

Photoprotective and Antiinflammatory Effects of Topical Glycolic Acid

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BACKGROUND. Concerns about photosensitizing potential of alpha hydroxy acids have been expressed. A previous study, however, reported topical glycolic acid showing the opposite potential, that is, photoprotective. This study was designed to test the antiinflammatory and photoprotective capabilities of glycolic acid.

OBJECTIVE. The effects of short-wave ultraviolet light (UVB) on skin treated with glycolic acid were evaluated in two different studies at two different locations.

METHODS. In the first study the antiinflammatory potential of topical glycolic acid was tested on erythematous templates on the backs of human volunteers. Erythema was induced by exposure to three times the minimum erythema dose (MED) of UVB. Glycolic acid cream in an oil-in-water vehicle at 12% partially neutralized with ammonium hydroxide to a pH of 4.2 was applied to the template beginning 4 hours postirradiation four times a day. A second template on the same subject was used as a vehicle control. After 48 hours a marked reduction of erythema was noted when compared with the vehicle control site. In the second study, four test sites were exposed to UVB light in the following manner. Site 1 was a nontreated control site and was used to establish the MED for the subjects being tested; site 2 was also exposed to a MED series but was treated 24 hours postirradiation for 7 days with two glycolic acid-based products (cleanser and oil-free moisture lotion, both containing 8.0%

glycolic acid at a pH of 3.25); site 3 was treated first with the two glycolic acid-based formulas for 3 weeks prior to being exposed to UVB light; and site 4 was treated as outlined in site 3, with the inclusion that the site was chemically peeled for 6 minutes (with a 50% glycolic solution at a pH of 2.75) 15 minutes prior to UVB exposure.

RESULTS. When UVB-burned skin was treated with glycolic acid daily for 7 days (site 2), a 16% reduction in irritation was observed compared to nontreated skin (site 1), implying that skin healed sooner when treated with glycolic acid. When a comparison of nontreated skin was made to skin treated with glycolic acid for 3 weeks prior to UVB exposure (site 1 vs site 3), a sun protection factor (SPF) of 2.4 was achieved. When a comparison of skin treated for 3 weeks was made to skin treated for 3 weeks and chemically peeled (site 3 vs site 4) the data implied that the chemical peel reduced the SPF value of skin treated with glycolic by approximately 50%, however, an SPF trend of 1.7 was still obtained when compared with untreated skin.

CONCLUSIONS. The studies demonstrated that topical glycolic acid provides a photoprotective effect to pretreated skin yielding an SPF of approximately 2.4. In addition, when glycolic acid is applied to irradiated skin, it accelerates resolution of erythema. The data obtained from both studies support the hypothesis that glycolic acids acts as an antioxidant. *Dermatol Surg* 1996;22: 435-437.

The use of the alpha hydroxy acids (AHAs) as a topical therapeutic and cosmetic agent has expanded dramatically over the last 5 years. Initially, AHAs were used primarily in treatment of hyperkeratotic skin disorders. As these agents gained popularity, additional benefits began to be observed and reported relating to photo-aging, hyperpigmentation, acne, pseudofolliculitis barbae, as well as general enhancements of normal skin. Because of these findings, approximately 45 companies are currently manufacturing over 200 different AHA-containing products. In addition to its use as a therapeutic and cosmetic ingredient, physicians and aestheticians are performing

chemical peels, using primarily glycolic acid in high concentrations. There has been growing concern about the widespread use of AHAs, because of their known ability to thin stratum corneum tissue,¹ which could result in a potential photosensitivity reaction and/or increased photo-trauma. Conversely, Perricone reported on the antiinflammatory effects of the topical glycolic acid on short wave ultraviolet light (UVB)-induced erythema,² a phenomenon that demonstrated the opposite potential of that which one would anticipate. This paper further reports on that research as well as explores the use of glycolic acid-containing products as a means of adding additional sun protection to the skin when applied prior to UVB irradiation.

Methods

This study was divided into two stages. The first segment of the study re-examined the therapeutic effect of topical glycolic acid after UVB exposure to skin. The second portion of the

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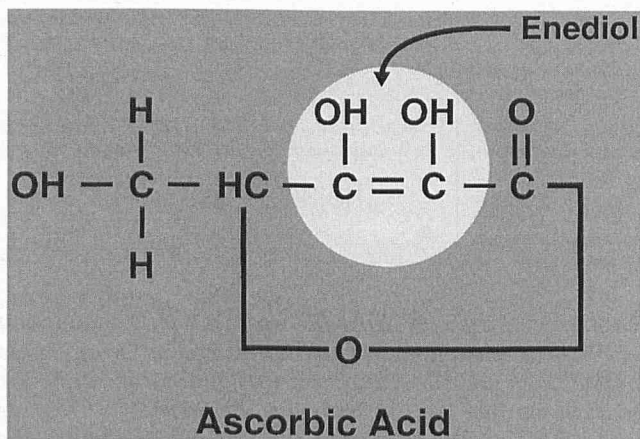


Figure 1. Schematic of an enediol structure characteristic of antioxidants such as Vitamin C.

study examined the effects of UVB exposure to skin previously treated with glycolic acid.

Segment 1

The antiinflammatory potential of topical glycolic acid was tested on erythematous templates on the backs of human volunteers. Erythema was induced on the backs of volunteers in a 2-cm template by exposure to three times the minimum erythema dose (MED) of UVB. Glycolic acid cream, in an oil-in-water vehicle at 12% partially neutralized with ammonium hydroxide to a pH of 4.2, was applied to the template beginning 4 hours postirradiation four times a day. A second template on the same subject was used as a vehicle control.

Segment 2

Five subjects were exposed to an MED series on nontreated skin using a xenon arc lamp on two adjacent test sites. Twenty-four hours after exposure, one site received daily applications of the two products containing 8.0% glycolic acid, partially neutralized with ammonium hydroxide to a pH of 3.25. Both test sites were graded for erythema after 1, 2, 3, 4, and 7 days postirradiation. A third site received daily applications of the two glycolic acid based formulas for 3 weeks. Twenty-four hours after the last product application, the test site was irradiated with an MED series and evaluated for erythema on days 1-7 post irradiation. A fourth site was treated in an identical manner as the third site, with the inclusion that 15 minutes prior to irradiation the area was chemically peeled with 50.0% glycolic acid, partially neutralized with ammonium hydroxide to a pH of 2.75.

Results

Segment 1

Five subjects treated with topical glycolic acid showed marked reduction of erythema at 48 hours when compared with the vehicle control site. At 72-96 hours, the treated site revealed hyperpigmentation, while the control site displayed erythema.

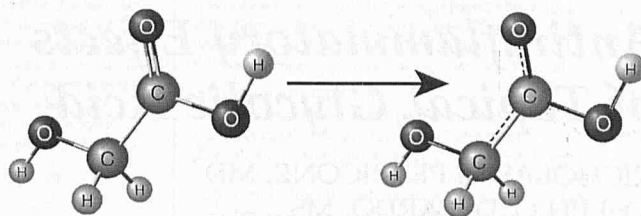


Figure 2. Illustration of hypothesized resonating double bond between carbons in glycolic acid, resulting in a transient enediol structure, which gives the molecule its antioxidant capabilities.

Segment 2

Comparison of the two untreated adjacent irradiated test sites demonstrated that a 7.0%, 13.0%, and 16.0% reduction in irritation can be achieved after daily application of the products to UVB-damaged skin. When the glycolic acid products were applied daily for 3 weeks and then irradiated by UVB, a sun protection factor (SPF) of 2.4 was achieved. In comparison, the site that was treated daily for three weeks with the two glycolic acid based products and then peeled 15 minutes prior to irradiation by UVB maintained an SPF trend of 1.7.

Discussion

These studies were conducted to illustrate the antiinflammatory effects of topical glycolic acid on UVB-irradiated skin. UV irradiation of skin results in erythema, which acts as an inflammatory model. UV irradiation of skin results in the generation of reactive oxygen species, which partially accounts for the appearance of erythema, indicating inflammation. The arachidonic acid cascade is activated by UV light, resulting in the production of inflammatory mediators, which perpetuate the production of free radicals. This quickly depletes the endogenous antioxidant defenses.³

Several studies have illustrated the ability of antioxidants to partially attenuate the erythema caused by UV radiation.^{4,5} Antioxidants act as antiinflammatories; however, not all antiinflammatories are antioxidants. These studies confirmed previous findings that topical glycolic acid can facilitate resolution of erythema after UVB exposure. This apparent antiinflammatory activity may be attributed to the molecule's ability to act as an antioxidant. Glycolic acid has a molecular structure similar to ascorbic acid, an antioxidant that owes its activity to the existence of an enediol within the molecule (Figure 1). Enediols are seen in many antioxidants and it is hypothesized that the double bond of the carboxylic acid group in glycolic may resonate between the two carbons, resulting in a transient enediol structure (Figure 2). Another possible explanation of the apparent antioxidant activity of glycolic acid may lie in its ability to chelate metals. Ferrous iron, which is found in skin,

acts as a prooxidant and thus can increase production of reactive oxygen species after ultraviolet radiation. Glycolic acid may chelate the free iron, and thus reduce free radical production by removal of this prooxidant in the skin. Additionally, when glycolic acid products are applied to the skin, prior to UVB irradiation, the skin appears to be more resilient to UVB damage, even after the skin was chemically peeled. The latter is a critical consideration when chemical peeling is desired to minimize any potential UV damage.

Conclusion

The studies demonstrated that topical glycolic acid provides a photoprotective effect to pretreated skin, yielding an SPF factor of approximately 2.4. In addition, when glycolic acid is applied to irradiated skin, it accelerates resolution of erythema. These data provide support for the hypothesis that glycolic acid acts as an

antioxidant. Despite the early concerns of the dangers of sun exposure on the thin stratum corneum secondary to AHA use, the study indicates a protective effect. The current trend of daily use of topical glycolic acid thus may provide some photoprotection and resultant decrease of photo-aging and perhaps carcinogenesis.

References

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