects.

#### **3. Medication Tolerability**

Medication tolerability is another crucial factor influencing the choice of acne treatments. Patients' previous experiences with acne medications, including any adverse reactions or allergies, must be taken into account to avoid similar issues [8]. Dermatologists should start with lower concentrations of potentially irritating treatments, such as retinoids or benzoyl peroxide, and gradually increase the dosage as tolerated [9]. When a patient presents with a history of poor tolerance to

certain medications, alternative treatments such as azelaic acid or sulfur-based products should be considered. The frequency of application and various lifestyle factors can pose challenges that might affect adherence, so the patient's ability to comply with the treatment regimen should be considered to ensure optimal outcomes. For example, those patients with busy schedules or those who engage in numerous outdoor activities may prefer treatments that are less time-consuming and do not increase photosensitivity [9]. Additionally, selecting formulations that enhance tolerability can further support adherence and effectiveness. Draelos et al. highlighted the significance of the medication vehicle in tolerability, demonstrating that a formulation containing glycerin and dimethicone added to clindamycin-benzoyl peroxide proved to be optimal compared to traditional formulations [10]. Medication tolerability aids in customizing the treatment plan to ensure it is both effective and manageable for the patient, enhancing adherence and overall treatment success.

#### **4. Comorbidities**

Comorbidities can significantly impact the selection and customization of acne treatments. Conditions such as hormonal imbalances, polycystic ovary syndrome (PCOS), and various endocrine disorders may require a comprehensive treatment approach that includes hormonal therapies in addition to traditional acne treatments. Understanding how these conditions interact is crucial. For instance, patients with PCOS may benefit from oral contraceptives or anti-androgen medications to help regulate the hormonal fluctuations contributing to acne [11]. Additionally, patients with a history of keloid scarring need tailored interventions to prevent exacerbation [12,13]. Researchers have emphasized the importance of customizing treatment plans to avoid worsening such scars, as traditional acne treatments might not be suitable [12,13]. This demonstrates the necessity of considering individual patient histories in treatment planning. Furthermore, coordinating care with other healthcare providers to manage underlying conditions that contribute to acne can ensure comprehensive care and optimize treatment outcomes for related conditions [13]. The patient's lifestyle factors such as diet, sleeping patterns, and stress levels should also be considered, as they can influence acne severity and treatment response. Comorbidities are an essential part of the holistic understanding of the patient's overall health, enabling dermatologists to devise an effective and safe acne treatment plan.

### *Topical Therapies for Acne Vulgaris*

The prevalent dermatological condition, acne vulgaris, is treated with a diverse array of topical therapies. These range from retinoids, benzoyl peroxide, salicylic acid, and topical antibiotics, each with their own distinct mechanisms of action and formulations. By targeting various specific pathways—such as follicular hyperkeratinization, inflammation, keratolysis, and bacterial reduction—these topical treatments can reduce the formation of new lesions and minimize the risk of scarring.

#### *Retinoids*

Retinoids are a class of compounds derived from vitamin A and are widely used in topical formulations for various dermatological conditions, including acne, photoaging, and hyperpigmentation. Retinoids promote acne lesion resolution through several mechanisms that target different aspects of acne pathophysiology. These compounds exert their effects by binding to retinoic acid receptors (RARs) in the cell nucleus,

leading to the regulation of gene transcription [14]. This action reduces keratinocyte cohesiveness and decreases follicular keratinization, thereby preventing follicular occlusion and the formation of comedones, fundamental steps in acne development [15]. Trifarotene, a novel topical retinoid selective for the RAR- $\gamma$  receptor, has demonstrated significant efficacy in treating both facial and truncal acne, highlighting its ability to modulate 67 genes involved in cellular migration, adaptive immunity, inflammation, and matrix reorganization, which are not affected in spontaneously resolving acne lesions [14]. This underscores the advanced therapeutic potential of Trifarotene, offering targeted action on key genetic pathways and providing a robust treatment for acne that does not naturally resolve on its own. Retinoids have additionally been shown to modulate inflammatory responses by inhibiting leukocyte migration, toll-like receptors, and Activator Protein (AP)-1, thereby reducing inflammation associated with acne lesions [15]. This highlights their role in not only promoting skin cell turnover but also in addressing the underlying inflammatory processes, making them a comprehensive treatment option for acne.

Among the most commonly used retinoids, tretinoin (all-trans retinoic acid) is considered the most effective for anti-aging treatments, with proven efficacy in reducing facial wrinkles and hyperpigmentation [17]. This reduction in hyperpigmentation is particularly important for individuals seeking to improve skin tone uniformity and address discoloration issues. Adapalene, another popular retinoid, is primarily used for acne treatment due to its ability to decrease follicular keratinization and reduce comedone formation [15]. Tazarotene, a receptor-selective retinoid prodrug, is effective in managing plaque psoriasis, acne vulgaris, and photoaging, and is noted for its minimal side effects and convenient once-daily application [18]. Tazarotene has been shown to be less irritating compared to other retinoids like adapalene and the fourth-generation retinoid Trifarotene, making it a favorable option for patients with sensitive skin. The clinical evidence supporting the use of these retinoids varies, with the most robust data on tretinoin, while other retinoids like tazarotene and adapalene also show promising results in clinical evaluations for antiaging effects [17].

Despite their benefits, retinoids pose challenges such as instability, low penetration, and potential skin irritation, prompting the development of novel delivery systems based on nanotechnology to enhance their efficacy and user compliance [17]. Use of this class of compounds is often accompanied by several additional adverse effects, including dryness (xerosis), erythema, peeling, and photosensitivity, which can significantly impact patient adherence and treatment efficacy. These side effects are dose-related and can manifest as irritant dermatitis, characterized by skin irritation and discomfort [19]. Photosensitivity is particularly concerning as retinoids increase the rate of skin cell turnover, exposing new skin cells to solar damage, thereby heightening the risk of sunburn and hyperpigmentation [20]. To mitigate these adverse effects, several strategies can be employed. The use of moisturizers in conjunction with retinoid therapy is highly recommended as they help maintain skin hydration and can enhance the therapeutic effects of retinoids. Additionally, incorporating sunscreens with broad-spectrum protection (SPF 50 PA++++) can protect the sensitive skin from UV damage and reduce erythema and dryness. Products like the “EI PRO Retinol Sunscreen,” which include soothing agents such as carrot seed oil and sodium hyaluronate, have been shown to minimize

irritation and are proven to be non-irritant [20]. Furthermore, patient education on the proper use of retinoids, including gradual introduction and nighttime application, can help reduce the severity of side effects. By combining these strategies, the adverse effects of retinoids can be effectively managed, ensuring better patient compliance and therapeutic outcomes.

Clinical guidelines consistently recommend the use of retinoids as the cornerstone of acne treatment due to their ability to address multiple facets of acne pathogenesis, including the reduction of sebum production, inhibition of *C. acnes* colonization, and prolongation of remission periods by preventing new lesion formation and bacterial resistance [15]. Despite their proven efficacy, retinoids are underprescribed, highlighting a gap between clinical recommendations and actual practice [15]. The choice of retinoid in topical formulations depends on the specific skin condition being treated, the patient’s skin type, and the retinoid’s irritation potential, with ongoing research aimed at optimizing their formulations and delivery methods to maximize therapeutic outcomes. Overall, the various actions of retinoids make them indispensable in the effective management and resolution of acne lesions.

#### *Benzoyl Peroxide*

Benzoyl peroxide (BPO) is a widely recognized topical agent for the treatment of acne vulgaris due to its potent bactericidal and comedolytic properties. Its bactericidal action is primarily attributed to its ability to release free oxygen radicals, which are lethal to *C. acnes* [21]. This antibacterial effect is complemented by its mild anti-inflammatory properties, which help reduce the inflammation associated with acne lesions [21]. Additionally, BPO exhibits keratolytic activity, promoting the shedding of the outer layer of the skin and preventing the formation of comedones [22]. BPO as monotherapy or add-on treatment has been found to be more effective than placebo or no treatment, although it may increase the risk of adverse events, most of which are mild to moderate, including erythema and pruritus [23]. Nevertheless, clinical studies have demonstrated that BPO is effective as a monotherapy for mild-to-moderate acne, significantly reducing both inflammatory and non-inflammatory lesions [24,25].

The selection of BPO formulations for acne treatment is influenced by several factors, including concentration, vehicle type, and combination with other acne treatments. Concentration is crucial as higher concentrations of BPO, such as 5%, can cause more irritation compared to lower concentrations, for example, 2.5%, which have been shown to provide similar efficacy with better tolerability [26]. Vehicle type also plays a significant role; advanced formulations that optimize drug concentration and utilize improved delivery vehicles can enhance tolerability and efficacy, allowing for less frequent application or co-application of drugs that were previously considered incompatible [27]. Therefore, the choice of BPO formulation should consider the balance between efficacy and tolerability, the type of vehicle used, and the potential benefits of combination therapy to ensure optimal patient outcomes and adherence to treatment regimens.

Despite its effectiveness, BPO is associated with several adverse effects. Commonly reported adverse effects include skin irritation and contact dermatitis. Skin irritation often manifests as redness, burning, and itching at the application site. Allergic contact dermatitis, although less common, can occur in up to 6.5% of individuals with a history of exposure to BPO and can

be severe enough to require hospitalization and systemic treatment in some cases [28]. This highlights the importance of recognizing potential severe reactions and the need for appropriate patient education and monitoring. Another notable adverse effect is the bleaching of clothing and hair, which occurs due to the oxidative properties of BPO. This can be particularly troublesome for users, as it can lead to the discoloration of fabrics and hair upon contact [29]. Despite these adverse effects, the overall risk associated with over-the-counter BPO products remains low, with a reporting rate of under 1% for adverse events over a 20-year period [30]. Therefore, while BPO is effective for acne treatment, users should be aware of its potential to cause skin irritation, allergic reactions, and bleaching of fabrics and hair, and they should take appropriate precautions to minimize these risks.

### *Salicylic Acid*

Salicylic acid (SA) is a beta-hydroxy acid widely recognized for its keratolytic and anti-inflammatory properties, making it an effective treatment for acne. Its primary mechanism involves desmolytic activity, which facilitates the exfoliation of the stratum corneum by breaking down desmosomes, the structures that hold skin cells together, rather than acting as a true keratolytic agent [31]. This exfoliative property allows SA to penetrate the pilosebaceous unit effectively. Its keratolytic action involves breaking down the bonds between dead skin cells, promoting exfoliation and preventing clogged pores [32,33].

SA's anti-inflammatory effects are significant in reducing acne-related inflammation. It achieves this by two mechanisms: (1) downregulating the adenosine monophosphate-activated protein kinase (AMPK)/sterol response element-binding protein-1 (SREBP-1) pathway, which decreases sebocyte lipogenesis, and (2) suppressing the NF- $\kappa$ B pathway, thereby reducing the production of inflammatory cytokines in sebocytes [33]. This dual action not only reduces sebum production but also decreases inflammation. SA has also been shown to downregulate the AMPK/SREBP-1 pathway, leading to reduced lipogenesis in sebocytes [33]. The AMPK/SREBP-1 pathway has utility in the treatment of acne, attributable to its central role in the processes of cellular energy homeostasis regulation and lipid metabolism. Additionally, studies on 30% supramolecular salicylic acid (SSA) peels have shown that SA can modulate the skin microbiome, reducing the proportion of acne-causing bacteria like *C. acnes* and *Staphylococcus* [34]. Improving the skin microenvironment further helps to reduce local inflammation and promote overall skin health. This modulation of the skin microbiome is significant, as it not only targets the bacteria directly involved in acne pathogenesis but also supports a balanced and healthier skin ecosystem.

As SA also possesses preservative properties, this adds to its versatility in cosmetic formulations. However, it is essential to use SA cautiously, especially at high concentrations or over large surface areas, to avoid potential side effects like salicylism and skin dyschromias [35]. In clinical practice, healthcare providers should evaluate individual risk factors for dyschromias, such as skin type and history of pigmentary disorders, before recommending SA treatments. Additionally, SA should be avoided in individuals with a known allergy to salicylates, as it can trigger allergic hypersensitivity reactions, including itching, redness, and swelling. For individuals with sensitive skin, lower concentrations of SA are recommended to minimize irritation. Overuse or improper application of SA can lead to excessive drying and peeling of the skin, which may exacerbate certain skin conditions such as eczema or rosacea.

Despite these precautions, overall, SA's ability to exfoliate, penetrate the pilosebaceous unit, and reduce inflammation deems it a potent agent in the treatment of various skin conditions, particularly acne vulgaris.

### *Topical Antibiotics*

Topical antibiotics play a crucial role in dermatology by reducing cutaneous bacterial colonization, suppressing inflammatory responses, and preventing acne exacerbations. In particular, clindamycin and erythromycin, are frequently employed in the treatment of acne vulgaris due to their effectiveness against the Gram-positive bacterium *C. acnes*. Clindamycin and erythromycin work by inhibiting bacterial protein synthesis, thereby reducing the bacterial load and subsequent inflammation associated with acne lesions [36]. These medications are commonly used to manage various skin conditions, including acne vulgaris, wound infections, and impetigo, due to their ability to target specific bacterial pathogens and reduce microbial load on the skin [37,38]. However, despite the potency of antibiotics, their effectiveness is compromised against resistant strains, highlighting the need for combination therapies or alternative treatments to mitigate issues of resistance [39]. Current guidelines recommend avoiding antibiotic monotherapy and suggest combining antibiotics with other agents such as retinoids or BPO to enhance treatment efficacy and evade the development of resistance [40]. Thus, antibiotic use must be carefully managed to prevent further resistance and maintain their therapeutic benefits.

Antibiotic resistance has become a global public health crisis, with antibiotic-resistant bacteria causing over 700,000 deaths annually worldwide, including more than 25,000 deaths in the European Union alone [41]. Resistance diminishes the efficacy of these antibiotics, necessitating the exploration of alternative treatments. The repeated use of topical antibiotics can result in contact sensitization, which is particularly problematic for patients with barrier-damaged skin, pre-existing dermatosis, or occupational exposure [42]. This contact allergy can limit the future use of systemic antibiotics, further complicating treatment options [42]. These local delayed hypersensitivity reactions are a growing concern among dermatologists, especially in managing conditions such as acne, rosacea, and impetigo, in which topical antibiotics are frequently used [37]. Despite these challenges, when used appropriately, antibiotics have proven efficacy and remain a crucial component in the treatment of acne.

### *Exploration of Combination Therapies*

Combination therapy in acne treatment involves using various medications to promote broader therapeutic coverage and enhance treatment efficacy. This approach leverages the strengths of various classes of acne treatments, addressing several pathogenic factors simultaneously. Given that acne vulgaris is a multifactorial disease, the combination of different treatments is not only justified but essential for comprehensive management.

Benzoyl peroxide is often used in combination products for the treatment of acne vulgaris. Kircik et al. evaluated a triple combination therapy of topical clindamycin 1.2% with adapalene 0.15% and benzoyl peroxide 3.1% gel, known as CAB gel. With this combination, both inflammatory and non-inflammatory lesions improved, marking it as the first fixed-dose, triple-combination topical treatment for acne vulgaris [8]. Furthermore, it demonstrated a suitable safety profile, indicating that combination therapies can maximize therapeutic benefits

while minimizing adverse effects. This permits greater accessibility for patients with sensitive skin. Moreover, the addition of niacinamide to BPO not only improves acne outcomes but also reduces facial sebum production, post-inflammatory hyperpigmentation, and erythema, which are common concerns in acne patients [43]. Although BPO and tretinoin are known to effectively reduce inflammatory and non-inflammatory lesions, their combined chemical instability and skin irritability have limited their use together. However, emerging research has investigated methods to overcome these barriers. Del Rosso et al. conducted two multicenter, double-blind, vehicle-controlled trials studies of 3% microencapsulated BPO with 0.1% microencapsulated tretinoin (E-BPO/T), demonstrating that microencapsulation can reduce the total number of lesions and increase tolerability when compared to traditional formulations., E-BPO/T cream showed superior results compared to the vehicle, with a notable reduction in inflammatory lesion counts (-21.6 vs. -14.8 and -16.2 vs. -14.1) and non-inflammatory lesions (-29.7 vs. -19.8 and -24.2 vs. -17.4) [44]. This innovative approach highlights the potential for microencapsulation to improve both the effectiveness and patient adherence to combination therapies in acne treatment.

The combination of SA with other bioactive compounds, such as magnolol, has also demonstrated enhanced antibacterial and anti-inflammatory effects, providing a synergistic approach to acne treatment [45]. This is important, as magnolol, a natural compound extracted from Magnolia bark, not only exhibits strong antimicrobial properties but also has potent antioxidant and anti-inflammatory effects, which can further enhance skin health and improve treatment outcomes for acne patients. Combination topical products such as facial masks present another innovative approach to acne management. A randomized controlled trial in Shanghai, China, assessed a facial serum and mask containing SA and lipohydroxy acid, showing substantial improvements in acne severity, comedones, post-inflammatory erythema (PIE), and hyperpigmentation (PIH) over eight weeks, with the addition of the mask accelerating these effects without adverse reactions [46]. These masks enhance the delivery and effectiveness of active ingredients, providing an intensified treatment experience. Additionally, cleansing the skin is just as important to manage as what is applied afterward, because it sets the foundation for the absorption and efficacy of subsequent treatments [10]. One cleansing gel containing 2% SA, zinc gluconate, and lipohydroxy acid demonstrated a significant reduction in both inflammatory and non-inflammatory truncal acne lesions over 84 days, with improved skin barrier function and no reported adverse events [47]. This highlights the critical role of a well-formulated cleanser in maintaining skin health, reducing acne severity, and preparing the skin for further treatment steps, effectively adding another layer of combination therapy by optimizing the skin's readiness for subsequent treatments.

Enhancements to the current treatment standards for acne vulgaris are constantly being explored and studied to increase efficacy and safety. Technology continues to shape these advancements, and polymeric emulsion technology (PET) is an example of this. PET is a newer development incorporated into retinoids such as tazarotene, allowing for even distribution onto the skin in order to decrease side effects while maintaining efficacy. The implications of PET are significant, as this technology could lead to more consistent treatment outcomes and greater patient comfort. Furthermore, since tazarotene

0.045% cream has been approved to treat acne vulgaris in individuals older than nine years, this expansion plays an important role in reducing adverse events and improving patient adherence even in younger populations [48]. Technology is important for the future of dermatology to keep pace with the evolving needs of patients, offering innovative solutions that improve both the effectiveness and tolerability of treatments.

These findings collectively demonstrate the potential for combination therapies to optimize acne treatment by enhancing efficacy and minimizing adverse effects. By integrating various topical agents and advanced technologies, dermatologists can offer more effective, personalized treatment regimens that address the multifactorial nature of acne.

#### **Areas for Future Research**

Many studies have been conducted to determine the most effective, safe, and accessible topical treatments for the dermatologic condition of acne vulgaris. Research ranges from evaluating improvements in commonly used topical therapies to exploring new regimens that may shape the future of acne vulgaris treatment.

Several proposed combinations and modifications to existing therapies have been supported by the literature and warrant deeper exploration.

Novel therapies and applications for acne vulgaris present another promising area for future investigations. Clascoterone cream 1% is a newer formulation approved by the FDA for treating acne vulgaris in patients older than 12 years. In a study by Eichenfield et al., clascoterone cream 1% was applied to the face twice daily for 12 weeks. They also performed a nine-month extension study which supported the long-term safety and efficacy of this agent. Clascoterone's adverse side effects were commonly mild, consisting of erythema, pruritus, dryness, and burning. These effects did not worsen over increased length of use, making clascoterone suitable for long-term use [49]. Overall, this study supported the use of clascoterone cream 1% as a treatment for acne vulgaris while adding information to support its long-term use and outcomes. Topical metformin 30% gel is also being explored for its potential in controlling acne. This was evaluated in a split-faced, placebo-controlled study which found that metformin in a 30% topical nanoemulsion formulation was effective in decreasing inflammatory and non-inflammatory lesions without producing adverse effects [50]. Although this study's sample size was small with a limited follow-up period, it still shows promising ideas for the future.

Much of the research done to evaluate the topical treatments of acne vulgaris could be improved by tracking further follow-ups to evaluate longer-term results and increasing the diversity in the subject pool to ensure it represents all patient populations. The advancements discussed highlight the progress made thus far, but also underscore the importance of continued innovation and comprehensive research. Future studies should focus on developing novel treatment formulations, exploring synergistic combinations, and integrating cutting-edge technologies to optimize therapeutic outcomes. By addressing these areas, the dermatological community can ensure that acne treatments are both effective and accessible, ultimately improving the quality of life for those affected by this common skin condition.

## Conclusion

Acne vulgaris is a multifaceted dermatological condition that affects a significant portion of the global population. This review has highlighted the complexities of its treatment, focusing on the efficacy, safety, and evolving therapeutic strategies of topical treatments. Future research should focus on long-term studies to evaluate the safety and efficacy of these regimens, ensuring they meet the needs of diverse populations. Continued exploration of combination therapies, personalized treatment approaches, and emerging technologies will be crucial in addressing the multifactorial nature of acne and enhancing patient outcomes. Through a comprehensive and dynamic approach, the future of acne treatment looks promising, with the potential to significantly improve patient care and satisfaction.

## References

1. Brown, S. K., & Shalita, A. R. (1998, June 20). *Acne Vulgaris*. *TheLancet*. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(98\)01046-0/abstract](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(98)01046-0/abstract).
2. Tan, J. K., & Bhat, K. (2015). A global perspective on the epidemiology of acne. *British Journal of Dermatology*, *172*(S1), 3-12. <https://doi.org/10.1111/bjd.13462>.
3. Skin conditions by the numbers. *American Academy of Dermatology*. <https://www.aad.org/media/stats-numbers>.
4. Zhang, H., & Zhang, Z. (2023). Genetic variants associated with acne vulgaris. *International Journal of General Medicine*, *16*, 3843–3856. <https://doi.org/10.2147/IJGM.S421835>.
5. Reynolds, R. V., Yeung, H., Cheng, C. E., Cook-Bolden, F., Desai, S. R., Druby, K. M., Freeman, E. E., Keri, J. E., Stein Gold, L. F., Tan, J. K. L., Tollefson, M. M., Weiss, J. S., Wu, P. A., Zaenglein, A. L., Han, J. M., & Barbieri, J. S. (2024). Guidelines of care for the management of acne vulgaris. *Journal of the American Academy of Dermatology*, *90*(5), 1006.e1–1006.e30. <https://doi.org/10.1016/j.jaad.2023.12.017>.
6. Goberdhan, L. T., Schneider, K., Makino, E. T., & Mehta, R. C. (2023). Combining diamond-tip dermabrasion treatments and topical skincare in participants with dry, hyperpigmented, photodamaged or acne-prone/oily facial skin: A clinical usage study. *Clinical, Cosmetic and Investigational Dermatology*, *16*, 2645–2657. <https://doi.org/10.2147/CCID.S423688>.
7. Youn, S. W., Na, J. I., Choi, S. Y., Huh, C. H., & Park, K. C. (2005). Regional and seasonal variations in facial sebum secretions: A proposal for the definition of combination skin type. *Skin Research and Technology: Official Journal of International Society for Bioengineering and the Skin (ISBS) [and] International Society for Digital Imaging of Skin (ISDIS) [and] International Society for Skin Imaging (ISSI)*, *11*(3), 189–195. <https://doi.org/10.1111/j.1600-0846.2005.00119.x>.
8. Kircik, L. H., Stein Gold, L., Gold, M., Weiss, J. S., Harper, J. C., Del Rosso, J. Q., Bunick, C. G., Bhatia, N., Tangheiti, E. A., Eichenfield, L. F., Baldwin, H., Draelos, Z. D., Callender, V. D., Han, G., Gooderham, M. J., Sadick, N., Lupo, M. P., Lain, E. T., & Werschler, W. P. (2024). Triple combination clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% for acne: Efficacy and safety from a pooled phase 3 analysis. *Dermatology and Therapy*, *14*(5), 1211–1227. <https://doi.org/10.1007/s13555-024-01155-7>.
9. Eicher, L., Knop, M., Aszodi, N., Senner, S., French, L. E., & Wollenberg, A. (2019). A systematic review of factors influencing treatment adherence in chronic inflammatory skin disease - Strategies for optimizing treatment outcome. *Journal of the European Academy of Dermatology and Venereology: JEADV*, *33*(12), 2253–2263. <https://doi.org/10.1111/jdv.15913>
10. Draelos, Z. D., Callender, V., Young, C., & Dhawan, S. S. (2008). The effect of vehicle formulation on acne medication tolerability. *Cutis*, *82*(4), 281–284. <https://pubmed.ncbi.nlm.nih.gov/19055172/>.
11. Thekho, A.J., Sarkar, R. (2024). PCOD-Management of ACNE. In: Singh, R., Sharma, N. (eds) *A Guide to Hormonal Dermatology*. Springer, Singapore. [https://doi.org/10.1007/978-981-99-7715-4\\_8](https://doi.org/10.1007/978-981-99-7715-4_8).
12. Kim, G. H., Lee, W. J., Jung, J. M., Won, C. H., Chang, S. E., Lee, M. W., & Moon, I. J. (2024). Morphological characteristics of facial scars: A retrospective analysis according to scar location, onset, age, and cause. *International Wound Journal*, *21*(4), e14453. <https://doi.org/10.1111/iwj.14453>.
13. Smart, K., Rodriguez, I., Worswick, S. (2024). Comorbidities and treatment options for acne keloidalis nuchae. *Dermatologic Therapy*. <https://doi.org/10.1155/2024/8336926>.
14. Dreno, B., Kang, S., Leyden, J., & York, J. (2022). Update: Mechanisms of topical retinoids in acne. *Journal of Drugs in Dermatology: JDD*, *21*(7), 734–740. <https://doi.org/10.36849/JDD.6890>.
15. Leyden, J., Stein-Gold, L., & Weiss, J. (2017). Why topical retinoids are mainstay of therapy for acne. *Dermatology and Therapy*, *7*(3), 293–304. <https://doi.org/10.1007/s13555-017-0185-2>.
16. Schmidt, N., & Gans, E. H. (2011). Tretinoin: A review of its anti-inflammatory properties in the treatment of acne. *The Journal of Clinical and Aesthetic Dermatology*, *4*(11), 22–29.
17. Milosheska, D., & Roškar, R. (2022). Use of retinoids in topical antiaging treatments: A focused review of clinical evidence for conventional and nanoformulations. *Advances in Therapy*, *39*(12), 5351–5375. <https://doi.org/10.1007/s12325-022-02319-7>.
18. Draelos Z. D. (2023). Low irritation potential of tazarotene 0.045% lotion: Head-to-head comparison to adapalene 0.3% gel and trifarotene 0.005% cream in two studies. *The Journal of Dermatological Treatment*, *34*(1), 2166346. <https://doi.org/10.1080/09546634.2023.2166346>.
19. Kim, B. H., Lee, Y. S., & Kang, K. S. (2003). The mechanism of retinol-induced irritation and its application to anti-irritant development. *Toxicology Letters*, *146*(1), 65–73. <https://doi.org/10.1016/j.toxlet.2003.09.001>.
20. Panda, P., Muppidi, S., Karuturi, K., Reddy Moranganti, M., & Mukkamala, S. (2023). Assessment of the SPF and anti-irritating properties of sunscreen designed for retinol users. *International Journal of Experimental Research and Review*, *30*(1). <https://doi.org/10.52756/ijerr.2023.v30.017>.
21. Dutil M. (2010). Benzoyl peroxide: Enhancing antibiotic efficacy in acne management. *Skin Therapy Letter*, *15*(10), 5–7.

22. Brammann, C., & Müller-Goymann, C. C. (2020). An update on formulation strategies of benzoyl peroxide in efficient acne therapy with special focus on minimizing undesired effects. *International Journal of Pharmaceutics*, 578, 119074. <https://doi.org/10.1016/j.ijpharm.2020.119074>.
23. Yang, Z., Zhang, Y., Lazic Mosler, E., Hu, J., Li, H., Zhang, Y., Liu, J., & Zhang, Q. (2020). Topical benzoyl peroxide for acne. *The Cochrane Database of Systematic Reviews*, 3(3), CD011154. <https://doi.org/10.1002/14651858.CD011154.pub2>.
24. Kawashima, M., Nagare, T., & Doi, M. (2017). Clinical efficacy and safety of benzoyl peroxide for acne vulgaris: Comparison between Japanese and Western patients. *The Journal of Dermatology*, 44(11), 1212–1218. <https://doi.org/10.1111/1346-8138.13996>.
25. Rosso, J.Q. (2008). What is the role of benzoyl peroxide cleansers in acne management?: Do they decrease Propionibacterium acnes counts? Do they reduce acne lesions?. *The Journal of Clinical and Aesthetic Dermatology*, 1(4), 48–51.
26. Zeichner, J. A., Bhatt, V., & Pillai, R. (2013). In vitro percutaneous absorption of benzoyl peroxide from three fixed combination acne formulations. *The Journal of Clinical and Aesthetic Dermatology*, 6(8), 19–22.
27. Stein Gold, L., Kwong, P., Draelos, Z., Arekapudi, K. L., Levy-Hacham, O., Erlich, M., & Desai, S. R. (2023). Impact of topical vehicles and cutaneous delivery technologies on patient adherence and treatment outcomes in acne and rosacea. *The Journal of Clinical and Aesthetic Dermatology*, 16(5), 26–34.
28. Sandre, M., Skotnicki-Grant, S. (2018). A case of a paediatric patient with allergic contact dermatitis to benzoyl peroxide. *Journal of Cutaneous Medicine and Surgery*, 22(2), 226–228. <https://doi.org/10.1177/1203475417733462>.
29. Fluhr, J.W. (2014). Benzoyl peroxide. In: Zouboulis, C., Katsambas, A., Kligman, A. (eds) *Pathogenesis and Treatment of Acne and Rosacea*. Springer, Berlin, Heidelberg. [https://doi.org/10.1007/978-3-540-69375-8\\_56](https://doi.org/10.1007/978-3-540-69375-8_56).
30. Szymanski, L., & Arekapudi, K. L. (2022). Adverse-event reports in over-the-counter topical acne drug products containing benzoyl peroxide from a specific pharmaceutical company in the USA. *Dermatology and Therapy*, 12(11), 2397–2400. <https://doi.org/10.1007/s13555-022-00808-9>.
31. Sylwia, K., Katarzyna, D. (2023). Salicylic acid and its use in cosmetology. *Aesthetic Cosmetology and Medicine*, 12(3), 91–95. <https://doi.org/10.52336/acm.2023.011>.
32. Măgeruşan, Ş.E., Hancu, G., & Rusu, A. (2023). A comprehensive bibliographic review concerning the efficacy of organic acids for chemical peels treating acne vulgaris. *Molecules*, 28(20), 7219. <https://doi.org/10.3390/molecules28207219>.
33. Lu, J., Cong, T., Wen, X., Li, X., Du, D., He, G., & Jiang, X. (2019). Salicylic acid treats acne vulgaris by suppressing AMPK/SREBP1 pathway in sebocytes. *Experimental Dermatology*, 28(7), 786–794. <https://doi.org/10.1111/exd.13934>.
34. Shao, X., Chen, Y., Zhang, L., Zhang, Y., Ariyawati, A., Chen, T., Chen, J., Liu, L., Pu, Y., Li, Y., & Chen, J. (2023). Effect of 30% supramolecular salicylic acid peel on skin microbiota and inflammation in patients with moderate-to-severe acne vulgaris. *Dermatology and Therapy*, 13(1), 155–168. <https://doi.org/10.1007/s13555-022-00844-5>.
35. Madan, R. K., & Levitt, J. (2014). A review of toxicity from topical salicylic acid preparations. *Journal of the American Academy of Dermatology*, 70(4), 788–792. <https://doi.org/10.1016/j.jaad.2013.12.005>.
36. Dessinioti, C., & Katsambas, A. (2022). Antibiotics and antimicrobial resistance in acne: Epidemiological trends and clinical practice considerations. *The Yale Journal of Biology and Medicine*, 95(4), 429–443.
37. Dallo, M., Patel, K., & Hebert, A. A. (2023). Topical antibiotic treatment in dermatology. *Antibiotics*, 12(2), 188. <https://doi.org/10.3390/antibiotics12020188>.
38. Bandyopadhyay D. (2021). Topical antibacterials in dermatology. *Indian Journal of Dermatology*, 66(2), 117–125. [https://doi.org/10.4103/ijdr.IJD\\_99\\_18](https://doi.org/10.4103/ijdr.IJD_99_18).
39. Muteeb, G., Rehman, M. T., Shahwan, M., & Aatif, M. (2023). Origin of antibiotics and antibiotic resistance, and their impacts on drug development: A narrative review. *Pharmaceutics*, 16(11), 1615. <https://doi.org/10.3390/ph16111615>.
40. Gupta, R., & Sharma, S. (2022). Role of alternatives to antibiotics in mitigating the antimicrobial resistance crisis. *The Indian Journal of Medical Research*, 156(3), 464–477. [https://doi.org/10.4103/ijmr.IJMR\\_3514\\_20](https://doi.org/10.4103/ijmr.IJMR_3514_20).
41. Bennani, H., Mateus, A., Mays, N., Eastmure, E., Stärk, K. D. C., & Häsler, B. (2020). Overview of evidence of antimicrobial use and antimicrobial resistance in the food chain. *Antibiotics*, 9(2), 49. <https://doi.org/10.3390/antibiotics9020049>.
42. Kreft, B., & Wohlrab, J. (2022). Contact allergies to topical antibiotic applications. *Allergologie Select*, 6, 18–26. <https://doi.org/10.5414/ALX02253E>.
43. Kaewsanit, T., Chakkavittumrong, P., & Waranuch, N. (2021). Clinical comparison of topical 2.5% benzoyl peroxide plus 5% niacinamide to 2.5% benzoyl peroxide alone in the treatment of mild to moderate facial acne vulgaris. *The Journal of Clinical and Aesthetic Dermatology*, 14(6), 35–41.
44. Del Rosso, J., Sugarman, J., Green, L., Lain, T., Levy-Hacham, O., Mizrahi, R., & Gold, L. S. (2023). Efficacy and safety of microencapsulated benzoyl peroxide and microencapsulated tretinoin for the treatment of acne vulgaris: Results from two phase 3 double-blind, randomized, vehicle-controlled studies. *Journal of the American Academy of Dermatology*, 89(4), 719–727. <https://doi.org/10.1016/j.jaad.2023.05.093>.
45. Kwon, K. C., Won, J. G., Kim, M. S., Shin, Y. W., Park, S. W., & Song, Y. S. (2023). Anti-acne activity of carnitine salicylate and magnolol through the regulation of exfoliation, lipogenesis, bacterial growth and inflammation. *Skin Research and Technology: Official Journal of International Society for Bioengineering and the Skin (ISBS) [and] International Society for Digital Imaging of Skin (ISDIS) [and] International Society for Skin Imaging (ISSI)*, 29(7), e13406. <https://doi.org/10.1111/srt.13406>.
46. Li, S., He, X., Zhang, Z., Zhang, X. S., Niu, Y. G., Steel, A., & Wang, H. T. (2023). Efficacy and safety of a facial serum and a mask containing salicylic acid and lipohydroxy acid in acne management: A randomized controlled trial. *Journal of Cosmetic Dermatology*, 22(9), 2502–2511. <https://doi.org/10.1111/jocd.15746>.

47. Towersey, L., Correia, P., Fajgenbaum Feiges, M., Euzébio Gonçalves Junior, J., Sant'Anna, B., Kerob, D., & Le Floch, C. (2023). Assessment of the benefit of a deep cleansing gel containing salicylic Acid 2%, zinc gluconate 0.2% and lipohydroxy acids 0.05% in patients with mild to moderate truncal acne: Results from an exploratory study. *Clinical, Cosmetic and Investigational Dermatology*, *16*, 119–123. <https://doi.org/10.2147/CCID.S394123>.
48. Mohney, L. A., Singh, R., & Feldman, S. R. (2022). Tazarotene 0.045% lotion: A novel retinoid formulation. *The Annals of Pharmacotherapy*, *56*(10), 1174–1180. <https://doi.org/10.1177/10600280211072155>.
49. Eichenfield, L. F., Hebert, A. A., Gold, L. S., Cartwright, M., Moro, L., Han, J., Squittieri, N., & Mazzetti, A. (2023). Long-term safety and efficacy of twice-daily topical clascoterone cream 1% in patients greater than or equal to 12 years of age with acne vulgaris. *Journal of Drugs in Dermatology: JDD*, *22*(8), 810–816. <https://doi-org.icom.idm.oclc.org/10.36849/jdd.7592>
50. El-Komy, M. H. M., Abdo, N. M. K., Shamma, R. N., & Bedair, N. I. (2023). Topical metformin 30% gel in the treatment of acne vulgaris in women, a split face, placebo-controlled study. *Experimental Dermatology*, *32*(10), 1663–1673. <https://doi-org.icom.idm.oclc.org/10.1111/exd.14868>.

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