Glycolic Acid Skin Care Literature Review
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Alpha-hydroxy acids (AHAs), particularly glycolic acid, are widely used in skin care products and are claimed to reduce wrinkles and the signs of aging and to improve the overall look and feel of skin. Over-the-counter AHA-based products are currently limited to 10% AHA. However, glycolic acid at concentrations up to 25% is in use for chemical peels in the clinical setting of the dermatologist’s office. Glycolic acid is also used as an adjuvant to enhance the efficacy of other therapeutic agents in clinical applications. This essay summarizes published findings related to the efficacy of glycolic acid in skin care products.

This summary covers literature extending from 1994 to 2009, emphasizing review articles in the scientific and medical literature. The scope includes investigations of glycolic acid itself, as well as comparison to other AHAs, retinoids, peptides, and botanicals. The investigations cited in this literature summary include clinical studies with human volunteers, histological evaluations, animal studies, in vitro mechanistic studies, and use of AHAs as adjuvants for other active ingredients.

Some investigators classify AHAs as examples of “cosmeceuticals”, which are cosmetic products claimed to have biologically active ingredients with medicinal or drug-like benefits. Functions of various cosmeceuticals include: Skin-whitening / depigmenting, Moisturizing, Antiwrinkling, and Antiphotoaging. Clinicians warn that certain cosmeceuticals can cause unwanted problems including skin irritation, contact dermatitis, photosensitivity, comedogenicity (acne generating), hair and nail damage, hyper- and hypo-pigmentation, infectivity, carcinogenicity, and even systemic adverse effects. Therefore, proper cosmeceuticals use must weigh the benefits against any possible risks. This consideration illustrates the need for proper scientific validation of the claims of skin care agents. Retinoids, peptides, and botanical extracts likewise fall under the category of cosmeceuticals.

Anti-Aging Effects

Clinicians distinguish between intrinsic (natural) aging and extrinsic aging, which is generally due to sun exposure. Sunlight generates reactive oxygen molecules which degrade connective tissue in the skin, especially collagen and keratin, causing the extrinsic aging effects. Over-the-counter skin care products are aimed at reversing the effects of aging due to sun exposure.

The skin care effects of glycolic acid are manifold, including reducing cell cohesiveness in the stratum corneum layer of the epidermis. The stratum corneum is the outermost layer of the epidermis, consisting of remnants of dead cells that are large and flat, being filled with keratin. The reduction in cohesiveness of cells in the stratum corneum results in exfoliation and cell turnover. Deeper in the epidermis, skin
normalization includes increasing thickness, improving the differentiation of the cell times among the layers of the epidermis, and evening out pigmentation. Glycolic acid brings about an increase in the undulating patterns that occur between the epidermis and the dermis of the skin. It promotes elastic fiber distribution, increased collagen synthesis, and hyaluronic synthesis. All of these effects result in a more youthful appearance.

Several studies establish the histological basis of these anti-aging effects. Direct evidence for modulation of skin keratinization and biosynthesis of dermal components has been derived from data on skin thickening of human subjects. The effect is not due to edema or other undesirable reaction to the AHAs because the effect persists for many weeks to months after the end of therapy. In a statistically designed study of 65 patients treated with 15% glycolic acid for 6 months, the skin thickening increased 27% over control (p < 0.01), even greater than the effect induced by 0.01% estradiol applied similarly. Electrical conductivity studies of skin show the moisturization effects of glycolic acid, electrical conductivity tracking the moisture content of the stratum corneum. A double-blind vehicle control study of photoaged skin treated with 50% glycolic acid showed a decrease in rough texture and fine wrinkling, fewer solar keratoses [sunspots on the skin], and a slight lightening of solar lentigenes [age spots]. Some histologic specimens revealed an increase in collagen thickness in the dermis.

A clinical study by the NeoStrata group confirms that glycolic acid treatment increases type 1 collagen mRNA and hyaluronic acid content of human skin, after a treatment regimen consisting of 20% glycolic acid lotion applied to the skin of the human forearm twice daily for 3 months in comparison to a vehicle control. These findings are corroborated by other in vivo studies supplemented by an in vitro study revealing the increase of collagen synthesis in cell culture as induced by glycolic acid. The pH and concentration dependence of glycolic acid induced skin repairing effects of glycolic acid shows that increasing the pH may increase efficacy, while glycolic acid is effective across a broad pH range.

In comparison to physical exfoliation, glycolic acid based exfoliation peel improves the cosmetic appearance of photo-aged skin as revealed in a clinical study. In this study, 28 patients with moderate to severe photodamaged skin on the back of the hands were evaluated. After 10 weeks, 95% of the GA-treated hands showed significant improvement. Another clinical study of glycolic acid peels revealed that 9 of the 10 patients in the trial showed overall significant improvement in photodamaged skin, including pigmentation, fine wrinkling, and roughness. No difference was found between a treatment regimen consisting of monthly serial 70% glycolic acid peel over 4 months versus application of a 10% glycolic acid based moisturizer twice daily. Efficacy was likewise established in a clinical study of glycolic acid in combination with tretinoin or L-ascorbic acid in the treatment of unpigmented stretch marks (Striae Alba).

An animal study shows that the rate of uptake of glycolic acid is influenced by formulation type. This is consistent with the NeoStrata report that un-ionized glycolic acid is more rapidly absorbed than ionized glycolic acid and that oleophilic glycolic acid derivatives are more rapidly absorbed.
Activity against Acne

A relatively large clinical trial of 80 women (mean age 22.7) revealed that glycolic acid chemical peels are an effective treatment for all types of acne, inducing rapid improvement and restoration to normal types of skin.\textsuperscript{15}

Skin Lightening Effects

A further cosmetic application of glycolic acid is to promote skin lightening. The studies cited here pertain to the treatment of melasma, which is the hyperpigmentation of the face. Incumbent treatments include Jessner’s solution, which is salicylate, lactate, and rescorcinol in ethanol. One clinical study compared efficacy of Jessner’s solution to 70% glycolic acid combined with tretinoin (retinoic acid) and hydroquinone used between the glycolic acid peels. This study of human subjects quantified the effects colorimetrically. Large variability in the results is evident in the large standard deviations in the average lightening, which are $3.14 \pm 3.1$ on the glycolic acid-treated side and $2.96 \pm 4.84$ on the Jessner’s solution-treated side. The authors state that there was an overall decrease in melasma area and severity of 63\%.\textsuperscript{16}

Another clinical study was focused on melasma treatment specifically for Asian women, including glycolic acid peels in the treatment.\textsuperscript{17} While the results show that glycolic acid provides large improvement subjectively, the investigators caution that the improvement does not reach statistical significance due to small samples size ($N = 10$).

Photoprotective Effects

Several studies have evaluated use of glycolic acid in photoprotection and in its relationship to sun sensitivity. One trial with human subjects evaluated glycolic acid’s effects in commercial skin creams on thickness of the stratum corneum and on the sensitivity to UVR, concluding that glycolic acid does not compromise skin sensitivity to sunlight.\textsuperscript{18} In contrast, another clinical study evaluating topical glycolic acid suggested that some individuals may have enhanced sun sensitivity resulting from the use of glycolic acid, although the investigators also conclude that the effects are reversed within one week. They further indicate that this could be due to “subclinical – that is, nonerythematous – irritation”, the implications of this being unclear in this writer’s view.\textsuperscript{19}

Another clinical study indicates that glycolic acid may have a photoprotective effect equivalent to spf 2.4. This study showed that glycolic acid applied to irradiated skin accelerates resolution of the redness or erythema.\textsuperscript{20} While the authors of the study suggested that these observations could be due to a mild antioxidant effect of glycolic
acid, it would not seem to be consistent with the bulk of the literature which indicates that there is little or no antioxidant character of glycolic acid.

Retinoids, Peptides, Botanicals

While few direct comparisons of relative efficacy of glycolic acid to the retinoids, peptides, and botanicals exist, published data reveals the efficacy of certain retinoids, peptides, and botanicals. Like glycolic acid, these materials are also frequently classified as cosmeceuticals. The literature points to advantages in formulating with glycolic acid over natural products such as the botanicals. Specific advantages of glycolic acid over the botanicals result from the complexity of the plant extracts, being complex mixtures, and varying in composition and also varying according to the season. A key review has pointed out these considerations and the fact that this is not reflected in the labeling. Nonetheless, active ingredients in the botanicals often have beneficial effects in skin care.

Many peptides are bioactive in skin care, modulating cell proliferation, cell migration, inflammation, angiogenesis, melanogenesis, and protein synthesis and regulation. These peptides fall into three main categories: signal peptides, neurotransmitter-affecting peptides and carrier peptides.

Our search revealed no references that compare glycolic acid to peptides. However, several articles review the use of peptides in skin care. The simplest of these is hydrolyzed keratin (sometimes from wool) and have high cystine content, which is sometimes S-sulphonated. In vivo studies appear to indicate an improvement in the skin’s water-holding capacity, hydration, and elasticity for volunteers with dry skin as a result of the keratin peptide treatment. Another study indicates that “A combination of the keratin peptide with the IWL [internal wool lipids] showed beneficial effects, indicating that this combination is suitable for designing new cosmetics products. The effects appear to be hydration and elasticity.” Both the keratin hydrolysates and the hair lipids provide moisturizing effects on skin, according to these investigators.

Glycolic acid as an Adjuvant for Other Therapeutic Agents

A key role of glycolic acid as an adjuvant is in pre-treatment of skin prior to application of therapeutic agents, resulting in enhanced activity of the therapeutic agent. For example, photodynamic therapy, which is the use of light for the localized treatment of diseases such as skin cancer, is sometimes limited by hyperkeratosis, or the excessive deposition of keratin. One clinical study demonstrates that pre-treatment with glycolic acid can relieve the effects of hyperkeratosis leading to enhanced efficacy of photodynamic therapy. The authors of this clinical study caution that there are a significant number of pre-treatment adjuvant agents and that current data is insufficient to determine which is the most safe and effective method.
Another study has shown that glycolic acid included in benzoyl peroxide containing acne gels can give improved results. Likewise, glycolic acid can improve the results provided by hydroquinone and kojic acid in the treatment of melasma, those being the dark skin lesions resulting from over exposure to sunlight.

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