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Review Article

Beyond Scrubs: Azelaic Acid's Chemical Exfoliation Journey In Cosmetic Dermatology

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ABSTRACT

Azelaic acid's role as a peeling agent in cosmetic dermatology, examining its historical significance and contemporary applications. The compound's gentle keratolytic mechanism enhances skin texture renewal by eliminating dead skin cells. Its unique chemistry engages water and lipid layers, enhancing efficacy across various skin conditions. Examining its anti-inflammatory properties, this analysis highlights its ability to inhibit tyrosinase, reducing melanin synthesis and addressing conditions like rosacea. Its anti-keratinizing effects alter epidermal keratinization, offering benefits in acne management, notably reducing comedone formation. Discussing chemical peeling as a proven method for skin rejuvenation, azelaic acid is positioned as a safe and cost-effective option. Comparing it with alternative peeling agents, emphasis is placed on its versatility and effectiveness. Azelaic acid's solubility in water and lipids contributes to its unique therapeutic profile, impacting keratinocyte DNA synthesis and cellular processes. Addressing the safety profile, minimal adverse effects are noted, along with compatibility with darker skin types. Combining azelaic acid with agents like retinol and glycolic acid is explored for enhanced efficacy in addressing dermatological concerns. In conclusion, azelaic acid emerges as a safe, effective, and versatile therapeutic agent in dermatology and cosmetics, offering solutions for conditions like acne, melasma, rosacea, and hyperpigmentation.

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INTRODUCTION

Exfoliation is a process that enhances skin texture by removing dead skin cells, dirt, and excess oil from the skin surface. Its origins date back to ancient Egypt, where pumice and alabaster stones, as well as sand and plant-based scrubs, were employed for exfoliation. China and Asia also embraced this technique. During the Middle Ages, wine containing tartaric acid served as a chemical exfoliant. While traditional methods have evolved, contemporary exfoliation includes scrubs, chemical peels, and cosmetics.1 Chemical peeling is a proven, safe, and cost-effective method for addressing various skin concerns and improving cosmetic appearance. The process involves controlled chemical injury to prompt skin rejuvenation, resulting in a smoother texture. Chemical peels are categorized based on the level of skin injury they induce: superficial, medium-depth, and deep. Superficial peels target the epidermis, addressing conditions like melasma and acne. Medium-depth peels penetrate the papillary dermis, suitable for solar keratoses and pigment disorders. Deep peels, causing necrosis to the reticular dermis, are indicated for severe photoaging, deep scars, and wrinkles¬¬.2 The purpose of this review is to provide a comprehensive examination of azelaic acid's role as a peeling agent in cosmetic dermatology. Additionally, the review addresses inquiries about azelaic acid's position among other skin acids, elucidates its keratolytic mechanism of action, and assesses its safety, particularly in individuals with darker skin tones.

DENOTATION OF CHEMICAL PEELING

Chemical peeling is the deliberate process of causing controlled chemical injury to the skin, impacting either the partial or complete layers of the epidermis, with or without the involvement of the dermis. This is achieved through the application of a chemical peeling agent, prompting the exfoliation of the skin's superficial layers. As a result, superficial lesions are removed, and the regeneration of new epidermal and dermal tissues is initiated.3

AZELAIC-PEEL

Azelaic acid employs gentle keratolysis to effectively eliminate dead skin cells. By slowing down keratin production, the protein forming the outer skin layer, facilitates natural shedding, revealing fresh, radiant cells underneath and imparting a soft, smooth feel. As a naturally occurring dicarboxylic acid, azelaic acid has a rich history in traditional medicine spanning centuries. Its versatile properties make it a valuable treatment for skin conditions such as acne, rosacea, and hyperpigmentation.4 Operating through keratolysis, it dissolves or breaks down keratin, the protein in the outermost skin layer, known as the stratum corneum. This natural process is integral to regular skin shedding, resulting in mild exfoliation contributing to skin texture renewal.5

CHEMISTRY AND PROPERTIES

Azelaic acid, chemically identified as nonanedioic acid, is an alpha, omega-dicarboxylic acid characterized by carboxy groups substituted at positions 1 and 7 of heptane.6 It functions as a conjugate acid of azelate (2-) and an azelaate, forming a key chemical structure.7 It possesses a unique characteristic as it demonstrates solubility in both water and lipids, setting it apart from other topical medications. This dual solubility enables the compound to effectively engage with both the aqueous and lipid layers of the skin, potentially enhancing its efficacy in addressing various skin conditions.8 In its water-soluble form, azelaic acid is capable of permeating the stratum corneum, the outermost layer of the skin. Within this layer, it engages with keratinocytes, the predominant skin cells, and specifically targets enzymes. On the other hand, its lipid-soluble nature allows it to penetrate deeper skin layers, reaching areas such as hair follicles and sebaceous glands. These regions are particularly relevant in the context of addressing concerns like acne and hyperpigmentation.9 It exhibits the capability to diminish the adhesion of corneocytes, which are the deceased skin cells found on the outermost layer of the skin. Through this reduction in corneocyte adhesion, azelaic acid induces the loosening and subsequent detachment of these cells from the skin's surface. This exfoliating action plays a role in clearing pores, eliminating whiteheads and blackheads, and averting future breakouts. Furthermore, it facilitates the generation of new cells, contributing to the skin's cellular turnover process.10

RELATIONSHIP BETWEEN KERATINIZATION AND INFLAMMATION

Keratinization and inflammation in the skin are intricate and often interlinked. Keratinization is the process by which skin cells produce keratin, a fibrous protein that forms the structural basis for the outermost layer of the skin. This process is normal and essential for maintaining skin integrity. However, when dysregulated keratinization can contribute to inflammation and various skin conditions.

ANTI-INFLAMMATORY PROPERTY

Azelaic acid gently inhibits tyrosinase, an enzyme responsible for melanin production, thereby reducing melanin synthesis and lightening the skin tone. Furthermore, the treatment has anti-inflammatory properties, effectively reducing inflammation that can contribute to hyperpigmentation.11 It proves to be a valuable asset in effectively managing rosacea, an inflammatory skin condition. Its efficacy stems from its dual capability: inhibiting the generation of reactive oxygen species (ROS) by neutrophils, a key contributor to rosacea inflammation, and downregulating inflammatory pathways within skin cells. This dual action makes azelaic acid a versatile and promising solution for the control and alleviation of rosacea symptoms.12 The optimal range for the most pronounced anti-inflammatory effect of azelaic Acid is found within concentrations ranging from 15% to 20%.13 The trial investigated the molecular mechanisms underlying the anti-inflammatory properties of azelaic acid in normal human keratinocytes. The findings revealed that azelaic acid effectively inhibited the UVB-induced expression of interleukins IL-1β and IL-6, along with the messenger ribonucleic acid (mRNA) expression and protein secretion of TNF-α.14

ANTI-KERATINIZING PROPERTY

Azelaic Acid functions as an anti-keratinizing agent, altering epidermal keratinization upon application. It specifically affects the concluding stages of epidermal differentiation, resulting in a proportional decrease in both the size and quantity of keratohyalin granules and tonofilament bundles.15-16 It lowers filaggrin expression within the stratum granulosum in individuals with acne. Consequently, there is a notable decrease in the thickness of the horny layer in the acro-infundibular regions, and the cytoplasmic content of horny cells displays a wide and irregular distribution.17 Immunocytochemistry studies have revealed a significant impact of azelaic acid on the terminal phases of keratinization. The distribution of filaggrin in acne and seborrheic skin exhibited notable alterations, with the most pronounced changes observed. Following exposure to azelaic acid, the filaggrin distribution returned to normal.18-19 Comparable outcomes were reported in a trial that involved the application of 20% Azelaic Acid, where transmission electron microscopy examinations of the follicular epithelium were conducted. In this study, the use of azelaic acid led to a decrease in the thickness of the horny layer, accompanied by a significant reduction in both the number and size of keratohyalin granules.20 Azelaic Acid has been noted to exert a level of influence on diminishing follicular hyperkeratosis akin to that observed with retinoids. Additionally, the concurrent use of azelaic acid, tretinoin, and benzoyl peroxide resulted in an increased presence of Odland bodies, contributing to reduction in the adhesion of horny cells.21-24 In experimental studies, Azelaic Acid showcased a reduction in keratinocyte DNA synthesis, with the extent of the effect dependent on both dosage and duration. Moreover, azelaic acid played a role in influencing the differentiation of the human epidermis and in the synthesis of proteins weighing 95 and 36 kDa, demonstrating its multifaceted impact on cellular processes.25-26 These findings imply that Azelaic Acid can produce reversible antiproliferative effects on keratinocytes. It acts as a competitive inhibitor for essential enzymes in the mitochondrial respiratory chain, including reduced NADH dehydrogenase, succinic dehydrogenase, and reduced ubiquinone cytochrome c oxidoreductase.27-29 To sum up, post-treatment with azelaic acid, individuals with acne display distinct alterations in the infundibular epidermis. These changes encompass a notable thinning of the horny layer, an enlargement of the horny cell cytoplasm, the presence of transitional corneal cells, and the restoration of filaggrin distribution. Furthermore, comedones in these individuals show a decrease in both bacteria and spores, contributing to a more controlled and regulated process of skin shedding.30-31 In everyday clinical scenarios, the anti-keratinizing effect of azelaic acid has demonstrated an inhibitory impact on comedone formation. Among individuals with mild-to-moderate acne, a substantial 87% decrease in comedones was noted following a 45-day treatment period with 20% Azelaic Acid.32 During a trial with adolescent acne patients, the application of azelaic acid for four months resulted in an almost 26% reduction in comedones as revealed by scanning electron microscopy.33 The effectiveness of 20% Azelaic Acid cream in reducing the number of comedones was on par with that of 0.05% tretinoin cream, showing a similar overall response rate.34 In a simulated model inducing comedone formation in rabbit ears through tetradecane, the administration of azelaic acid significantly decreased the size of comedones. This reduction can be attributed, at least partially, to the exfoliation of the skin.35

COMPARATIVE INVESTIGATIONS EXAMINING THE OUTCOMES OF AZELAIC ACID IN CONTRAST TO ALTERNATIVE PEELING AGENTS IN DIVERSE STUDIES:

Abdel Hay et al36 (2019) The study sought to compare the efficacy of a combined solution comprising 20% azelaic acid and 20% salicylic acid against a 25% trichloroacetic acid (TCA) peel in addressing acne. A total of 34 participants underwent four treatment sessions spaced two weeks apart. One side of each participant's face received treatment with the combined salicylic acid and azelaic acid solution, while the other side underwent a 25% TCA peel. Evaluation criteria included physician-reported clinical improvement, dermoscopic assessment of erythema, and patient satisfaction. Both treatments resulted in a significant alleviation of acne, with no notable disparity in clinical improvement. Notably, patients reported more discomfort on the TCA-treated side. The combined salicylic acid and azelaic acid solution is recommended for early-stage treatment, particularly when inflammatory lesions predominate. In contrast, TCA is suggested for cases with a higher prevalence of non-inflammatory lesions. Patient feedback indicated greater satisfaction with the salicylic acid–azelaic acid-treated side, suggesting that this combination may offer a more comfortable and gratifying treatment experience compared to TCA. Chilicka K. et al37 (2020) The research aimed to compare the efficacy of azelaic acid and pyruvic acid peels in the treatment of acne vulgaris, involving 120 young female participants with mild to moderate papulopustular acne. Over six peeling sessions at two-week intervals, a parallel clinical design was employed, with one group receiving azelaic acid treatment and the other pyruvic acid. Following the sessions, clinical examination indicated a significant reduction in acne severity symptoms and a decrease in desquamation and skin oiliness for both groups. Notably, pyruvic acid exhibited superior effectiveness in reducing greasy skin compared to azelaic acid. The investigators noted a nearly equivalent enhancement in quality-of-life scores with pyruvic acid compared to a peeling treatment using azelaic acid.38 The peeling formula, which combines glycolic acid with lactic acid and azelaic acid, integrates multiple alpha hydroxy acids (AHAs) to facilitate skin exfoliation, diminish acne scars and hyperpigmentation, and stimulate cell turnover. Azelaic acid enhances the formula with its antibacterial and anti-inflammatory properties, making it particularly effective for acne-prone skin. Compared to glycolic and lactic acid, azelaic acid offers unique advantages due to its specific antibacterial and anti-inflammatory attributes. While glycolic and lactic acids contribute to exfoliation and overall skin improvement, adding azelaic acid provides targeted benefits for individuals with acne-prone skin, enhancing the formula's efficacy in addressing both exfoliation and specific concerns related to acne.39 An alternative instance involves the blending of mandelic acid with azelaic acid in a chemical peel. Mandelic acid, classified as an AHA, stands out for its lower irritation potential compared to glycolic or lactic acid, rendering it suitable for individuals with sensitive skin. On the other hand, azelaic acid exhibits antibacterial properties and effectiveness against acne-causing bacteria. This combined formulation aims to mitigate acne breakouts, enhance skin texture, and target pigmentation concerns.40

SIDE EFFECTS

Azelaic acid stands out for its minimal occurrence of adverse effects on the skin and its absence of systemic toxicity, providing a notable edge over alternative agents employed for treating skin prone to acne. Generally acknowledged as safe for topical application, it presents mild side effects, including itching, burning, and dryness, which have been reported by some individuals. Moreover, the combination of azelaic acid with additional therapeutic approaches proves to be more effective in addressing acne-prone skin and yields superior clinical results.41

CONCLUSION

Azelaic acid emerges as a safe and effective therapeutic agent with notable applications in both dermatology and cosmetics, as its skin exfoliating properties could be a significant contributor to its therapeutic activity would addressing various concerns such as acne vulgaris, melasma, rosacea, hyperpigmentation, and skin aging. Notably, it is deemed safe for use on darker skin types. Combining Azelaic acid with formulations containing retinol, glycolic acid, lactic acid, kojic acid, tranexamic acid, and salicylic acid has demonstrated enhanced efficacy in tackling dermatological issues, establishing it as a potent cosmetic agent.

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