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# A Comprehensive Review on Cosmeceutical

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**Abstract:** *Cosmeceutical” is not a term formally recognized by regulatory bodies. It was a term introduced in the 1980s to describe an emerging type of PCP with therapeutic potential, sold for topical use but with claimed performance characteristics more aligned with pharmaceutical actions (Martin and Glaser, 2011; Draelos, 2015; Sotiropoulou et al., 2021) (see Chapter 4). As such, cosmeceuticals confound the distinction between cosmetic and drug, but they remain at the current time viewed by regulatory agencies as cosmetic products with ingredients regulated as for any other ingredients of PCPs. This status quo raises two questions, firstly of the evidence for the purported medical benefit and secondly of possible side effects from inappropriate usage. Without regulatory scrutiny, claimed medical benefits of these biologically active ingredients are not externally validated and could be misleading to consumers. On the other hand, supply of these products without any guidance as to quantity or frequency of use could result in adverse side effects. Pharmaceuticals are always provided with considerable information to the user concerning dosage and possible side effects, and with purported biological activity, cosmeceuticals need the same provision if misuse is to be avoided.*

**Keywords:** *Cosmeceuticals, cosmeceutical chemistry, regulatory aspects, skin cosmeceutical*

## I. INTRODUCTION

A cosmeceutical is a cosmetic product that contains bioactive ingredients purported to have medical or health benefits for the skin, beyond just cosmetic appearance. They bridge the gap between cosmetics and pharmaceuticals, acting as topical products with therapeutic potential, such as correcting skin concerns like acne or aging, say Vinner Labs, ScienceDirect.com, and Bentham Science Publisher. Examples of active ingredients include retinol, vitamin C, and hyaluronic acid.

### A. Key Characteristics

- 1) Bioactive ingredients: Contain scientifically-backed ingredients that can affect biological functions of the skin, according to ScienceDirect.com.
- 2) Therapeutic potential: Aim to address specific skin conditions or concerns and may offer long-term, visible results, notes Symphonic M.D..
- 3) Topical application: Are applied to the skin in a similar way to traditional cosmetics, according to Bentham Science Publisher.
- 4) Examples of ingredients: May include antioxidants like vitamin C and green tea, anti-aging ingredients like retinol and hyaluronic acid, and ingredients for specific issues like salicylic acid, according to [Collins Dictionary](#) and [YouTube](#).

### B. Regulatory Status

- 1) Despite their therapeutic claims, the "cosmeceutical" category is not formally recognized by regulatory bodies like the [US-FDA](#) or the European Union, states National Institutes of Health (.gov).
- 2) In the U.S., there is no legal requirement to prove that cosmeceutical products live up to their claims, notes [Wikipedia](#).
- 3) This lack of formal regulation can lead to controversy regarding the actual effectiveness and validation of their claims, according to National Institutes of Health (.gov).



There remains much controversy surrounding the “active ingredients” found within cosmeceutical products, particularly in regards to their mechanism of action, formulation, optimal concentration, penetration and retention in skin. Some clinical trials and tests have been done to address these questions, but on the whole there is little validation to support cosmeceutical claims. In vitro testing for some products has shown that these ingredients do have a protective and repairing effect on aging skin; however, there has been little translation of this evidence into in vivo testing to determine the possibility of delivering adequate doses to skin that will produce clinical or histologic results.<sup>1</sup>

### C. Vitamins

Many cosmeceutical agents are developed and advertised for prevention and treatment of aging skin, particularly photoaging skin. Photoaging refers to the damage that is done to the skin from prolonged exposure, over a person’s lifetime, to solar UV radiation. While the most important protective measure against photoaged skin is the daily application of UVA and UVB sunscreen, potential treatment options for already damaged skin involve the use of topical antioxidants and compounds that help repair DNA and stimulate collagen synthesis. Topical vitamins are substances that are purported to provide some of these benefits.

The efficacy of topical synthetic Vitamin A or retinoids—in various forms such as tretinoin, adapalene, and tazarotene—is evidence-based, and the cosmetic benefits of these prescription retinoids are well supported by ample research.<sup>2,3</sup> Tretinoin induces production of type I and II procollagen in skin and reduces collagen breakdown by inhibiting metalloproteinases. The overall effect is a thickening of the dermis as the skin is “filled in” with glycosaminoglycans, helping to reduce fine lines and wrinkles.

Other retinoids, such as retinaldehyde, retinol, and the retinyl esters, are marketed as over-the-counter cosmeceuticals and may have similar actions to their prescription counterparts despite having less evidence proving their efficacy.<sup>1</sup> Patients should be cautioned that all of the retinoids are able to produce skin irritation and dryness, even in over-the-counter formulations, although the latter much less than prescription-strength products.

Vitamin E is another vitamin that is purported to have advantageous cosmetic effects on skin. Functioning as an epidermal antioxidant by absorbing the solar spectrum of UV light, endogenous Vitamin E becomes depleted after years of excessive exposure to free radicals, with resulting oxidative damage.

Thus, many studies have looked at the benefit of applying topical Vitamin E, especially in its most active form alpha-tocopherol, as a means of protecting against sunburn and improving the wrinkling and hyperpigmentation caused by free radicals. Studies in human subjects have demonstrated its efficacy in preventing UV-induced skin erythema, with topical 2% Vitamin E reducing the redness value by approximately 20%.<sup>4</sup> A four-month facial study of topical 5% vitamin E resulted in improved wrinkling and UV-caused inflammation around the eye area.<sup>5</sup> Importantly, Vitamin E can reduce UV-associated erythema and edema when applied before UV exposure, with little benefit noted if Vitamin E is applied after the exposure.<sup>6</sup> Also, almost no side effects have been reported from the use of topically applied vitamin E.

One of the most recently recognized “cosmeceutical vitamins” is Vitamin B<sub>3</sub>, also called nicotinamide or niacinamide. A precursor to the key metabolic cofactor NAD(P) and its powerful reduced form NAD(P)H, niacinamide’s role as a key player in antioxidantizing reactions has been the focus of most of the studies. Well-tolerated in topical form, niacinamide has been shown to improve skin barrier by increasing lipids and epidermal protein.<sup>7</sup> This action leaves skin more resistant to irritation and blotchiness, most likely by decreasing water loss from skin. Niacinamide also reduces facial dyspigmentation via a mechanism that inhibits melanosome transfer from melanocytes to keratinocytes.<sup>8</sup> Other beneficial effects with chronic topical niacinamide application include improvement and prevention of skin yellowing and a smoothing of skin texture. However, even with these benefits, topical niacinamide remains one-third to one-fifth as effective as topical 0.025% tretinoin.<sup>9</sup>

Vitamin C, also known as L-ascorbic acid, is one of the vitamins that humans must obtain from dietary sources. However, oral supplementation of Vitamin C only minimally increases its concentration in skin. Thus, topical Vitamin C application is a popular research area. In addition to its well-known and essential contribution to collagen biosynthesis, research data demonstrates that topical Vitamin C has anti-inflammatory and antioxidant properties,<sup>10</sup> such that it has been used to reduce the erythema associated with postoperative laser resurfacing. A double-blind, placebo-controlled, splitface 12-week study examining the effects of topical 3% ascorbic acid showed that Vitamin C is well-tolerated in topical application and causes a reduction in facial wrinkles.<sup>11</sup> Higher doses of 5–17% ascorbic acid revealed improved skin texture and the appearance of photoaging. With ongoing research confirming and maximizing the benefits of topical Vitamin C and the other cosmeceutical vitamins, these agents will continue to grow in their usefulness and value in protection and restoration of skin.

#### D. Hydroxy Acids

The hydroxyacids—comprised of the  $\alpha$ -hydroxyacids,  $\beta$ -hydroxyacids, polyhydroxyacids, and bionic acids—represent a class of compounds with unprecedented cosmetic benefits. The most well-known and commonly used is the  $\alpha$ -hydroxyacid glycolic acid for its proven antiaging benefit and ability to improve hyperpigmentation and acne-prone skin. Both the  $\alpha$ -hydroxyacids and  $\beta$ -hydroxyacids work by removing or decreasing hyperkeratinized skin and restoring the epidermis, making them useful for treatment of dry skin, verrucous growths, and ichthyosis.<sup>12</sup> Furthermore, application of hydroxyacids causes dermal thickening by stimulating biosynthesis of glycosaminoglycans, collagen, and elastic fibers, improving wrinkles and fine lines.<sup>13</sup> The polyhydroxyacids and bionic acids are newer agents with the same benefits as the  $\alpha$ - and  $\beta$ -hydroxyacids but without their characteristic irritation or burning and with additional antioxidant and barrier functions to improve moisturization. Their gentleness on skin makes them ideal for treating sensitive skin. Gluconolactone is a polyhydroxyacid widely used in skin care products that has been shown in vitro to protect against UV radiation by trapping free radicals.<sup>14</sup> The hydroxyacids, especially glycolic and lactic acid, are commonly used as peeling agents. Applied to the skin in high concentrations for short periods of time, hydroxyacid peels are increasingly used to accelerate exfoliation and to stimulate skin renewal to improve hyperpigmentation and texture of skin.

#### E. Peptides

The role of peptides in cosmeceuticals revolves around the hypothesis that peptide fragments of collagen and elastin can act as positive feedback signals for their own continued synthesis. Peptides are highly successful in the current cosmeceutical market, and there are increasing numbers of double-blinded, placebo-controlled studies to examine their effects on human skin. Peptides of interest include pal-KTTKS (Matrixyl), Ac-EEMQRR (Argireline), and Cu-GHK. The peptide pal-KTTKS is a fragment of dermal collagen that stimulates new collagen synthesis in vitro and is postulated to facilitate wound healing.<sup>15</sup> It has high potency and was shown to improve wrinkled skin when applied topically at very low doses and with minimal skin irritation. Cu-GHK is also a fragment of dermal collagen, and the copper moiety is a necessary cofactor for collagen synthesis. Many peptides, such as Ac-EEMQRR, mimic botulinum toxin and function to cause muscle relaxation by inhibiting neurotransmitter release;<sup>16</sup> however, a 2006 study comparing topical nonprescription products, including those containing peptides, to botulinum toxin type A injections concluded that the injections provided significantly greater efficacy and patient satisfaction in the treatment of glabellar frown lines.<sup>17</sup> The cost of all of these peptides remains a challenge to cosmeceutical companies, especially if the peptide has low potency and requires greater concentrations to achieve efficacy.

#### F. Growth Factors

Growth factors function as regulatory proteins that mediate signaling pathways, particularly those associated with wound healing. Kinetin, also known as N-6 furfuryladenine, is a plant growth factor studied in human skin fibroblast cultures. In vitro studies have demonstrated that the continuous application of kinetin may have the ability to delay the skin changes associated with aging as well as decrease the severity of these changes. Kinetin prevents the alteration in cell size and shape and delays growth rates and macromolecular synthesis associated with aging. Kinetin acts as both an inhibitor of free radical formation and a scavenger of reactive oxygen species by mimicking superoxide dismutase. Other clinical studies have suggested that topical kinetin may improve skin texture, decrease hyperpigmentation, and impede transepidermal water loss, but the mechanisms for these actions have much less evidence to support them.

#### G. Regulatory Status

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- 3) This lack of formal regulation can lead to controversy regarding the actual effectiveness and validation of their claims, according to National Institutes of Health (.gov).

## II. CONCLUSION

Cosmeceuticals are cosmetic products containing biologically active ingredients that provide pharmaceutical-like benefits, such as anti-aging or acne control, beyond simple aesthetic enhancement. The term is a portmanteau of "cosmetics" and "pharmaceuticals" and describes products intended to influence the skin's biological functions to improve its health and beauty. These products are not formally recognized as either a cosmetic or a drug by regulatory bodies like the US FDA or the EU.



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