

Functional Properties Of Cosmeceuticals: A Unified Chemist's Perspective On Urea, Salicylic Acid, Glycolic Acid, And Niacinamide

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Abstract:

Background: Cosmeceuticals are the skin care products which combine pharmaceutical and cosmetics. They provide physiologically active chemicals that have counter effect on skin aging and help in skin rejuvenation. These non-tested products which are regarded drugs, based studies of some active components. Their formulations, mode of action, clinical uses, and synergistic use has created a vast sector which has significant expansion in the cosmetic industry. In this article, we will discuss the insights of four important cosmeceuticals—urea, salicylic acid, glycolic acid, and niacinamide which are commonly used in cosmetic industry. When combined, their formulations represent the multifaceted approaches used in dermatological treatment to address various skin associated problems like pigmentation, photoaging, exfoliation, and skin hydration.

Key Word: Cosmeceuticals; Urea; Glycolic Acid; Citric Acid; Salicylic Acid; Niacinamide.

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I. Introduction

Cosmeceuticals are topical products that claim to enhance the skin appearance [1-5]. The Drug and Cosmetic Act, 1938 that clearly differentiated between 'Drug' and 'Cosmetics'. This document states that using ingredients or raw material in cosmetic products for "cleansing, beautifying and promoting the attractiveness" or "alternating the appearance" without the approval of a government agency permitted; however, medicinal claims for such product(s) may be made. Kilgman who coined the term cosmeceuticals believed that it should represent something which not only appears to improve skin tone, texture, also enhances its appearance but definitely less than a pharmaceutical drug [6]. That's why in recent decades demand for multipurpose skincare products, the cosmeceutical sector has gained significant expansion. This clearly indicates cosmeceuticals as bridging skincare (cosmetics) and dermatology. Various active substances that have noticeable physiological effects on the skin, skin rejuvenation and also provide effective treatment for diseases including xerosis, acne, hyperpigmentation, and photoaging etc are known [7]. In this article, we will focus on use of urea, salicylic acid, glycolic acid, and niacinamide which are common chemistry laboratory reagents also used in the skin care products. These substances are also known for their versatility in a variety of dermatological and cosmetic formulations. In addition to their unique mechanisms of action, which include keratolytic (skin Peeling), anti-inflammatory properties and exfoliative effects through inhibiting melanin production/ Melanosome transport enhanced epidermal turnover and barrier-repairing capabilities [8]. Alpha-hydroxy acids like glycolic acid are essential for anti-aging and pigmentation therapies because they encourage epidermal exfoliation and increased epidermal turnover. Vitamin B3 in the form of niacinamide has shown numerous dermatological advantages, such as improving the barrier, reducing hyperpigmentation [9]. Beta hydroxy acids BHA's like salicylic acid are widely used for acne control, skin repair, skin tag removal and anti-inflammatory effects. As a strong humectant and keratolytic, urea is especially useful for treating scaly, dry skin [10].

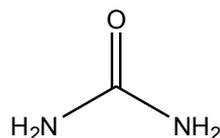
With a focus on their mechanisms of action, effective concentrations used in cosmeceuticals and dermatology, role of pH, shelf life this article provides a comprehensive study of these four active ingredients.

II. Result And Discussion

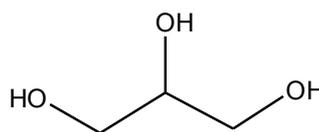
A humectant: Urea

Known for being the first organic compound synthesized in the laboratory, this low molecular weight organic substance urea, is a byproduct of protein degradation in the body. This important marker of liver and kidney's function, is important raw material for many different industries like fertilizer, the plastic production, pharmaceuticals, as nutritional supplement in livestock and even cosmetics. Owing to its hygroscopic properties,

urea is an important natural moisturizing factor (NMF) [3,11]. Due to its high-water solubility, it is used in dermatological and cosmetic procedures. Urea is mainly used as moisturizers in foot creams and hand creams, nail and cuticle softener, in the ointments for disorders like psoriasis, xerosis (dry skin) etc. However, its role is concentration dependent.



Urea (1)



Glycerol (2)

The concentrations of urea used determines its function in the cosmeceuticals. At concentrations below 10%, urea is predominantly utilized as a humectant. or a moisturizer. Concentrations exceeding 30% are utilized as keratolytics. The in between concentrations, i.e., 10-30% serves the purpose of both humectant and keratolytic agent. Research indicates that a urea-glycerol mixture serves as a superior moisturizer compared to lotions solely based on glycerol or paraffin [12].

Concentrations	Effect	Uses
<10%	As humectant	<ul style="list-style-type: none"> • as moisturizer, for skin and nail penetration • optimizing the action of topical drugs.
>30%	Topical drug enhancer	<ul style="list-style-type: none"> • In dermatology for treatment of nail disorder, dandruff etc. • Keratolytic agent (for skin peeling)
Between 10-30%	As humectant as well as keratolytic agent	<ul style="list-style-type: none"> • For maintaining hydrated skin. • Treating skin ailments like Psoriasis etc.

III. A Versatile Alpha Hydroxy Acid, AHA: Glycolic Acid

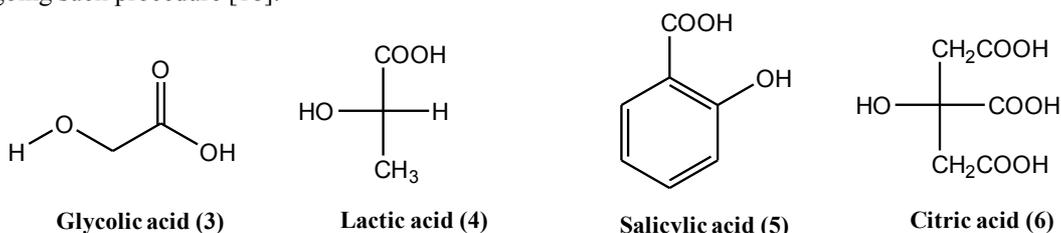
Glycolic acid (3), the smallest three carbon alpha-hydroxy acid (AHA), is naturally found in sugarcane, beets, kiwi, grapes and many other fruits. Although it can be naturally extracted from these sources but its extraction is tedious and expensive process. Infact most of the glycolic acid available in the markets is synthetically produced by the carbonylation of the formaldehyde [13] followed by purification. This too pose a problem as even after purification some of the formaldehyde is still present in the purified product. Most of the skin care agencies allow less than 0.2% of formaldehyde as impurity. Beyond this limit formaldehyde may cause allergic reactions in many people. Earlier concentrations as low as 200ppm have shown to cause dermatitis. Another method of its preparation is by hydrolysis of chloroacetic acid using alkali but that too pose problems associated with starting material [14]. Now a days fermentation, using microorganisms [15], is also being used for producing glycolic acid. This biobased glycolic acid is free from any impurity which can cause potential damage to user.

Glycolic acid works on its unique property that it can penetrate into the outermost layer of skin and breaks the matrix that keep the dead cells together. Due to its exfoliation property, it causes the cellular turnover leading to the smoother complexion and improvement of skin texture. Apart from this, it also boosts the collagen synthesis in the dermis. That is why it is helpful when applied topically to treat a range of skin disorders, such as acne, age spots, photoaging, and fine lines/ wrinkles [16-17]. The use of glycolic acid in the chemical peel to reduce the acne related inflammation is already reported [18]. B. K Yoon *et. al.* reported the pH dependent antimicrobial activity against *Cutibacterium acnes*. In contrast to the earlier conventional methods which use high concentration of glycolic acid, they reported the antiacne formulations with glycolic acid as low as 0.2% can be formulated but with a suitable pH condition [19]. Apart from Glycolic acid other AHA's like lactic acid, and citric acid also serve the same purpose. Various parameter like the optimal concentrations, optimum pH, shelf life, efficacy, sensitivity need investigation before using these AHA's in the formulations. They may have potential side effects like redness, inflammation irritation etc.

AHA's along with BHA's (Beta hydroxy acid's eg salicylic acid (5) or citric acid (6)) in skin care products is useful combination for treating many dermatological problems [20]. AHA'S like glycolic acid and lactic acid (4) work mainly on the skin surface by removing dead skin cells while BHA's like salicylic acid (5) infiltrate into the pores helping in the treatment of the acne. BHA's have a multi facet approach to skin care that can lead to improved skin tone, texture and clarity. With concentration between 5 to 10% and a 28-day regime has been known to substantially showing the positive results. Higher concentrations may be more effective in severe conditions but they may also pose the increased risk of skin irritation so for a majority of individual

lower concentrations are preferred. Not only this which vehicle we use for delivering AHA's is also very important. The gel form usually preferred because of the lightweight texture, rapid absorption. Gels are suitable for oiling acne brown skin but because of the high-water content and low lipid content they end up in quick drying and non-greasy finish. Even creams and lotions are preferred for their moisturizing property for dry and sensitive skin. So, while selecting the right type of AHA/BHA's we need to see the characteristic of skin like texture, type and the specific need of the individual.

The most common use of glycolic acid is in chemical peels, usually referred to as fruit acid peels. These peels are preferred as they are simple, inexpensive and short recovery period. The treatment of acne scars, hyperpigmentation photoaging etc using glycolic acid peel have been reported. Before undergoing such peel medical history, pre-peel analysis of skin type of the user is important. This helps in deciding the peel timings, and neutralization on-time and also ensures good results, without any side effects. The concentration and time for which the peel has been applied is important. The user must take these points into account before undergoing such procedure [18].



To optimize effectiveness and reduce side effects, a number of aspects need to be taken into account while creating glycolic acid-based solutions. These consist of:

Optimal concentration	While 5–10% concentrations are common in skincare, higher levels may be reserved for clinical treatments.
Skin tolerance	Potential side effects include irritation, redness, stinging, and increased sensitivity to ultraviolet radiation, which can heighten the risk of sunburn
pH balance	The efficacy of glycolic acid is heavily influenced by the formulation's pH. It works best between pH 3-5. Concentrations as low as 0.2 % is effective in this range
Vehicle selection	Gels, due to their lightweight and quick absorption, are often preferred for oily skin. However, they may lead to dryness due to low lipid content. Creams and lotions, by contrast, provide moisturizing benefits ideal for dry or sensitive skin

In spite of the effectiveness and the well tolerated application of glycolic acid in skin care products some adverse effects are also seen like skin irritation, stinging redness or burning sensation. The risk of sunburn and UV induced damage are some of problems associated with such treatments. In order to optimize the tolerability and reduce the side effect, a gradual approach involving use of lower concentration to higher concentration can be done. Incorporation of soothing and hydrating agents like aloe vera etc along with AHA's to improve the quality of the formulation.

IV. A Lipophilic Exfoliant: Salicylic Acid

Salicylic acid (5) (a Beta hydroxy acid, or BHA) is a substance that is found naturally in plants like white willow bark (salicin) and wintergreen leaves (methyl salicylate), also in vegetables like broccoli, avocado, tomatoes etc. They are formed in plants to protect them from insects and diseases [21]. Apart from conventional use in synthetic chemistry, salicylic acid is a precursor of the common medicinal drug acetylsalicylic acid, also known as Aspirin. Salicylates are known to have health benefits. For thousands of years salicylate extracts have been used as pain relievers and anti-inflammatory and acne-prone skin [22].

Black heads, white heads and acne often appears when hair follicle gets plugged with dead skin cells and oil. Salicylic acid penetrates deep into the skin (Stratum Corneum layer) and helps to dissolve the dead skin cells clogging the pores [23]. Its effect depends on the concentration in the skin care product [24]. Salicylic acid concentrations in cosmetic items vary depending on the type of product (except eyeshadow, eyeliners, mascara, deodorants and lipsticks). Salicylic acid or its derivative may be present up to 2%, while hair rinse products can contain concentrations of up to 3%. According to Commission Regulation (EU) 2019/1966 of 27 November 2019 salicylic acid must not be present in cosmetic products for children under three-year-old [1]. For certain dermatological uses, salicylic acid is also made in white soft paraffin bases or aqueous creams in concentrations between 2% and 12% [24].

Concentrations	Effect	Uses
Upto 10%	As keratoplastic effect	• In home care products
10-20%	As keratolytic (skin peeling)	• Chemical peeling -Keratolytic agent
Between 20-30%	keratolytic agent	• Used in cosmetic salons and dermatological surgeries.

Owing to its bactericidal and fungicidal nature, Salicylic acid serves as a preservative and an active therapeutic agent in the cosmetology. By lowering the pH, it improves product stability and prevents microbial growth. Because of its various benefits like antibacterial action, chemo exfoliation, and regulatory approval for a number of product range, salicylic acid remains a fundamental component of contemporary cosmetology.

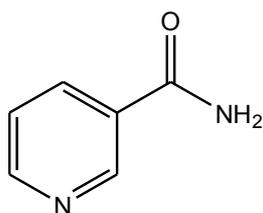
V. A Quintessential Companion: Niacinamide

Niacinamide (7), the biologically active form of vitamin B3, is an important part of our diet. Naturally found in foods like meat, fish, and grains, niacinamide can also be biosynthesized in the body from tryptophan. Its deficiency leads to pellagra with distinct symptoms like dermatitis, diarrhea, and dementia. It is important in dermatology and cosmetology because it provides a wide range of therapeutic and aesthetic effects. Niacinamide, a substituted pyridine derivative is one of the starting material for the oxidoreduction coenzymes nicotinamide adenine dinucleotide (NAD⁺) (9) and nicotinamide adenine dinucleotide phosphate (NADP⁺). These coenzymes are crucial for physiological functions like energy metabolism as they uptake electrons during glycolysis and TCA cycle and later transfer it during oxidative phosphorylation. Reports suggests that concentration of this fundamental currency of both catabolic and anabolic processes keeps on decreasing with aging. The localized supply of niacinamide helps to restore intracellular nicotinamide homeostasis.

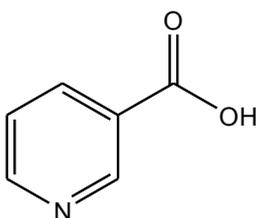
This Topical Agent has apparent role the dermatological therapeutic. its apparent roles are in the anti-acne, and up regulator of epidermal sphingolipids synthesis, an inducer of epidermal differentiation markers and cell growth within the dermis, also as a moderator of photo immune suppression and accompanied tumor genesis [24-26]. Its most recent role in modifying the aesthetic appearance of skin through inhibiting the melanin transfer leading to the reduction in skin pigmentation [27].

Niacinamide is especially crucial for collagen biosynthesis. Not only this, topical application of 2% niacinamide is also known to up-regulates the epidermal ceramides synthesis. With 5% concentration of Niacinamide application for a period of 12 weeks showed a significant effect on skin texture and hyperpigmentation [27]. By stimulating poly (ADP-ribose) polymerases (PARPs), niacinamide improves DNA repair topically, assisting in the repair of UV-induced damage and preventing photoaging.

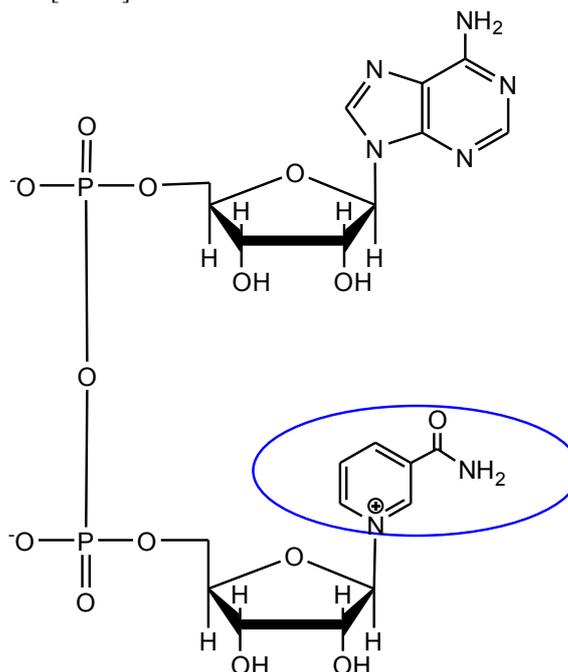
Unlike other active ingredients such as retinoids or vitamin C, niacinamide remains stable across a broad pH range and resistant to deterioration on light or air exposure. These characteristics make it perfect for use in combination with other active ingredients like retinoids, hyaluronic acid, BHAs, and AHAs. All skin types, even sensitive skin, can tolerate it well when applied in concentrations between 2 and 10%. Furthermore, it is compatible with sensitive skin, which broadens its use among different age groups and skin types. All the aforementioned effects on the skin makes niacinamide a primary ingredient in a variety of skin care products, including, cleansers serums, moisturizers and sunscreens [28-30].



Niacinamide (7)



Niacin (vitamin B3) (8)



Nicotinamide adenine dinucleotide (NAD⁺) (9)

VI. Conclusion

In conclusion we can say inclusion of these simple organic molecule in our daily skin care routine can help the user in many different ways. The choice of using the right AHA or BHA depends on the skin texture and using it in right amount is crucial. AHA's like Glycolic acid is known to remove fine lines, enlarged skin pores and also uneven skin tone. Its adaptability, effectiveness, and generally good safety makes it right for cosmeceuticals. For treating sun damaged or acne BHA's like salicylic acid is very effective. The mechanism of action on the skin of Glycolic acid and salicylic acid, are different. In all, we can say one can try both AHA and BHA as exfoliant alternatively in the morning evening skin care routine.

To maintain the natural moisturizing factor (NMF), urea is an important active ingredient. Due to its high-water solubility, it is in dermatological and cosmetic procedures. Urea is mainly used as moisturizers in foot creams and hand creams, nail and cuticle softener, in the ointments for disorders like psoriasis, xerosis etc. However, its role is concentration dependent.

In conclusion, niacinamide is most reliable, stable molecule having longer shelf life, and compatible to all age groups offers a broad range of dermatological and cosmetic formulations. The combination of other active ingredients like retinoids, hyaluronic acid, BHAs, and AHAs with niacinamide makes the products even better. All skin types, even sensitive skin, can tolerate it well when applied in concentrations between 2 and 10%. Following a skin care regime with these cosmeceuticals may help in skin appearance, hyperpigmentation and treating fine lines, thereby boosting the confidence of the user.

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