



## Review Article

# Hypochlorous Acid: Applications in Dermatology

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### Relevance

Hypochlorous acid (HClO) is a weak acid and powerful oxidant traditionally used as an active ingredient in various sanitizers and disinfectants. HClO is produced endogenously from activated leukocytes, and it was first exogenously synthesized in 1834, later to be used medicinally as a wound disinfectant during World War I and II.

### Objective

In this review, we aim to review the literature assessing the efficacy and safety of dermatologic uses of topical hypochlorous acid.

### Methods

A PubMed search for articles with the following keywords was performed: “hypochlorous acid” AND “dermatology” OR “dermis” OR “dermal.” Forty-one reports were included in the efficacy and safety analysis.

### Results

Hypochlorous acid exhibits antimicrobial properties and has been demonstrated to promote re-epithelialization in wound healing with low cytotoxicity to keratinocytes and fibroblasts. Recent work has highlighted its anti-inflammatory properties via modulation of the NF-κβ signaling pathway and downregulation of inflammatory cytokines; reports have discussed its application for the management of various inflammatory skin conditions including atopic dermatitis and psoriasis.

### Conclusion

Dermatologic application of hypochlorous acid includes infection prevention, wound care and scar management, inflammatory modulation, treatment in atopic dermatitis and pruritus. Emerging research has discussed potential applications in acne vulgaris, seborrheic dermatitis, and tumor suppression.

## INTRODUCTION

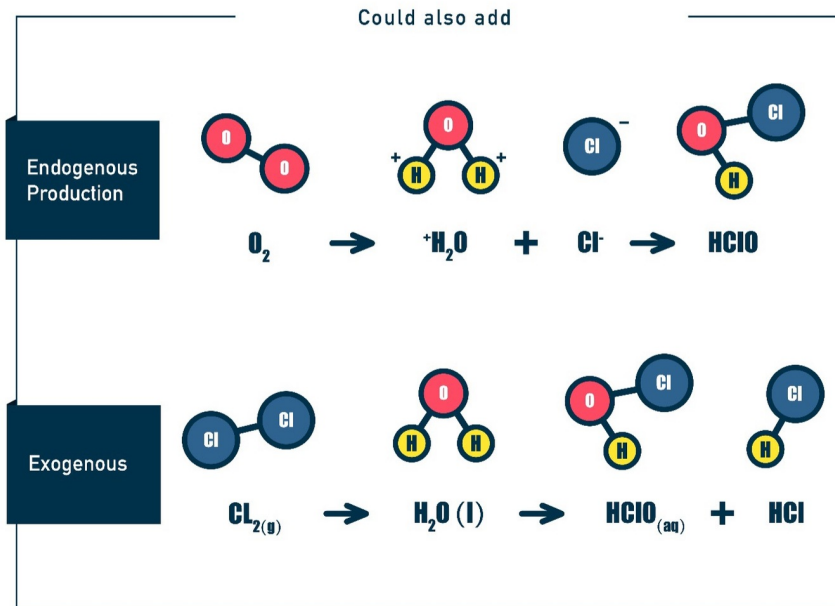
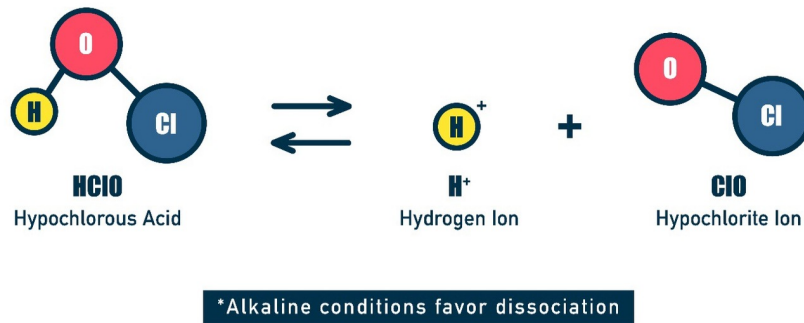
Hypochlorous acid (HClO) is a weak acid and powerful oxidant. It is formed when chlorine (Cl) dissolves in water,  $\text{Cl}_2(\text{g}) + \text{H}_2\text{O}(\text{l}) \rightarrow \text{HClO}(\text{aq}) + \text{HCl}$  (Figure 1). Chlorine dissolution in water is a common disinfecting technique for swimming pools due to the oxidizing and antimicrobial properties of hypochlorous acid. Endogenously, HClO is released from activated leukocytes via a heme enzyme, myeloperoxidase (MPO), which generates hypochlorous acid from hydrogen peroxide and chloride,  $\text{O}_2 \rightarrow \text{H}_2\text{O}_2$

$+ \text{Cl}^- \rightarrow \text{HClO}$ .<sup>1</sup> It thereby has an important function in the innate immune response.

Exogenous hypochlorous acid was first synthesized by a French chemist, Antoine Jérôme Balard, in 1834. Early medicinal application of hypochlorous acid is exemplified by its use as a wound disinfectant during World War I and II. The antimicrobial properties of hypochlorous acid have since been studied both *in vitro* and *in vivo*.<sup>2-7</sup> A study found hypochlorous acid to be effective against *Escherichia coli*, *Porphyromonas gingivalis*, *Enterococcus faecalis*, and *Streptococcus sanguinis* bacterial biofilms on titanium alloy surfaces; compared with sodium hypochlorite (NaOCl) and

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**Figure 1. The Production and Dissociation of Hypochlorous Acid (HClO).**

Hypochlorous acid is produced endogenously by myeloperoxidase, a heme enzyme, and exogenously via chlorine dissolution in water. Activated leukocytes endogenously produce hypochlorous acid from water and chloride. Exogenous chlorine dissolution in water produces hypochlorous acid and hydrogen chloride. Once hypochlorous acid is produced, alkaline conditions favor dissociation into hypochlorite and a hydrogen ion.

chlorhexidine (CHX), hypochlorous acid significantly lowered the lipopolysaccharide concentration of *P. gingivalis*, leading the authors to conclude that HOCl antiseptic may be effective for cleaning infected implant surfaces for medical use.<sup>2</sup>

*In vivo*, the microbicidal efficacy of hypochlorous acid has been evaluated among patients with wounds. A study found 300 or 500 mg/L concentrations of hypochlorous acid to be an effective antiseptic for wounds and mucous membranes after a 5-10 minute application.<sup>3</sup> Higher concentrations were found to be very effective both in the presence or absence of biofilms, with use acceptable on healthy skin for five minutes. Similarly, Hierbert and Robson demonstrated the ability of HClO to reduce bacterial counts in open wounds.<sup>4</sup> Both saline and hypochlorous acid irrigation initially reduced bacterial counts by 4-6 logs, although reduced bacterial counts were only maintained to the time of definitive closure with hypochlorous acid-irrigated wounds. While saline-irrigated wounds demonstrated bacterial

counts back to  $10^5$ , hypochlorous acid-irrigated wounds remained less than or equal to  $10^2$ .

The mechanism of action of hypochlorous acid's antimicrobial properties includes DNA synthesis inhibition, protein synthesis inhibition via oxidation of thiol-containing proteins and enzymes, and bacterial growth inhibition via reduced DNA replication and cell wall synthesis.<sup>8</sup> Furthermore, HClO can reduce ATP production and thereby directly affect microbial metabolism. The antimicrobial properties of HClO justify its use in numerous disinfecting and cleaning products, and its relative tolerability and nontoxicity to humans have fostered use in antiseptics and wound care. As such, the United States Food and Drug Administration (FDA) has cleared the use of over ten branded aqueous hypochlorous acid formulations for topical wound management within the last decade.<sup>9</sup> Novel research has sought to determine the efficacy and safety of topical hypochlorous acid in a variety of dermatologic conditions. In this review, we aim to review published literature detailing the effi-

cacy and safety of dermatologic uses of topical hypochlorous acid.

## MATERIALS AND METHODS

A PubMed search for articles with the following keywords was performed: “hypochlorous acid” AND “dermatology” OR “dermis” OR “dermal”, which yielded 304 articles. Upon review of article titles and abstracts, those with relevant subject matter were retrieved for full-text review. In addition, their associated references were scanned for relevant reports. Forty-one reports were included in the efficacy and safety analysis: 17 clinical studies or case reports with human subjects, 10 *in vitro* or animal-model studies, 9 reviews, and 5 reports discussing sodium hypochlorite for safety comparisons. The most common reasons for exclusion were 1) reports detailing sodium hypochlorite, rather than hypochlorous acid, and 2) non-dermatological application.

## RESULTS

### INFECTION PREVENTION

Hypochlorous acid has traditionally been used as a disinfectant and wound cleanser. Its antiseptic properties, coupled with cutaneous tolerability, contributes to its efficacy for use in wounds.<sup>10</sup> A comparative study assessed the efficacy of 0.01% hypochlorous acid, 5% povidone iodine (PI), 4% chlorhexidine gluconate (CHG), and 70% isopropyl alcohol (IPA) against common skin microorganisms using time-kill studies.<sup>5</sup> Researchers found 0.01% hypochlorous acid to be of equal or greater efficacy compared with PI, CHG, and IPA. HClO exhibited bactericidal effects against methicillin-resistant *S. aureus* and *S. epidermidis*; methicillin-susceptible *S. aureus*, *S. epidermidis*, and *S. capitis*; and *S. pyogenes*, *P. aeruginosa*, *C. acnes*, *C. albicans*, and *S. xylosus*.

A subsequent *in vivo* study assessed the antiseptic role of PI, CHG, IPA, and 0.01% hypochlorous acid on the facial skin of 21 participants.<sup>6</sup> Although CHG reduced bacterial growth to the greatest extent, there were no significant differences in bactericidal effects between HClO, PI, and IPA.<sup>6</sup> Whereas the prior study assessed bactericidal effects *in vitro*,<sup>5</sup> this study supports the role of hypochlorous acid as an antiseptic *in vivo*.<sup>6</sup>

Based on its antiseptic properties, researchers and clinicians have similarly assessed topical hypochlorous acid for specific skin conditions. In 2016, Howard et al describe a case in which a 60-year-old chemist with congenital erythropoietic porphyria (Gunther's disease) prepared a hypochlorous acid spray and hypochlorous acid gel.<sup>7</sup> The man exhibited lifelong photosensitivity, leading to multiple erosions with severe scarring and multiple secondary infections colonized with multi-resistant *Staphylococcus aureus*. During HClO treatment, the patient noted reduced frequency of antibiotic use, less redness and weeping, greater healing of erosions, and thinning of hyperkeratotic plaques; in addition, he reported increased well-being.<sup>7</sup> Although this is a single case, this report supports the investigation of topical hypochlorous acid for specific cutaneous

indications and highlights its potential utility in cases of increasing antimicrobial resistance.

Chapman et al further describe how the inability of bacteria to deactivate HClO and confer resistance makes hypochlorous acid particularly useful in some dermatologic procedures, such as cosmetic dermal fillers.<sup>11</sup> At their practice, the authors used a product containing hypochlorous acid and 120 parts per million of free available chlorine (FAC), to cleanse the skin prior to injection. A large, randomized controlled trial would be necessary to definitively conclude the prophylactic efficacy of topical hypochlorous acid prior to injection related procedures compared to other common topical pre-procedure antiseptics, such as isopropyl alcohol, chlorhexidine, and povidone-iodine; however, the studies conducted by Anagnostopoulos et al<sup>5</sup> and Tran et al<sup>6</sup> suggest hypochlorous acid to have similar efficacy *in vitro* and *in vivo*.

### WOUND CARE AND SCAR MANAGEMENT

Based on the antiseptic properties of hypochlorous acid, wound care is the most common medical application for HClO, and there is ample literature supporting its use for open wounds and diabetic ulcers. Furthermore, recent work has suggested such properties can similarly prevent adverse events and infections associated with skin grafting.<sup>12,13</sup> One significant benefit of hypochlorous acid application to infected wounds is the subsequent reduction in microbial load, reducing the need for systemic antibiotics, which can contribute to microflora dysbiosis and bacterial resistance.<sup>14</sup> Furthermore, the reduced bioburden can foster prompt healing. In contrast, whereas CHX and PI can similarly reduce the bioburden, their cytotoxic effect on keratinocyte may actually impede wound healing.<sup>15</sup>

Numerous reports have discussed or evaluated the efficacy of hypochlorous acid in reducing wound bioburden.<sup>16-21</sup> A study by Davis et al evaluated the efficacy of a hypochlorous acid-containing wound management solution (WMS) compared to sterile saline solution on methicillin-resistant *S. aureus* and healing in mouse models.<sup>19</sup> The authors found topical WMS and debridement to significantly reduce methicillin-resistant *S. aureus* contamination, and there was no difference between WMS and saline in epithelial thickness or granulation tissue formation. However, percent epithelization was significantly greater for the hypochlorous acid-containing WMS (78.3% vs. 67.8%,  $p \leq 0.05$ ), which is an important result as epithelization is considered a defining parameter of wound healing success.<sup>22</sup> Similarly findings have been demonstrated in human subjects. A randomized controlled trial including 308 patients and twelve study arms found efficacious bioburden reduction with various irrigation solutions; the authors ultimately suggested that solutions containing a combination of hypochlorite/hypochlorous acid or antiseptics such as polyhexanide, octenidine, or PI, should be considered for bioburden reduction.<sup>18</sup>

In addition to infection prophylaxis via reduced bioburden, the significantly increased percent epithelization of mouse wounds treated with hypochlorous acid compared to WMS, depicted by Davis et al,<sup>19</sup> suggests topical HClO may

directly foster wound healing success. Similarly, Burian et al conducted a randomized controlled trial with healthy volunteers and found hypochlorous acid to increase the degree of re-epithelization compared to the control solution, sterile 0.9% NaCl, with an estimated difference in re-epithelization degree of 14% (95% confidence interval 6.8-20%,  $p=0.00051$ ).<sup>21</sup> On day 10, however, this difference was non-significant, suggesting that topical hypochlorous acid is noninferior to sterile 0.9% NaCl, yet may foster a greater degree of initial re-epithelization.<sup>21</sup>

Additional studies are required to better understand the effect topical hypochlorous acid has on re-epithelization in comparison to other wound-cleansing agents. Furthermore, it is necessary to consider cytotoxicity and its impact on successful wound healing. A 2022 study evaluating cytotoxicity of common antiseptics found chlorhexidine gluconate and ethanol to significantly reduce the viability of keratinocytes; PI and chlorhexidine digluconate to significantly reduce fibroblast viability; and chlorhexidine gluconate, ethanol, and PI to each inhibit cell migration.<sup>23</sup> In contrast, sodium hypochlorite was the least destructive to both keratinocytes and fibroblasts.<sup>23</sup> Although hypochlorous acid was not included as a treatment group, it is possible that its cytotoxicity mirrors that of sodium hypochlorite. Future work is required to assess the cytotoxicity of topical HClO and the implications this may have on wound care.

Lastly, recent reports have suggested topical hypochlorous acid may be beneficial in the management of scars. A 2020 report from an expert panel composed of clinicians with cosmetic and surgical procedure experience concluded that topical stabilized HClO not only fosters wound healing but may also be optimal for reduced scarring, an important aspect in both dermatologic and plastic surgical procedures.<sup>24</sup> A 2015 randomized, double-blind study assessed the efficacy, safety, and tolerability of a hypochlorous acid scar gel, compared to 100% silicone gel, for the management of hypertrophic or keloid scars.<sup>25</sup> Outcome measures included the Vancouver Scar Scale (VSS), Investigator-assessed Subject Global Satisfaction, and Investigator Global Assessment (IGA) of Efficacy. At week 16, the hypochlorous acid-based scar gel demonstrated a greater average decrease in the vascularity, pliability, and height of scars, as measured by the VSS. Furthermore, whereas the IGA of efficacy at week 16 was good or very good in only 27.8% of patients receiving silicone gel, the IGA of efficacy was good or very good in 55% of patients receiving the scar gel. Both treatments were well tolerated.<sup>25</sup>

#### IMMUNOLOGIC ACTIVITY

Emerging clinical evidence supports the therapeutic use of hypochlorous acid formulations in the management and suppression of inflammatory skin conditions. Nuclear factor- $\kappa$ B, a regulator of cellular inflammation and aging, has been implicated in the pathogenesis of multiple cutaneous diseases including psoriasis and atopic dermatitis.<sup>26</sup> Prior work has demonstrated that hypochlorous acid-dependent cysteine oxidation inhibits the activity of IKK, a regulator of NF- $\kappa$ B activation, in mouse models.<sup>27</sup> Similarly, in hu-

man keratinocytes, HClO was found to reversibly inhibit the expression of two NF- $\kappa$ B-dependent genes.<sup>27</sup> By effectively targeting NF- $\kappa$ B signaling via inhibition of IKK, topical hypochlorous acid may provide therapeutic benefit for patients with inflammatory skin conditions.

Jandova et al discovered another potential mechanism for which topical hypochlorous acid can modulate dermatologic conditions.<sup>28</sup> Using SKH-1 mice, the researchers found topical HClO treatment to significantly downregulate inflammatory cytokine IL-19 mRNA and protein levels. As increased IL-19 expression has been associated with psoriasis, atopic dermatitis, and cutaneous T-cell lymphoma,<sup>29-31</sup> it is possible that IL-19 downregulation via HClO could effectively modulate disease-associated inflammation and tumorigenesis. In addition, topical HClO has been demonstrated to decrease tumor necrosis factor- $\alpha$ , interferon gamma, IL-2, and histamine.<sup>32</sup> Although the clinical benefit of topical hypochlorous acid for psoriasis remains largely hypothetical, mouse and human studies have depicted its potential efficacy in the management of atopic dermatitis, potentially due to the immunomodulatory mechanisms described by Jandova et al<sup>28</sup> and Vakharia et al.<sup>32</sup>

#### TREATMENT IN ATOPIC DERMATITIS AND PRURITUS

Sodium hypochlorite, commonly known as bleach, has been used to reduce bacterial colonization and severity of atopic dermatitis. Hypochlorous acid, however, is more reactive than sodium hypochlorite,<sup>33</sup> and its use for atopic dermatitis has been less extensively studied. Preclinical studies using mouse models have suggested topical HClO may reduce pruritus. A study utilizing mice with house dust mite-induced itch found significantly reduced scratching behavior in those treated with topical hypochlorous acid.<sup>34</sup> After full development of lesions, hypochlorous acid administration reduced scratching behavior nearly to the same extent as 0.1% betamethasone dipropionate ointment. The authors also observed reduced secretion of inflammatory cytokines in affected skin tissue, reduced IL-12 production in bone marrow-derived dendritic cells, and impaired response to pruritogens in excised dorsal root ganglia neurons. Taken together, these results suggest reduced inflammation and sensory response are implicated in hypochlorous acid's ability to significantly reduce itch.<sup>34</sup>

A 2018 study compared the efficacy of 0.1% hypochlorous acid in gel vs. tofacitinib, a Janus kinase inhibitor in human clinical studies for the treatment of atopic dermatitis, for the improvement of pruritus.<sup>35</sup> Both treatments reduced lesions and scratching behavior, and affected skin tissue showed diminished inflammatory cytokines. As demonstrated by Fukuyama et al in their prior study,<sup>34</sup> the dorsal root ganglia neurons showed a reduced response with both treatments compared to control mice.<sup>35</sup>

The potential utility of hypochlorous acid in atopic dermatitis has further been demonstrated in human subjects. In 2012, Draelos and Cash presented a case series in which twenty human subjects with atopic dermatitis experienced statistically significant reductions in pruritus at day 3 with topical HClO treatment; however, this case series omitted

a control group.<sup>36</sup> In 2017, Berman and Nestor showed that topical hypochlorous acid significantly reduced atopic dermatitis-associated itching in as little as 3 days in thirty participants.<sup>37</sup> The results demonstrated that 73.7% of subjects treated with hypochlorous acid experienced a reduction in itching between baseline and 72 hours post application, compared to 30.0% of the untreated control group. The authors concluded that HClO is cost-efficient and effective in the management of pruritus in patients with atopic dermatitis.

Lastly, a study involving twenty-two patients with atopic dermatitis assessed the efficacy of acid electrolytic water (AEW) on colony counts of *S. aureus* on skin lesions and grading scores of atopic dermatitis.<sup>38</sup> Electrolyzed water refers to the electrolysis of tap water containing dissolved sodium chloride, which produces hypochlorous acid. Grading scores of atopic dermatitis were significantly decreased in the AEW group ( $p < 0.01$ ), but not in the placebo group receiving tap water.<sup>38</sup> Furthermore, the authors found a significant reduction in *S. aureus* colony counts three minutes after spraying ( $p < 0.05$ ) and after one week of treatment ( $p < 0.01$ ) in the AEW group only. This suggests that *S. aureus* reduction may act as a mechanism for which topical hypochlorous acid can yield clinical improvement of atopic dermatitis.<sup>38</sup>

This hypothesis has similarly been discussed by Pelgrift and Friedman who propose two potential mechanisms by which hypochlorous acid can reduce pruritus associated with atopic dermatitis.<sup>39</sup> First, as previously discussed, hypochlorous acid is thought to be microbicidal to cutaneous pathogens associated with atopic dermatitis, such as *S. aureus*. Second, hypochlorous acid is anti-inflammatory and reduces the activity of histamine, leukotriene B<sub>4</sub>, and interleukin-2, which are collectively implicated in the pathophysiology of itch. Larger randomized controlled trials are required to further assess the efficacy of pruritus reduction in human subjects with atopic dermatitis, although this appears a promising field of novel research.

#### OTHER DERMATOLOGIC APPLICATIONS

Despite the relative scarcity of literature supporting hypochlorous acid use in other dermatologic conditions, published reports have assessed the efficacy of topical HClO for seborrheic dermatitis and acne vulgaris. In 2014, a safety and efficacy study evaluated the use of a hypochlorous acid-based topical product on 25 patients with mild to moderate facial and scalp seborrheic dermatitis.<sup>40</sup> The HClO-based gel depicted significant improvements from baseline in both the Investigator Global Assessment (IGA) and the Subject Global Assessment (SGA). On day 14, there was an average IGA improvement of 33% and an average SGA improvement of 217%, with further improvement noted in both measures on day 28. Few participants experienced a complete resolution of symptoms, although symptoms of burning, stinging, and itching decreased. Furthermore, the gel was tolerated by all subjects except one, who experienced increased erythema and scaling of the scalp. These results appear promising for the use of HClO for symptom management of seborrheic dermatitis, although

larger, randomized, and controlled trials are required to better assess efficacy compared to standard treatment.

Another study assessed the efficacy and tolerance of superoxidized solution in the treatment of mild to moderate inflammatory acne.<sup>41</sup> Superoxidized solutions (SOS) are created by passing an electric current through a solution of sodium chloride dissolved in water, and they contain hypochlorous acid. The study included benzoyl peroxide (BP), a topical antiseptic used for the treatment of acne, as a second treatment group. Excellent improvement was observed in 23% of SOS subjects and 21% of BP subjects; good improvement was observed in 54% of SOS subjects and 50% BP subjects. There was no significant difference in outcomes between the SOS and BP treatment groups, and both exhibited markedly superior results to placebo. This study depicted the potential efficacy of hypochlorous acid in the treatment of mild to moderate acne vulgaris and found no significant differences in efficacy between HClO and benzoyl peroxide.

#### TUMOR SUPPRESSION

A burgeoning area of research has focused on the role of HClO on tumor suppression.<sup>42,43</sup> The p53 gene is a tumor suppressor gene that stops the progression of uncontrolled cellular division leading to cancer. One study identified HClO as the oxidative compound responsible for an increase in p53 to aid at sites of inflammation.<sup>44</sup> HClO helped to upregulate the p53 protein in a dose-dependent manner in a culture of human skin fibroblasts containing MPO and H<sub>2</sub>O<sub>2</sub>.<sup>44</sup> Simultaneously, p53 was also produced by H<sub>2</sub>O<sub>2</sub> generated from glucose oxidase, but a flux 10-fold greater was required to produce similar levels of p53 increased by HClO from MPO and glucose oxidase.<sup>44</sup> This study was one of the first studies to demonstrate the role of HClO in suppressing tumor progression.

As a topical, HClO has early animal-based evidence for uses in solar-induced skin damage and melanoma. A study was conducted with transgenic SKH-1 mice to understand the potential therapeutic effects of topical HClO on tumorigenesis.<sup>28</sup> Without HClO, there was a pronounced upregulation of inflammatory genes associated with nitric oxide and prostaglandins activated in carcinogenesis.<sup>28</sup> However, pretreatment with topically applied HClO completely attenuated expression of these inflammatory genes.<sup>28</sup> Although only tested in a murine model, this study highlights the potential for HClO to be used in targeting early development of cutaneous cancerous progression. Further human clinical studies will help delineate the effects of topical HClO in relation to sun related cutaneous skin damage.

#### SAFETY

Although ample research has explored irritation factors associated with diluted sodium hypochlorite (bleach), there exists a relative scarcity of literature detailing the safety of topical hypochlorous acid. Although not directly toxic to the skin itself, dilute sodium hypochlorite can irritate the skin and eyes, and it has been associated with contact

dermatitis and other reactions.<sup>45–49</sup> However, hypochlorous acid has been deemed to have a good safety profile.<sup>50</sup>

Few reports have detailed adverse effects of topical hypochlorous acid. No evidence of ocular irritation was uncovered in Dutch pigmented rabbits with the application of 0.01%, 0.03%, and 0.1% hypochlorous acid.<sup>16</sup> Furthermore, application of multiple concentrations exhibited no evidence of dermal irritation.<sup>16</sup> In 1991, however, a cytotoxic effect of a higher concentration of hypochlorous acid, 0.25%, on dorsal Sprague Dawley rat tissue was shown.<sup>51</sup> Additional research is required to determine the safety profiles of differing concentrations of topical hypochlorous acid. A 2019 study assessed the safety profiles of different solutions of hypochlorite/hypochlorous acid.<sup>52</sup> However, as such solutions also contained sodium hypochlorite that is associated with irritation and contact dermatitis, it is difficult to conclude the effects of hypochlorous acid alone in that particular study.

In 2021, an *in vivo* study analyzed the safety of stabilized-hypochlorous acid in an acetic acid buffer for the treatment of wounds. Of twelve subjects, two reported frequent, but quickly resolving pain, and excellent wound healing was observed.<sup>53</sup> Ultimately, this pilot study provided support for the efficacy and tolerability of topical hypochlorous acid, although larger studies are required.

Additional work is required to determine the concentration of hypochlorous acid that maximizes efficacy yet minimizes irritation for specific indications, such as wound healing and atopic dermatitis. Pelgrift and Friedman warn that high-dose or prolonged cutaneous exposure may actually increase pruritus by causing conditions in which itching is a primary symptom, such as irritant contact dermatitis and allergic contact dermatitis.<sup>39</sup> Furthermore, due to the possibility of Type I and Type IV HClO-induced hypersensitivity reactions, and as rare cases of HClO-induced non-immunologic contact urticaria (NICU) have been reported, it is recommended that patients consider an open skin test or skin prick test to detect HClO-induced Type I hypersensitivity or HClO-induced NICU prior to use if there is concern for possible hypersensitivity.<sup>39</sup>

Overall, the literature suggests that topical hypochlorous acid is well-tolerated in low concentrations. As hypochlorous acid partially dissociates into its anion, hypochlorite, which has been associated with contact dermatitis and irritation, similar adverse effects may be associated with hypochlorous acid use, especially at higher concentrations.

## DISCUSSION AND CONCLUSION

There are two primary limitations of this review. First, the properties of hypochlorous acid in solution depend on the pH. Alterations in a solution's pH can cause hypochlorous acid to react, resulting in HClO in equilibrium with reaction products.<sup>39</sup> For example, in a solution of hypochlorous acid in aqueous 0.9% NaCl, HClO is stable at pH between 3.5 and 5.5; at higher pH levels, however, HClO donates its hydrogen atom and forms hypochlorite.<sup>39</sup> Current literature on the use of hypochlorous acid, both *in vitro* and *in vivo*, of-

ten does not address pH considerations. Secondly, reports have discussed the efficacy and safety of differing concentrations of hypochlorous acid, reducing the ability to make direct comparisons between studies.

Nonetheless, the results have depicted topical hypochlorous acid to be relatively safe and potentially useful in the management of infection, wounds, scarring, atopic dermatitis, pruritus, seborrheic dermatitis, and acne vulgaris. Safety results suggest that lower concentrations of hypochlorous acid may reduce cytotoxicity, and further research is required to evaluate topical formulations that maximize efficacy and minimize toxicity.

Furthermore, numerous studies evaluated the efficacy of hypochlorous acid against other approved topical formulations. An *in vitro* study found 0.01% hypochlorous acid to be of equal or greater efficacy as 5% povidone iodine, 4% chlorhexidine gluconate, and 70% isopropyl alcohol against common skin microorganisms.<sup>5</sup> *In vivo*, chlorhexidine gluconate reduced bacterial growth on facial skin to the greatest extent, although no significant differences existed between hypochlorous acid, povidone iodine, and isopropyl alcohol.<sup>6</sup> As PI, CHX, and IPA are commonly used as bactericides, the results suggest hypochlorous acid to be as efficacious as currently approved formulations. Furthermore, hypochlorous acid may be superior in cases of wound healing due to reduced keratinocyte cytotoxicity, which otherwise may impede wound healing.<sup>15</sup>

In addition, a study assessing the efficacy of superoxidized solution in the treatment of mild to moderate inflammatory acne included benzoyl peroxide as a second treatment group and found no significant differences in outcomes between the SOS and BP groups.<sup>39</sup> This is an important finding, as benzoyl peroxide has already been approved by the FDA for the treatment of acne. Ultimately, additional randomized, controlled trials with sufficient sample sizes are required to assess the efficacy of topical hypochlorous acid in comparison to approved treatments for such dermatologic conditions. However, the results of this review suggest hypochlorous acid may exhibit clinical utility in dermatology and dermatologic surgery and should be utilized in future dermatological clinical studies.

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None

## DISCLOSURES

Raja Sivamani, MD, MS, AP is a Scientific Advisor for Learn-Health, Codex Labs, and Arbonne and serves as a consultant for Burt's Bees, Novozymes, Nutrafol, Abbvie, Incyte, Fotona, Sanofi, Leo, UCB, Sun and Regeneron Pharmaceuticals. Jessica Maloh, ND, serves as a consultant for Codex Labs. The other authors report no conflicts.

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