Topical Hypochlorous Acid for Acne Vulgaris: Mechanisms, Clinical Evidence, and Therapeutic Potential

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PRACTICE **POINTS**

- First-line treatments for acne vulgaris are effective but often limited by local irritation, systemic adverse effects, and antibiotic resistance.
- Hypochlorous acid (HOCl) shows rapid, broad-spectrum antimicrobial and biofilm-disruptive activity against *Cutibacterium acnes* and other pathogens, with a low propensity for resistance.
- Emerging clinical data indicate HOCl formulations deliver efficacy comparable to standard topical treatments with superior tolerability and no barrier disruption, supporting its use as a well-tolerated adjunct in acne management.

Acne vulgaris is driven by *Cutibacterium acnes*, sebaceous activity, and innate immune activation, leading to inflammation, scarring, and reduced quality of life. Although standard topical and systemic therapies are effective, their use may be limited by irritation, adverse effects, and antimicrobial resistance. Hypochlorous acid (HOCl) exhibits antimicrobial, biofilm-disruptive, and anti-inflammatory activity through inhibition of nuclear factor kappa B (NF-κB) and mitogen-activated protein kinase (MAPK) signaling. Preliminary studies suggest HOCl provides lesion reductions comparable to benzoyl peroxide with superior tolerability and no barrier disruption, supporting its potential as an adjunctive acne therapy pending larger controlled trials.

Acne vulgaris, a chronic inflammatory disease of the pilosebaceous unit, is among the most prevalent dermatologic conditions worldwide. Though symptoms range in severity, patients can experience painful irritation and scarring that can lead to substantial psychological distress and impact quality of life. *Cutibacterium acnes* plays a central role in acne development through biofilm formation, lipase activity, and activation of innate immune pathways, which together contribute to a cycle of inflammation and comedogenesis.[1]

First-line treatments for acne vulgaris include topical benzoyl peroxide, topical retinoids, and topical antibiotics, while oral spironolactone and tetracyclines can be used alongside topical therapies for more extensive disease. Additionally, isotretinoin is generally reserved for severe or refractory cases. While these therapies are effective, each has notable limitations and adverse effects that in some cases limit adherence and efficacy. The most common adverse effects seen with topical acne therapies include irritation and dryness. Systemic therapies such as spironolactone can cause fatigue, dizziness, and birth defects, while prolonged antibiotic use can promote the risk for antimicrobial resistance.[2]

Hypochlorous acid (HOCl) is a naturally occurring weak acid produced by neutrophils and currently is approved by the US Food and Drug Administration for wound cleansing, burn management, and dermal lesion irrigation. Although it is not approved for the treatment of acne, stabilized HOCl formulations have been used off label in dermatology for this purpose. Interest in HOCl stems from its broad-spectrum antimicrobial activity against *C acnes*, anti-inflammatory properties, and favorable safety profile. This literature review examines the mechanism of action, clinical evidence, and potential role of HOCl in acne management, contextualizing its use relative to current standard therapies.

Methods

A narrative literature review was conducted to identify and synthesize peer-reviewed evidence on the use of HOCl in dermatology, with emphasis on its potential role in acne management. Searches were performed using PubMed and Scopus databases. Search terms included

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The authors have no relevant financial disclosures to report.

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Cutis. 2026 July;118(1):23-25. doi:10.12788/cutis.1419

combinations of *hypochlorous acid*, *acne*, *acne vulgaris*, *dermatology*, *antimicrobial*, *anti-inflammatory*, *biofilm*, and *skin barrier*. Eligible publications included original research articles, randomized controlled trials, retrospective studies, preclinical in vitro and in vivo studies, and systematic reviews published in English between January 2000 and December 2024. Titles and abstracts were screened for relevance, and the final selection included 16 peer-reviewed articles that met the inclusion criteria.

Results

Hypochlorous acid exhibits rapid, broad-spectrum antimicrobial activity against gram-positive and gram-negative bacteria and fungi. In vitro time-kill assays demonstrated that stabilized HOCl was bactericidal against a variety of pathogens, including methicillin-resistant *Staphylococcus aureus*, methicillin-sensitive *S aureus*, *Staphylococcus epidermidis*, *Corynebacterium* species, *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, *Candida albicans*, and *C acnes*. Specifically, HOCl achieved 99.99% or greater kill within 2 minutes.[3] Moreover, HOCl's antimicrobial efficacy against this panel of organisms was found to be comparable to or greater than that of commonly used antiseptics, including povidone-iodine, chlorhexidine gluconate, and isopropyl alcohol.[3] An additional study using HOCl stabilized in 0.9% saline (pH, 3.5-4.0) confirmed its rapid activity across gram-positive, gram-negative, and fungal species, again demonstrating 99.99 % or greater reduction within 1 to 2 minutes of exposure.[4]

Hypochlorous acid also has demonstrated substantial biofilm-disruptive properties. In vitro studies demonstrated that HOCl can penetrate and disrupt early-stage biofilms by oxidizing extracellular polymeric substances and damaging bacterial membranes; however, while HOCl was effective at destroying immature biofilms and preventing biofilm formation, its efficacy against mature, fully established biofilms was more limited.[5] Thus, topical HOCl may be most effective during the early colonization phase of acne, helping to prevent biofilm maturation and subsequent inflammatory lesion formation. Unlike traditional topical and oral antibiotics, HOCl's nonspecific oxidative mechanism of action is less likely to contribute to microbial resistance. These findings highlight HOCl as a rapid, broad-spectrum antimicrobial with additional biofilm-disruptive activity, supporting its potential role as an early-intervention therapeutic in acne treatment.

In addition to its antimicrobial effects, HOCl is a potent anti-inflammatory molecule that exerts its anti-inflammatory effects through several mechanisms. HOCl acts as a mast cell membrane stabilizer, inhibiting degranulation. Hypochlorous acid also has been demonstrated to reduce levels of leukotriene B4 and interleukin (IL) 2, which supports that HOCl has both antipruritic and anti-inflammatory properties.[6] In keratinocytes and immune cells, HOCl has been shown to suppress the transcription of multiple proinflammatory cytokines by oxidizing IκB kinase β, which then prevents the activation of the nuclear factor kappa B (NF-κB) signaling pathway.[7] Additionally, in a murine model of atopic dermatitis, treatment with HOCl resulted in a downregulation of key proinflammatory and Th2-associated cytokines, including IL-1β, IL-4, IL-6, IL-13, tumor necrosis factor α, thymus and activation-regulated chemokine, thymic stromal lymphopoietin, and IL-31. Parallel in vitro assays revealed that HOCl inhibited phosphorylation of mitogen-activated protein kinase (MAPK) and inhibitor of κB, which inhibits the downstream proinflammatory pathways, thereby elucidating a mechanistic basis for its anti-inflammatory effects.[8] *C acnes* has been shown to activate the toll-like receptor 2 pathway on keratinocytes and macrophages, triggering NF-κB–dependent release of IL-1β and tumor necrosis factor α.[9]

By inhibiting these same signaling pathways, HOCl may attenuate the inflammatory response associated with acne lesions while simultaneously reducing microbial load. These combined anti-inflammatory and antimicrobial effects also may contribute to improved healing outcomes. Emerging clinical evidence supports HOCl's benefit in minimizing scarring and postinflammatory sequelae. A comparative study evaluating a silicone-based scar gel containing HOCl vs silicone gel alone found that the HOCl-containing formulation produced greater improvement in hypertrophic and keloid scar appearance and overall scar texture.[10] These findings suggest that HOCl may have beneficial effects on wound healing and scar remodeling.

In murine models of acute radiation dermatitis, topical HOCl reduced NF-κB–dependent gene expression, decreased epidermal ulceration, and promoted re-epithelialization to near-normal histologic appearance.[7] A double-blind, randomized controlled trial evaluating topical sodium hypochlorite 0.005%, which is a compound in equilibrium with HOCl under physiologic pH, demonstrated a statistically significant reduction in papules among patients with mild to moderate acne after 1 month of treatment ($P<.0001$). Female participants exhibited greater lesion improvement, suggesting possible hormonal or immunologic modulation of response.[11] Although limited in scale, this literature review provides preliminary clinical support for the therapeutic potential of HOCl in the treatment of acne. Collectively, these findings highlight the potential of HOCl as an emerging treatment in acne and other dermatologic conditions.

Comment

Traditional acne therapies include topical agents such as benzoyl peroxide, topical retinoids (eg, tretinoin, adapalene), and salicylic acid, as well as systemic agents such as oral antibiotics, spironolactone, and isotretinoin. While these treatments are effective, their use may be limited by irritation, antibiotic resistance, and systemic adverse effects.

Hypochlorous acid is a potential adjunctive option that acts locally with minimal irritation and without

hormonal or systemic activity.[12] Its antimicrobial and anti-inflammatory mechanisms target key pathogenic pathways in acne while maintaining excellent cutaneous tolerability. In a randomized, double-blind, placebo-controlled trial of 89 patients comparing topical HOCl solution with benzoyl peroxide for mild to moderate acne, HOCl demonstrated comparable improvement in lesion counts.[13] Importantly, no local adverse effects were reported in either group and no dose adjustments were needed during the 12-week treatment period. Although both agents were effective, the absence of irritation with HOCl contrasts with the dryness and erythema frequently associated with benzoyl peroxide.

Additionally, a clinical trial comparing HOCl 0.01% with standard antiseptics, including isopropyl alcohol, povidone-iodine, and chlorhexidine gluconate, showed that HOCl achieved comparable antibacterial reductions while remaining well tolerated and free of facial adverse effects.[14] Similarly, studies evaluating HOCl's antimicrobial efficacy have confirmed that it is nontoxic to periocular and facial tissues, further supporting its safety for use on delicate skin regions.[3] Importantly, in an experimental model evaluating both healthy skin and skin with experimentally induced irritant contact dermatitis, repeated application of an HOCl-based formulation did not impair skin barrier function, underscoring its excellent cutaneous compatibility even under inflammatory conditions.[15] Ultimately, these findings suggest that HOCl offers efficacy comparable to benzoyl peroxide and retinoids while eliminating the irritation and barrier disruption that can limit the use of these first-line agents.

Topical antibiotics such as clindamycin and erythromycin are used widely for their antimicrobial and anti-inflammatory properties but increasingly are undermined by antibiotic resistance. In contrast, HOCl has been shown to reduce bacterial load without altering microbial diversity, supporting its role as a resistance-neutral antimicrobial option for acne management.[16] These characteristics position HOCl as a well-tolerated, resistance-neutral adjunctive treatment that warrants further investigation through larger, controlled trials.

Topical HOCl formulations, particularly those available as sprays or misting solutions, have gained attention on social media for their ease of use and versatility. Although formal studies evaluating adherence or outcomes in this context are currently limited, this emerging consumer trend underscores the perceived convenience of HOCl compared with traditional acne therapies. These formulations can be applied throughout the day, including between exercise and work, supporting adherence among patients with active lifestyles. In contrast to many conventional topical agents that require specific application timing, cleansing routines, or avoidance of cosmetic products, HOCl sprays offer flexible use without disrupting daily activities. These characteristics highlight HOCl's potential as a user-friendly option that may support consistent application and optimize therapeutic outcomes.

Conclusion

The addition of HOCl to acne treatment regimens offers several potential benefits. Its antimicrobial and anti-inflammatory properties may help prevent new papules and pustules, while its favorable tolerability profile minimizes irritation and systemic adverse effects. Preliminary data also suggest efficacy in androgen-mediated acne, though additional studies are needed to confirm these findings.[11] Current evidence remains limited by small sample sizes, short follow-up durations, and a lack of comparative studies among available formulations. Accordingly, HOCl should be considered an adjunctive rather than replacement therapy pending larger studies with longer follow-up.

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