doi:10.36849/JDD.2025.NVRN0525

NEWS, VIEWS, AND REVIEWS

All Things Acid: A Primer on Alpha Hydroxy, Beta Hydroxy, and Polyhydroxy Acids

Savanna I. Vidal BS, Nikita Menta BA, Adam Friedman MD FAAD

Department of Dermatology, George Washington University School of Medicine and Health Sciences, Washington, DC

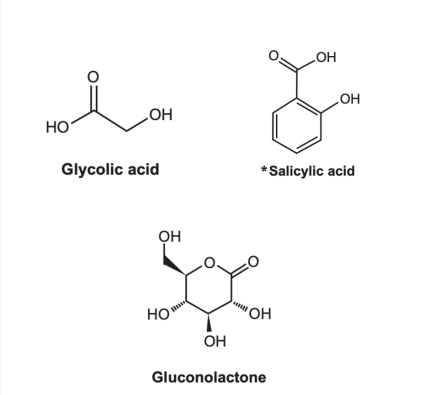
INTRODUCTION

Hydroxy acids (HAs) are a diverse class of topical agents with a decades-long tenure in dermatology, used for acne, ichthyosis, keratoses, warts, psoriasis, and photoaging. HAs are classified into alpha HAs (AHAs), beta HAs (BHAs), and polyhydroxy acids (PHAs). AHAs, introduced in the 1970s, promote cell turnover and collagen synthesis, while BHAs provide keratolytic, antimicrobial, and anti-inflammatory benefits. PHAs, a newer generation HA, offer similar effects to AHAs with added humectant properties and less irritation. HAs are formulated in low concentrations for over-the-counter (OTC) skincare, and higher concentrations for prescription chemical peels.[1] Given their long-standing and widespread use, dermatologists must understand their nuances to optimize treatment recommendations and patient safety.

Chemical Structure and Properties

HAs are classified by the position of their hydroxyl (-OH) group relative to their carboxyl (-COOH) group, influencing solubility, penetration, and biological activity. AHAs and BHAs are carboxylic acids with a hydroxyl group at the α-position and β-position, respectively. PHAs contain two or more hydroxyl groups, including at least one in the α-position (Figure 1).[1]

Figure 1. Structures of a representative AHA (glycolic acid), BHA* (salicylic acid), and PHA (gluconolactone).[1]



*Controversy exists regarding salicylic acid's classification as a BHA.

Low molecular weight AHAs, such as glycolic acid (GA) and lactic acid (LA), penetrate the skin most effectively, whereas larger AHAs, like tartaric and mandelic acid (MA), offer milder exfoliation with less irritation. Most AHAs are water-soluble, though lipophilic AHAs like MA better penetrate the skin.[2,3] Salicylic acid (SA), the most well-known BHA, is technically misclassified as such due to structural and functional differences. Being lipid-soluble, BHAs penetrate sebaceous follicles, while PHAs' increased molecular size limits deeper penetration. Gluconolactone, a PHA, metabolizes into an AHA, possessing similar benefits to AHAs while also acting as a humectant and antioxidant.[1,4]

Mechanisms of Action

AHAs promote exfoliation by disrupting cellular adhesions within the epidermis, likely through calcium ion chelation, weakening intercellular adhesion and facilitating desquamation. In vitro and ex vivo investigations demonstrate GA's role in enhancing collagen synthesis, modulating matrix degradation, increasing epidermal thickness, and upregulating hyaluronic acid production. LA has been shown to increase vascular endothelial growth factor and contribute to wound healing. Both GA and LA accelerate epidermal turnover and inhibit tyrosinase, improving superficial pigmented lesions. PHAs offer skin-smoothing, anti-aging, and moisturizing effects without skin irritation, while gluconolactone has demonstrated photoprotective properties.[1]

SA, a keratolytic, possesses photoprotective and antimicrobial properties. Both animal and human studies have shown SA can lessen ultraviolet penetration, while preclinical studies showed its ability to modulate and downregulate bacterial virulence factors. β-lipohydroxy acid, an SA derivative, exhibits antibacterial, antifungal, anti-inflammatory, and anti-comedogenic activity.[1]

Clinical Applications

HAs are widely used to treat various dermatologic conditions. GA is effective for hyperpigmentation, including post-inflammatory hyperpigmentation (PIH), melasma, and sun-induced discoloration. While GA aids in acne treatment through exfoliation, SA's anti-inflammatory and antimicrobial properties make it particularly

beneficial for treating acne and psoriasis. PHAs are useful for photoaging and rosacea, especially in individuals with comorbid sensitive skin (SS).[1]

For acne vulgaris, both AHAs and BHAs show efficacy, though SA is often preferred. While widely used, evidence supporting their use is often limited to small, single-center studies. In a study of 97 adults with acne, a daily cream with low-potency AHAs and BHAs combined with a topical retinoid significantly reduced acne lesions (P<0.001) over 12 weeks compared to moisturizers alone. Another study of 17 patients using a daily 2% SA cleanser and spot treatment with a barrier gel cream showed improvements in acne-related erythema in all enrollees over 6 weeks.[5,6] Notably, GA outperforms SA for the treatment of PIH secondary to acne. In a randomized trial, 45% of 20 patients treated with 50% GA showed >75% PIH reduction, while none of the 20 patients treated with 30% SA exhibited improvement.[7]

For photoaging, AHAs like GA improve skin texture by increasing collagen synthesis and epidermal turnover.[1] PHAs are comparable to SA in treating photoaging, and are preferable for SS.[1,3,8] In one study of a topical lotion containing MA, SA, and gluconolactone, applied daily to 389 subjects (116 with SS), significant exfoliation was noted by day 3 (P<0.05), with clinical improvements in skin texture and tone both immediately after the first application and after 28 days (P<0.05). The lotion was well tolerated, with an 89% global SS score reduction among participants.[9] A similar study in 30 patients using a combination of AHA/BHA/PHA topical showed improved skin appearance without irritation nor sensitization.[10]

Beyond photoaging, gluconolactone can improve the signs and symptoms of rosacea. In a study of 67 females with rosacea, a 4% gluconolactone facial cleanser and 10% gluconolactone moisturizing cream combined with 15% azelaic acid gel outperformed azelaic acid gel alone in reducing mean erythema score (P=0.012 at week 8, P=0.001 at week 12). Participants in the gluconolactone-treated group also exhibited reported pronounced improvements in skin itching (week 8, P=0.045) and stinging (week 12, P=0.029).[4]

Safety Considerations

The concentration-dependent effects of HAs determine their clinical efficacy and tolerability. To minimize skin irritation and/or dryness, lower concentrations (<10% for AHAs and <3% for BHAs) and an AHA pH at or above 3.5 were recommended for use in cosmetic formulations by the Cosmetic Ingredient Review Expert Panel in 1998. Higher concentrations are reserved for professional chemical peels as with increasing concentrations, efficacy improves, but so does the risk of adverse effects. Despite the potential for GA to enhance barrier function, excessive exfoliation may lead to barrier impairment, resulting in greater transepidermal water loss and sensitivity. Additionally, increases in skin renewal may disrupt the balance between cell proliferation and differentiation, potentially compromising skin integrity.[1]

A key limitation of these acids is their potential to increase skin sensitization in response to external stressors. In a study of 26 subjects, 10% GA was shown to enhance the skin's sensitivity to solar-simulated radiation (SSR), increasing the risk of UV-induced damage. While this effect was reversible upon discontinuation, it underscores the importance of consistent sunscreen use when incorporating AHAs into skincare routines and the need for careful patient counseling to ensure appropriately timed application. Studies in murine models suggest that GA does not enhance photocarcinogenesis, while SA 4% has a potential photoprotective effect through the reduction of erythema response, lessening the carcinogenicity of SSR.[1] Elucidation of the effects of long-term ultraviolet exposure in human skin treated with HAs requires further investigation.

CONCLUSION

HAs remain a cornerstone of dermatologic care, offering diverse benefits from exfoliation to anti-aging effects. Their efficacy varies by active ingredient and concentration, requiring individualized selection of HA type, formulation, and potency to elicit desired results. Future research should focus on investigating long-term safety, enhancing formulations, and promoting the responsible use of HAs to maximize efficacy and minimize adverse effects.

DISCLOSURE

SIV's work is funded through an independent research grant from Galderma. NM's work is funded through independent research grants from Incyte and Johnson & Johnson. AF is a member of the Galderma Sensitive Skincare Faculty.

REFERENCES

1. Kornhauser A, Coelho SG, Hearing VJ. Applications of hydroxy acids: classification, mechanisms, and photoactivity. *Clin Cosmet Investig Dermatol.* 2010;3:135-142. Published 2010 Nov 24.
2. Almeman AA. Evaluating the Efficacy and Safety of Alpha-Hydroxy Acids in Dermatological Practice: A Comprehensive Clinical and Legal Review [published correction appears in Clin Cosmet Investig Dermatol. 2024 Aug 30;17:1973-1974. doi: 10.2147/CCID.S493491.]. *Clin Cosmet Investig Dermatol.* 2024;17:1661-1685. Published 2024 Jul 16.
3. Green BA, Yu RJ, Van Scott EJ. Clinical and cosmeceutical uses of hydroxyacids. *Clin Dermatol.* 2009;27(5):495-501.
4. Draelos ZD, Green BA, Edison BL. An evaluation of a polyhydroxy acid skin care regimen in combination with azelaic acid 15% gel in rosacea patients. *J Cosmet Dermatol.* 2006;5(1):23-29.
5. Chlebus E, Serafin M, Chlebus M. Is maintenance treatment in adult acne important? Benefits from maintenance therapy with adapalene, and low doses of alpha and beta hydroxy acids. *J Dermatolog Treat.* 2019;30(6):568-571.
6. Bhatia N, Donald A, Mariwalla K. Efficacy and Consumer Perception of Topical Over-the-Counter Regimens Involving Beta-Hydroxy Acid for Acne Vulgaris. *J Drugs Dermatol.* 2025;24(2):162-166.
7. Ravikumar B, Indradevi R, Pillai D. Efficacy of alpha and beta hydroxy acid chemical peels in postacne pigmentation: a double blinded, randomized, controlled trial. *J Clin Aesthet Dermatol.* 2022;15(1):48-52.
8. Edison BL, Green BA, Wildnauer RH, et al. A polyhydroxy acid skin care regimen provides antiaging effects comparable to an alpha-hydroxyacid regimen. *Cutis.* 2004;73(2 Suppl):14-17.
9. Morsel M, Zielinski Y, Grivet-Seyvel M, et al. Addressing an unmet need for sensitive skin: A formulation to enable daily exfoliation. Presented at the *American Academy of D Poster Exhibition.* March 2025.
10. Konisky H, Bowe WP, Yang P, et al. The clinical efficacy and tolerability of a novel triple acid exfoliating blend for reducing signs of photoaging in sensitive skin. *J Cosmet Dermatol.* 2024;23(9):2982-2988.

AUTHOR CORRESPONDENCE

Adam Friedman MD FAAD

E-mail:.....ajfriedman@mfa.gwu.edu