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Review

Topical AHA in Dermatology: Formulations, Mechanisms of Action, Efficacy, and Future Perspectives

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Abstract: The utilization of topical formulations containing alpha hydroxy acids (AHAs) has garnered considerable attention. This review summarizes the effectiveness of the most common topical AHA formulations, including mechanisms of action and future research directions. AHAs have a dramatic impact on diverse skin conditions, enhancing texture and stimulating collagen synthesis. Uncertainties persist regarding optimal concentration, pH, and vehicle for maximum efficacy. Advancements in formulation technologies offer opportunities for AHA penetration and stability. Understanding mechanisms is vital for skincare optimization. The review covers AHAs, their concentrations, formulation considerations, safety measures, and future directions.

Keywords: AHA; glycolic acid; lactic acid; citric acid; photoaging; hyperpigmentation; acne

1. Introduction

Topical formulations containing alpha hydroxy acids (AHAs) have garnered significant interest in the field of skincare owing to their exfoliative and rejuvenating properties [1]. This comprehensive review aims to assess the efficacy of AHA formulations, explicate their underlying mechanisms of action, and delineate prospective avenues for further research and clinical applications.

AHAs have been subjected to extensive investigation regarding their potential to ameliorate various skin conditions such as photoaging, hyperpigmentation, and acne [2]. Accordingly, within the cosmeceutical industry, these benefits have led to a proliferation of AHA-containing anti-aging products [2]. Numerous clinical studies have substantiated their effectiveness in improving skin texture, diminishing fine lines and wrinkles, and enhancing overall skin tone [2,3]. By stimulating collagen synthesis and facilitating skin cell turnover, AHAs engender a more refined and youthful appearance [1]. Clinically, this phenomenon has precipitated a notable surge in procedural interventions conducted by dermatologists and skincare professionals. These interventions are meticulously designed to address a wide spectrum of dermatological afflictions and aesthetic concerns, encompassing but not limited to the following: chemical peels, acne management, amelioration of hyperpigmentation, therapeutic intervention for actinic keratosis, intricate skin rejuvenation procedures, attenuation of fine lines and wrinkles, targeted mitigation of dry skin conditions, and the adept management of cutaneous manifestations stemming from solar-induced damage [4]. Therefore, gaining a comprehensive understanding of the mechanisms underlying the action of AHAs assumes paramount importance in order to optimize their application in the realm of skincare within the cosmeceutical industry.

AHAs, including glycolic acid, lactic acid, and citric acid, function by penetrating the stratum corneum, the outermost layer of the epidermis, and interacting with desmosomes, thus promoting desquamation [1]. This exfoliative action facilitates the removal of dead skin cells, resulting in a smoother complexion and an improvement in skin texture [1].

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Furthermore, AHAs stimulate collagen synthesis in the dermis, the deeper layer of the skin, by activating fibroblasts and upregulating the production of collagen and other extracellular matrix proteins [1]. Enhanced collagen deposition contributes to improved skin elasticity, firmness, and the attenuation of fine lines and wrinkles [1].

To optimize the utilization of AHAs in skincare, further research is warranted in several areas. Firstly, investigations into the optimal concentration of AHAs in formulations are necessary to strike a balance between efficacy and potential side effects, such as irritation and sensitivity [3]. Additionally, exploring the compatibility of AHAs with other skincare ingredients and evaluating their potential synergistic effects could enhance their therapeutic efficacy [3]. Furthermore, investigating the impact of different formulation vehicles on the stability and delivery of AHAs could contribute to their enhanced bioavailability and efficacy [3].

Notwithstanding the extensive research conducted on AHAs, queries persist regarding their optimal formulation characteristics remain. One such question pertains to the appropriate concentration of AHAs to achieve the desired therapeutic effects while minimizing the risk of adverse reactions, such as skin irritation and sensitivity [3]. Additionally, the pH of AHA formulations has been a subject of inquiry, as it can influence the stability and efficacy of these compounds [5]. Achieving the ideal balance between efficacy and tolerability requires a meticulous understanding of these factors.

Moreover, the choice of vehicle plays a pivotal role in the delivery and efficacy of AHA formulations. Advancements in formulation technologies offer opportunities to optimize the penetration and stability of AHAs. These advancements include novel delivery systems that can enhance the bioavailability and skin permeation of AHAs, thereby improving their therapeutic outcomes [5]. Exploring and harnessing these advancements may lead to significant improvements in the formulation of AHAs for enhanced efficacy and tolerability.

The present review aims to address these outstanding queries and shed light on the optimal use of AHA formulations in skincare. By critically evaluating the effectiveness of AHA formulations and providing insights into their mechanisms of action, this review seeks to contribute to the existing body of knowledge and guide future research endeavors. Moreover, by outlining potential research directions and clinical applications, it aims to pave the way for further advancements in this field.

2. Types of AHAs

The exfoliative and rejuvenating properties of alpha hydroxy acids (AHAs) have propelled their widespread utilization in the field of skincare. Among the various types of AHAs, glycolic acid, lactic acid, and citric acid have emerged as salient contenders (Table 1). Glycolic acid, derived from sugarcane, stands out due to its small molecular size, which enables effective skin penetration, promotion of cell turnover, and enhancement of skin texture [6]. Lactic acid, sourced from milk or fermented plant derivatives, is another sought-after AHA known for its gentle exfoliative properties and compatibility with sensitive skin types [4]. Its mechanism of action involves breaking down intercellular bonds, resulting in smoother and more radiant skin [7]. Citric acid, derived from citrus fruits, possesses antioxidant attributes and contributes to improved skin brightness and texture [8].

The concentration of AHAs in topical formulations varies depending on the desired effect and individual skin tolerance. Lower concentrations, typically ranging from 5–10%, are commonly found in daily skincare products, facilitating mild exfoliation and the maintenance of skin health [9]. These lower concentrations are generally well-tolerated by the majority of individuals and contribute to the enhancement of skin tone and texture [9]. In contrast, higher concentrations, such as 20–30%, are often utilized in professional chemical peels performed by dermatologists or skincare specialists to achieve more significant skin resurfacing and rejuvenation [6]. It is important to note that determining the optimal concentration of AHAs requires consideration of individual skin types and the specific condition being treated.

Recent advancements in skincare have brought forth the emergence of novel AHAs. Mandelic acid, sourced from bitter almonds, has garnered attention due to its exfoliative and antibacterial properties, making it beneficial in the treatment of acne-prone skin [10]. Another nascent AHA is malic acid, which is abundantly found in fruits such as apples and pears. Malic acid imparts hydrating and exfoliative effects, making it particularly suitable for individuals with dry or mature skin [11].

In summary, AHAs have gained prominence in the field of skincare due to their exfoliative and rejuvenating properties. Glycolic acid, lactic acid, and citric acid are prominent examples, each with unique characteristics and mechanisms of action. The concentration of AHAs in topical formulations can vary to achieve the desired effect, with lower concentrations commonly used for daily skincare products and higher concentrations employed in professional settings. Furthermore, novel AHAs, such as mandelic acid and malic acid, have emerged, offering additional benefits for specific skin conditions and types. These advancements in AHAs contribute to the expanding repertoire of skincare interventions and provide further opportunities for customization and tailored treatments.

3. Efficacy of Topical AHA Formulations

Clinical studies have provided compelling evidence supporting the efficacy of topical alpha hydroxy acid formulations in improving a diverse range of skin conditions. One prominent area of focus for AHA research has been photoaging, which is characterized by fine lines, wrinkles, and uneven skin texture. Noteworthy studies have demonstrated the effectiveness of AHAs in addressing these concerns. In a randomized clinical trial conducted by Prestes et al. [12], the application of 70% glycolic acid and 85% lactic acid in monthly peels exhibited notable efficacy in diminishing fine wrinkles. Moreover, a recent clinical trial by Narda et al. [13] revealed a significant increase in total collagen levels following the administration of glycolic acid, providing compelling evidence for its beneficial effects in skin rejuvenation and establishing its potential as a valuable therapeutic agent in dermatology. Similarly, Kornhauser et al. [14] reported that a lactic acid-containing formulation improved skin roughness and stimulated collagen synthesis in photoaged skin.

In addition to addressing photoaging, AHAs have demonstrated remarkable efficacy in treating hyperpigmentation concerns. Ravikumar et al. [15] emphasized the positive outcomes of AHA treatments for hyperpigmentation, citing the notable reduction in pigmentation intensity and overall improvement in skin tone observed in patients with melasma treated with topical glycolic acid formulations, as reported by Conforti et al. [16] Furthermore, Campos et al. [17] highlighted the effectiveness of citric acid formulations in lightening post-inflammatory hyperpigmentation, further establishing the role of AHAs in promoting a more even skin complexion.

Beyond their effectiveness in photoaging and hyperpigmentation, AHAs have also shown efficacy in managing acne. Glycolic acid formulations, in particular, aid in reducing acne lesions, improving skin texture, and preventing comedone formation [18]. The exfoliating properties of AHAs contribute to unclogging pores and reducing the appearance of acne scars, as supported by Sarkar and colleagues' findings [18]. Moreover, a more recent study by Arif [19] demonstrated a significant reduction in inflammatory acne lesions and an overall improvement in acne severity with a combination of glycolic acid and salicylic acid, a beta hydroxy acid.

The exploration of novel AHAs has further expanded the range of treatment options for various skin conditions. Mandelic acid, a naturally derived AHA, has been used in the treatment of hyperpigmentation and melasma due to its anti-inflammatory properties, which make it less irritating than other peels and thus safer for sensitive skin [20]. These findings underscore the potential of novel AHAs in dermatology.

Overall, the existing body of clinical evidence strongly supports the efficacy of topical AHA formulations in improving various skin conditions, including photoaging, hyperpigmentation, and acne management. These formulations consistently demonstrate their ability to enhance skin texture, reduce fine lines and wrinkles, lighten hyperpigmentation,

and address acne concerns. However, further studies investigating optimal concentration, frequency of use, and formulation characteristics are necessary to refine the therapeutic potential of AHAs in dermatology. By continuing to investigate and optimize the use of AHAs, dermatologists can offer patients effective treatment options for a wide range of skin conditions.

4. Mechanisms of Action

Elucidating the underlying mechanisms through which AHAs exert their effects on the skin is essential for comprehending their therapeutic potential. AHAs primarily act by virtue of their exfoliating properties, which involve the disruption of intercellular adhesions between corneocytes, the outermost layer of skin cells, leading to the elimination of dead skin cells and the facilitation of cell turnover [21]. Notably, glycolic acid, extensively investigated among AHAs, has been found to augment desquamation by stimulating the activity of enzymes implicated in the degradation of corneodesmosomes, the structures responsible for maintaining the integrity of the stratum corneum [22]. This process engenders the removal of superficial damaged layers, unveiling a smoother and more vibrant skin texture [22].

Beyond their exfoliative role, AHAs also play a pivotal role in stimulating collagen synthesis, a crucial determinant of skin elasticity and firmness. Research studies have established that AHAs, such as glycolic acid and lactic acid, can induce upregulation of collagen production in the dermis, the deeper layer of the skin [1]. This stimulation transpires through diverse mechanisms, encompassing the activation of fibroblasts, heightened expression of collagen-related genes, and modulation of signaling pathways implicated in collagen synthesis [23]. Consequently, the employment of AHAs can contribute to the amelioration of fine lines, wrinkles, and overall skin texture [1].

AHAs have also been shown to enhance the skin's barrier function and hydration. AHAs promote the synthesis of epidermal lipids, such as ceramides and cholesterol, which assume a vital role in upholding a healthy skin barrier, acting as a protective shield against external aggressors and maintaining moisture balance [14]. By fortifying the barrier function, AHAs assist in averting transepidermal water loss and maintaining optimal hydration levels in the skin. This attribute holds particular significance for individuals with dry or dehydrated skin, as AHAs can aid in the restoration and retention of moisture, thereby yielding a smoother and well-hydrated complexion [14].

The combination of AHAs and beta-hydroxy acids (BHAs) represents a compelling synergy in skincare formulations, exhibiting remarkable potential for enhancing overall skin health and addressing various dermatological concerns. AHAs, such as glycolic acid and lactic acid, work predominantly on the skin's surface by exfoliating dead skin cells and promoting cellular turnover, while BHAs, notably salicylic acid, penetrate deeper into the pores, aiding in the treatment of acne [4]. The complementary actions of AHAs and BHAs offer a multifaceted approach to skincare, yielding synergistic effects that can result in improved skin texture, tone, and clarity [4]. Recent research endeavors have delved into the mechanisms of action of AHAs. Lupu et al. [24] investigated a topical formulation containing both AHAs and BHAs, along with anti-inflammatory and antibacterial molecules. Following a 28-day regimen, a substantial decrease in the number of dilated infundibula, infundibula filled with keratotic material, and infundibula with thickened bright borders were observed. These findings offer promising prospects for ameliorating various inflammatory skin conditions, such as rosacea [25].

AHAs have also been shown to modulate the expression of genes implicated in skin pigmentation, leading to an overall reduction in melanin synthesis and an improvement in hyperpigmentation [26]. In a systematic review investigating treatments for lentigines, a common form of hyperpigmentation, 58% of individuals experienced a complete or partial response following chemical peels with AHA/BHAs [27]. These findings further underscore the multifaceted mechanisms by which AHAs exert their beneficial effects on the skin.

Overall, the mechanisms of action of AHAs on the skin encompass exfoliation, stimulation of collagen synthesis, enhancement of the skin's barrier function and hydration, as well as anti-inflammatory and depigmenting effects. By employing these mechanisms, dermatologists can harness the therapeutic potential of AHAs for a broad spectrum of dermatological conditions, including textural skin changes and photoaging, hyperpigmentation, and inflammatory skin disorders.

5. Formulation Considerations

Formulating topical products containing AHAs requires meticulous attention to various key factors that significantly impact their effectiveness and tolerability. Among these factors, the pH of the formulation plays a critical role. While an exact pH value has not been universally established, it is widely acknowledged that AHAs exhibit optimal efficacy within a lower pH range, typically ranging from 3 to 5 [28]. This acidic environment plays a crucial role in amplifying the exfoliative attributes of AHAs and facilitating their penetration into the cutaneous layers of the skin.

Maintaining the optimal pH range is essential to ensure the desired therapeutic effects of AHAs while minimizing potential skin irritation. The acidic pH of AHA formulations acts as a catalyst in enhancing their exfoliative properties. It creates an environment that promotes the breakdown of intercellular adhesions between corneocytes, the outermost layer of skin cells [28]. This process, known as desquamation, facilitates the effective removal of dead skin cells, unveiling a smoother and more rejuvenated skin texture [28]. Furthermore, the acidic environment created by AHAs aids in enhancing their penetration into the deeper layers of the skin, known as the cutaneous layers. This penetration allows AHAs to exert their beneficial effects, such as stimulating collagen synthesis and promoting cell turnover, resulting in improved skin texture and the reduction of various skin concerns [28].

Concentration represents another pivotal factor to consider in formulating topical AHA products. Higher concentrations of AHAs generally yield more profound skin exfoliation and therapeutic benefits; however, they may also heighten the risk of skin irritation [29]. Extensive research indicates that concentrations ranging from 5% to 10% are commonly employed in clinical practice, with higher concentrations typically reserved for in-office or professional treatments [29,30]. Determining the appropriate concentration necessitates considering specific factors such as the skin condition being treated, individual tolerance, and desired treatment outcomes.

Choosing the optimal concentration of AHAs is a delicate balance. Higher concentrations can deliver more robust exfoliation and therapeutic effects, particularly for more severe skin conditions. However, they also pose an increased risk of skin irritation, making them more suitable for professional use under the supervision of dermatologists or skincare specialists. Lower concentrations, on the other hand, are commonly found in over-the-counter skincare products and are typically well-tolerated by the majority of individuals. These concentrations provide milder exfoliation and therapeutic benefits, contributing to the enhancement of skin tone and texture [30].

In addition to pH and concentration, the selection of an appropriate vehicle plays a pivotal role in the formulation of topical products containing AHAs. The ideal vehicle should optimize the stability and penetration of AHAs while providing a pleasing sensory experience for the patient. Various vehicles, such as gels, creams, lotions, and serums, have been employed to deliver AHAs [30]. Each vehicle type possesses its own advantages and limitations in terms of AHA stability, skin penetration, and cosmetic elegance.

Gel formulations are often favored due to their lightweight texture and rapid absorption, making them suitable for oily or acne-prone skin types [9]. Gels typically have a high-water content and a low lipid content, allowing for quick drying and a non-greasy finish. This formulation type is well-suited for individuals who prefer lightweight and non-comedogenic products. Moreover, gels provide a cooling effect upon application, offering a refreshing sensory experience [9].

On the other hand, creams or lotions may be preferred for their moisturizing properties, making them suitable for individuals with dry or sensitive skin (Leyden et al., 2009). Creams have a higher lipid content and provide a more emollient texture, offering enhanced moisturization and barrier protection [30]. This formulation type is beneficial for individuals with dry or dehydrated skin, as it helps replenish moisture and restore the skin's natural lipid barrier. Lotions, which have a lighter consistency than creams, offer a balance between hydration and lightness, making them suitable for individuals who desire a more fluid texture [31].

The selection of the appropriate vehicle for AHA formulations depends on the specific needs of the patient and the characteristics of their skin. The vehicle should not only enhance the stability and penetration of AHAs but also align with the patient's preferences and skin type. By considering factors such as the desired texture, level of moisturization, and compatibility with different skin types, dermatologists can customize the formulation to address specific skin conditions and individual patient needs.

Optimizing the formulation of topical AHA products is critical in achieving the desired therapeutic effects while mitigating potential adverse reactions. By meticulously considering factors such as pH, concentration, and vehicle selection, dermatologists can tailor the formulation to the unique requirements of each patient. This ensures optimal stability, penetration, and overall treatment outcomes. The selection of the appropriate vehicle, alongside pH and concentration considerations, further enhances the efficacy and tolerability of AHA products, contributing to improved patient satisfaction and treatment results.

6. Safety and Side Effects

The comprehension of the safety profile associated with topical formulations containing alpha hydroxy acids AHAs holds paramount significance in ensuring not only their effectiveness but also their well-tolerated application within the field of dermatology. AHAs, although generally acknowledged as safe, possess exfoliating properties that may give rise to specific side effects. Notably, commonly reported adverse reactions encompass mild skin irritation, redness, as well as stinging or burning sensations upon application [32,33]. These side effects, however, are typically transient in nature and tend to subside with continued usage of AHAs or through the adjustment of their concentration or frequency of application [32].

It is important to understand the underlying mechanisms behind the reported side effects of AHAs. AHAs, such as glycolic acid, lactic acid, and citric acid, possess the ability to induce controlled exfoliation of the outermost layer of the skin, the stratum corneum. This exfoliation process promotes the removal of dead skin cells, resulting in a smoother and more even skin texture [33]. However, this exfoliation can also lead to mild skin irritation, manifesting as redness, and the sensation of stinging or burning upon application. These reactions are thought to arise from the disruption of the skin barrier function, causing increased transepidermal water loss and heightened sensitivity [32]. Nevertheless, these effects are generally well-tolerated and subside as the skin adjusts to the treatment or when the concentration or frequency of AHA application is modified.

In addition to the potential for skin irritation, AHAs have been shown to increase the skin's sensitivity to ultraviolet (UV) radiation, thereby increasing the risk of sunburn and UV-induced damage. This is primarily due to their exfoliating properties, which thin the stratum corneum, reducing its ability to provide a natural barrier against UV rays. Consequently, the skin becomes more susceptible to sunburn and UV-induced damage, including premature aging and an increased risk of skin cancer [14]. It is, therefore, crucial for healthcare providers to educate patients undergoing AHA treatment about the importance of sun protection. This involves advising the regular use of broad-spectrum sunscreens with high sun protection factors, the adoption of protective clothing, and the avoidance of prolonged sun exposure, especially during peak hours [14].

In order to optimize tolerability and mitigate the occurrence of side effects, several strategies can be implemented. A gradual initiation approach involving lower concen-

trations of AHAs is particularly beneficial for individuals with sensitive or reactive skin. This method allows the skin to acclimate gradually, reducing the likelihood of adverse reactions [32]. Additionally, formulating AHA products at a lower pH level has the potential to enhance their efficacy while minimizing skin irritation [30]. By adjusting the pH, the exfoliating properties of AHAs can be maintained while minimizing their potential to disrupt the skin barrier and cause irritation.

The incorporation of soothing and hydrating ingredients alongside AHAs can further improve the tolerability of topical formulations and reinforce the skin barrier function. Ingredients such as ceramides or hyaluronic acid possess hydrating and moisturizing properties that can counteract the potential drying effects of AHAs and enhance the overall tolerability of the treatment [34]. By combining these ingredients with AHAs, the formulation can provide dual benefits of exfoliation and hydration, resulting in a more comfortable and well-tolerated experience for patients.

Regular monitoring and close follow-up of patients using topical AHA formulations are of utmost importance to promptly identify any signs of intolerance or adverse reactions. This allows healthcare professionals to intervene and adjust the treatment as needed, ensuring patient safety and satisfaction. Additionally, providing appropriate skincare recommendations to patients undergoing AHA treatment plays a crucial role in overall tolerability. Recommending the use of gentle cleansers that do not strip the skin of its natural oils and moisturizers that help restore hydration and maintain the skin's moisture barrier can contribute to a more comfortable experience for patients [4,32]. By implementing these strategies, dermatologists and skincare professionals can optimize the safety and tolerability of topical AHA formulations. These measures not only minimize the risk of side effects but also ensure effective treatment outcomes. Moreover, they contribute to the overall satisfaction and well-being of patients undergoing AHA therapy.

The utilization of AHAs in skincare has sparked considerable interest, leading to the development of distinct approaches for in-office or home chemical peels compared to daily active or maintenance treatments using creams or serums. In professional settings, chemical peels incorporating AHAs provide a controlled and intensive exfoliation process. These peels facilitate the removal of dead skin cells, stimulate collagen production, and promote cellular turnover [35]. By utilizing higher concentrations and customized formulations, these peels enable deeper penetration and deliver more significant results, making them particularly suitable for addressing specific concerns such as hyperpigmentation, fine lines, and uneven texture [35].

Conversely, daily active or maintenance treatments involving AHAs typically involve creams or serums with lower concentrations. The objective of this approach is to ensure gradual and consistent exfoliation while preserving the skin's barrier [26]. By formulating AHAs into creams or serums with lower concentrations, the aim is to enhance skin radiance, promote a smoother complexion, and minimize the risk of adverse reactions associated with stronger peels [26]. This approach offers individuals the opportunity to incorporate AHAs into their daily skincare routine without the need for intensive exfoliation or prolonged recovery periods.

The tailored use of AHAs in both in-office or home chemical peels and daily active/maintenance treatments through cream or serum formulations provides practitioners and individuals with flexible options to address specific skincare needs. The availability of higher concentrations in chemical peels allows for a more targeted and intensive approach, providing noticeable results for specific skin concerns. On the other hand, the use of lower concentrations in daily treatments emphasizes a gentle and gradual exfoliation process, prioritizing the long-term health of the skin and minimizing the risk of adverse reactions. By considering factors such as treatment intensity, convenience, and long-term skin health, individuals can select the most suitable AHA regimen to achieve their desired skincare outcomes.

7. Future Directions

Topical formulations containing AHAs have shown remarkable efficacy in improving various skin conditions. To further advance the field of AHAs in skincare, ongoing research should focus on the development of innovative delivery systems, such as liposomes or nanoparticles, to enhance the penetration and stability of these compounds [30,32]. Encapsulating AHAs within liposomes or nanoparticles offers several advantages that can optimize their therapeutic potential. Firstly, these delivery systems enable controlled release, allowing for a gradual and sustained delivery of AHAs to the skin compounds [30,32]. This controlled release mechanism ensures a prolonged activity of AHAs, enhancing their effectiveness in addressing specific skin concerns. Moreover, by utilizing liposomes or nanoparticles as carriers, the stability of AHAs can be improved, preventing their degradation and enhancing their shelf life compounds [30,32]. The encapsulation of AHAs within these nanocarriers provides a protective environment, shielding the active ingredients from external factors that may compromise their stability, such as light and air exposure [32]. This results in more reliable and consistent delivery of AHAs, ensuring their optimal functionality and therapeutic efficacy.

In addition to enhancing the delivery and stability of AHAs, further exploration of their synergistic effects with other active ingredients holds great promise for skincare advancements. Combining AHAs with complementary agents, such as retinoids, has shown significant potential in addressing a range of skin concerns, including photoaging and acne [36]. By targeting multiple pathways involved in skin aging, these combination therapies can yield enhanced and comprehensive results, surpassing the benefits of individual treatments alone. Furthermore, investigating the integration of AHAs with emerging technologies like micro-needling or laser therapy represents another fruitful avenue for future research [30,37]. Such combination approaches have the potential to create synergistic effects by promoting deeper penetration of AHAs into the skin and facilitating their interaction with targeted tissues. This may lead to the development of novel treatment modalities that offer improved efficacy and safety profiles, opening up new possibilities for addressing various skin conditions.

Further investigation is imperative to gain a comprehensive understanding of the role of AHAs in addressing specific skin concerns, such as melasma or post-inflammatory hyperpigmentation [38]. To develop more effective treatment strategies, there is a need to optimize AHA formulations and explore their combination with other depigmenting agents [39]. By combining AHAs with complementary compounds, it is possible to target multiple pathways involved in pigmentation regulation, leading to enhanced treatment outcomes.

Furthermore, personalized approaches that consider individual variations in skin type and genetic factors have emerged as an area of interest. Understanding the genetic factors influencing individual responses to AHA treatment can enable the development of personalized skincare regimens [4,30]. By tailoring AHA formulations based on individual characteristics, healthcare professionals can optimize treatment outcomes and minimize adverse reactions, leading to higher patient satisfaction.

The future of topical AHA formulation lies in continuous research efforts in understanding the role of AHAs in: specific skin concerns, optimizing formulations, exploring combination therapies, and implementing personalized approaches that will shape the future of topical AHA treatments. Advancements in delivery systems, combination therapies, and personalized approaches will contribute to improving the efficacy, tolerability, and individualization of AHA treatments, benefiting individuals seeking to enhance their skin health and appearance.

8. Conclusions

Topical formulations containing AHAs have demonstrated their effectiveness as interventions for various dermatological conditions, including photoaging, hyperpigmentation, and acne [4,36,37]. AHAs exert their beneficial effects by enhancing dermal texture, stimu-

lating collagen synthesis, and improving skin tone (Table 1) [6]. These mechanisms involve disrupting intercellular adhesions, promoting cellular turnover, and strengthening the skin barrier (Figure 1) [6]. Of note, the stability and efficacy of AHA formulations are significantly influenced by formulation considerations, such as pH and vehicle selection.

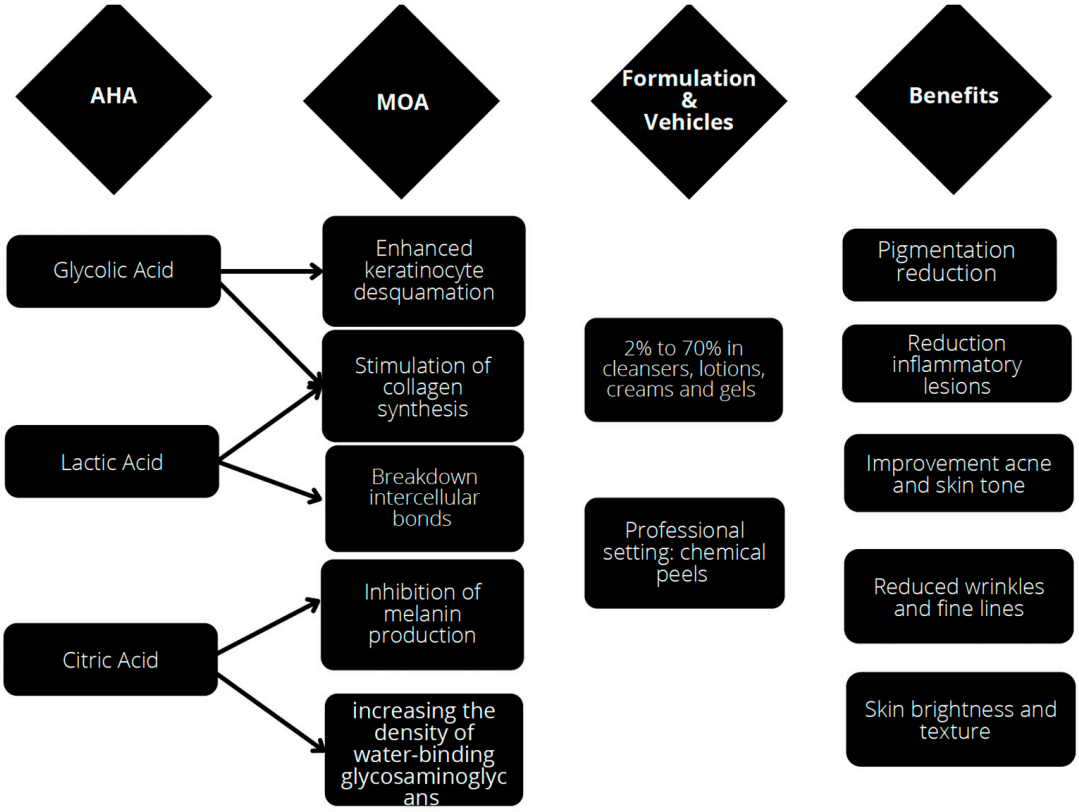

Figure 1. Alpha-hydroxy acids in dermatology—formulations, mechanisms of action, and efficacy.

To further advance the field of AHA utilization, future research should focus on the development of innovative delivery systems, including encapsulation technologies, to enhance the penetration and stability of AHAs. Encapsulation of AHAs within liposomes or nanoparticles, for instance, can improve their stability, control release kinetics, and enhance their overall efficacy [30,32]. By enhancing the delivery of AHAs into the skin, these innovative delivery systems can maximize their therapeutic potential and provide improved treatment outcomes.

Exploring synergistic combinations of AHAs with other active ingredients, such as retinoids, holds promise for the development of more comprehensive and effective therapies. The combination of AHAs with retinoids has shown significant potential in addressing a wide range of skin concerns, including photoaging and acne, by targeting multiple pathways involved in skin aging and promoting cellular renewal [36]. Investigating the synergistic effects of such combinations can lead to the development of novel treatment modalities with enhanced efficacy and better clinical outcomes.

Furthermore, personalized skincare strategies guided by genetic markers or biomarkers represent an exciting area of future research. Understanding the genetic factors and individual variations that influence the response to AHA treatments can enable the development of tailored skincare regimens [37]. By considering individual genetic profiles and specific biomarkers, healthcare professionals can optimize AHA formulations to suit individual needs, improving treatment outcomes and minimizing the risk of adverse reactions.

To fully harness the potential of AHAs, further investigation is necessary to better understand their role in treating specific skin concerns, such as melasma, and to explore

the potential benefits of combining AHAs with emerging technologies like micro-needling or laser therapy [39]. Research efforts in these areas can pave the way for the development of novel and more effective treatment approaches [39].

In conclusion, topical AHA formulations offer effective remedies for a wide range of dermatological conditions. Understanding their multifaceted mechanisms, taking into account formulation considerations, and directing future research towards innovative delivery systems, synergistic combinations, and personalized skincare strategies will enhance our understanding of AHAs and contribute to the development of safe and efficacious skincare interventions for patients.

Table 1. Alpha-hydroxy acids in dermatology—formulations, mechanisms of action, and efficacy.

AHA Type	Mode of Action	Formulations /Vehicles	Efficacy
Glycolic Acid	Augmentation of desquamation by stimulating the activity of enzymes implicated in the degradation of corneodesmosomes [22]	Concentrations of vary from 2% to 70% in cleansers, lotions, creams and gels [6,40]	Reduction in pigmentation intensity [16]
	Stimulation of collagen synthesis [1]	Professional setting: chemical peels [13]	Significant reduction in inflammatory acne lesions and overall improvement in acne severity and skin tone [16,19] Increased epidermal and dermal firmness and thickness [41]
Lactic Acid	Breakdown intercellular bonds [1,42]	Concentrations of vary from 2% to 70% in cleansers, lotions, creams, and gels [6]	Reduce the number and depth of fine lines and wrinkles [43]
	Stimulation of collagen synthesis [1,6]	Professional setting: chemical peels [13]	Improve skin texture and acne [43] Increased epidermal and dermal firmness and thickness [41,43]
Citric Acid	Increasing collagen synthesis, improving the quality of elastic fibers and increasing the density of water-binding glycosaminoglycans [8] Inhibition of melanin production due to regulation of tyrosinase [44]	Concentrations vary from 2% to 70% in cleansers, lotions, creams, and gels [6]	Lightens post-inflammatory hyperpigmentation [17]
			Increased epidermal and dermal firmness and thickness [41]
			Augment skin brightness and texture [8]

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