

Review Article

## Insights into Cosmeceuticals

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### ABSTRACT

A cosmetic is “intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance” while a drug is “intended for use in diagnosis, cure, mitigation, or prevention of disease, i.e. it affects the structure and function of the body.” Cosmeceuticals attempt to interface between a pure cosmetic and a drug. They are those which lie between a prescription and a non-prescription over-the-counter product. They are medical products, which are cosmetics, with functional benefits for the skin, hair, and nails. Cosmeceuticals are disease-treating and disease-modifying. Dermatologists form a unique interface between products with perceived advantages and those with proven efficacy. In an attempt to hard-sell products with minimal side effects, certain compounds may contain subtherapeutic doses of topical agents hence rendering them ineffective. On the other hand, certain products may form a useful bridge with a safety profile better than cosmetics in their class. This article reviews commonly available and evolving cosmeceuticals, their rationale, side effects, and use in dermatology practice with the aim to sensitize dermatologists about their perceived usefulness.

**Keywords:** Cosmeceutical, Nutraceuticals, Supplements, Phytochemicals

### INTRODUCTION

The word cosmeceutical is derived from the words, “cosmetic” and “pharmaceutical” and is a gray area between the two.<sup>[1]</sup> Cosmeceuticals are akin to jokers in the pack, acting as substitutes for that “missing link” needed to bridge the gap between specific and holistic treatment of the skin, hair, and nails.

A cosmetic is “intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance,”<sup>[2]</sup> whereas, a drug is “intended for use in diagnosis, cure, mitigation, treatment, or prevention of disease,” thus affecting the structure and function of the body.<sup>[3]</sup>

Cosmeceuticals hence attempt an interface between a pure cosmetic like a lipstick and a pure drug like Vitamin E. They are those which lie between a prescription and a non-prescription over-the-counter (OTC) product. They are medical products, which are also cosmetics, with functional benefits for the skin, hair, and nails. They are fortified with certain medicated actives which have disease-modifying or disease-treating properties. In actual terms, even water, when applied on the skin, is said to have therapeutic benefits.<sup>[4]</sup>

They are also called dermocosmetics, but an appropriate term could also be “Medical Cosmetics.” They have a very unsure standing, as the US FDA does not recognize any such term as a “cosmeceutical.”<sup>[5]</sup> The strengths of the medical actives present are not equivalent to prescription

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medication. They are mostly developed for home use. Despite this, the boom in the cosmeceutical market is glaring. This is mainly because cosmeceuticals are procured as non-prescription products available as OTC and regulations regarding their market release are flimsy.

The history of cosmeceuticals dates to the Egyptians in the 1600s, who described the use of cosmeceutical-like products in their medical papyrus “Ebers.”<sup>[6]</sup> Their productivity and usefulness has thus been known since ancient times. Raymond Reed, the founder of the US society of cosmetic chemists, was the one who proposed the term cosmeceutical after recognizing their functional benefits. It was Kligman, in the late 1970s, who propagated the term and took forward the use of cosmeceuticals.<sup>[7,8]</sup> He based his theories mainly on his work done with retinoic acid on UV damaged skin.

Cosmeceutical development has seen an exponential increase in research and development. Modern cosmeceutical formulations are thoroughly researched and tested in laboratories using many methods such as on fibroblast gene chips. A positive result is followed by application of cultured fibroblasts to a mice model, following which human trials are done.

## NOMENCLATURE

Relevant to their nomenclature it is necessary to be familiar with certain terms:

### Cosmeceuticals

Topical agents are applied to the skin, hair, or nails. They have functional properties and act beyond the time of application. They have certain properties, which make them penetrate deeper than cosmetics.

### Nutraceuticals

These are oral supplements, which are ingested to maintain the overall health of the skin, hair, and nails. They have issues of absorption and first- pass metabolism, hence have unpredictable bioavailability.<sup>[9]</sup>

### Nutricosmetics

Nutraceutical ingredients are put into topical delivery systems with the elegance of cosmetics, so they can be applied to the skin.<sup>[10]</sup>

## MAJOR FUNCTIONS OF COSMECEUTICALS

The main functions of these “Jacks of all trades” are anti-aging, photoprotection, anti-inflammatory, antioxidant, skin lightening, skin brightening, texture improvement, hair growth enhancing, and nail care.

## CLASSIFICATION

1. Cosmeceuticals can be divided into those with functional benefits for the skin and hair, which continue their action beyond the time of application, such as sunscreens, depigmenting agents, moisturizers, and shampoos and those to adorn the skin, which act till the time of application, such as lipsticks, toothpastes, talc, and hair serums.
2. They can also be divided according to their major functions due to various mechanisms of actions of the main ingredients in the product. Examples are sunscreens, moisturizers, hydroxy acids, retinoids, antioxidants, etc.
3. Division into pure topical cosmeceuticals, such as Vitamin C serum, or nutricosmetics such as glutathione, coenzyme Q10, lycopene, and omega 3 fatty acids may also be considered.<sup>[11,12]</sup>
4. Cosmeceuticals may be synthetic or natural products, such as hydroquinone or botanicals, respectively.

## MECHANISM OF ACTION

1. Antioxidant: Where they scavenge free radicals (coenzyme Q10, Vitamin C, and Vitamin E) and act as anticancer and anti-aging molecules.<sup>[13]</sup>
2. Anti-inflammatory: By inhibiting COX-2, PGE2 (aloe), inhibiting leukotriene B4 (chamomile).<sup>[14]</sup>
3. Anti-aging – lightening: By inhibiting tyrosinase (hydroquinone).  
Anti-aging – rhytides reduction: By stimulating fibroblasts and collagen synthesis (retinoids, peptides), improve exfoliation (alpha, beta, or poly hydroxy acids), prevent UV damage (soy), improve hydration of the stratum corneum, and improve barrier function (moisturizers based on silicone, petrolatum, ceramides, or white soft paraffin).<sup>[15]</sup>
4. Prevent apoptosis: Retinoids, phytochemicals.<sup>[13,16]</sup> Prevent UV damage induced apoptosis.
5. Photoprotection: By deflection or absorption (sunscreens with avobenzone, micronized zinc, and titanium).
6. Regulating cellular mechanisms: Providing cellular messengers or modulating cellular mechanisms through enzymatic interplay to produce more extracellular matrix (peptides).<sup>[17]</sup>

## COSMECEUTICALS IN USE

Cosmeceuticals contain active ingredients called “actives” which are usually weaker in strength compared to prescription drugs [Figure 1]. They are basically sold as OTC products and hence contain strengths which do not qualify them to be called drugs. This way, they circumvent the regulatory procedures pertaining to their entry and sale in the retail markets.

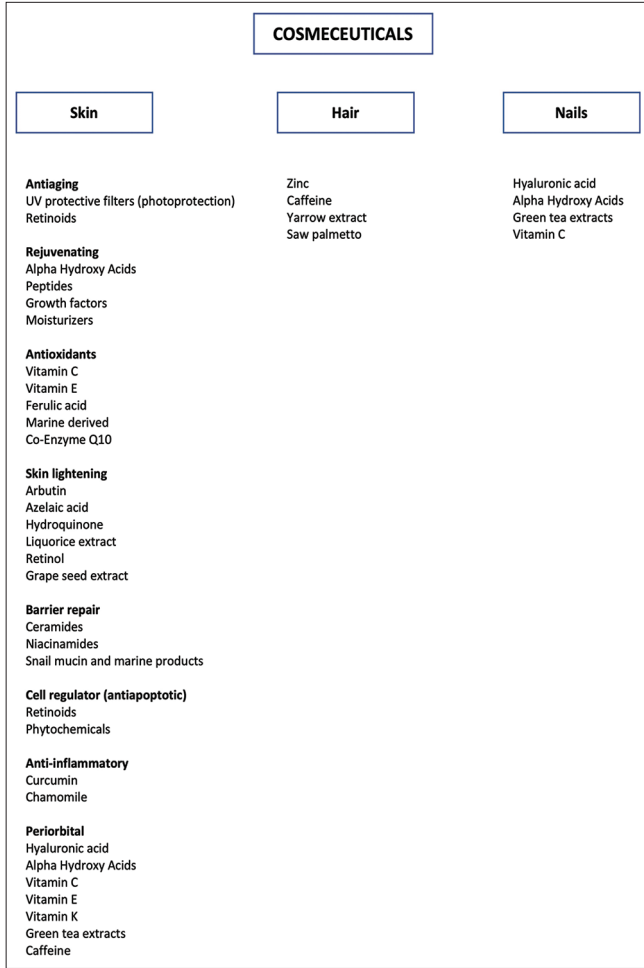


Figure 1: Cosmeceuticals in use.

## SUNSCREENS

They help to reduce photoaging, pigmentation, and skin cancers.

These may be physical or chemical. Physical ones contain inorganic filters such as micro-ionized or nanoparticles of metal oxides such as zinc, titanium, or iron. They deflect ultraviolet rays. Absorption of the active ingredients is a cause of concern as reported in literature.<sup>[18]</sup>

Chemical sunscreens have organic filters such as avobenzene, benzophenones, or methyl anthranilate which act on UVA spectrum, and salicylates or cinnamates which act on the UVB spectrum. The chemical filters absorb ultraviolet rays and dissipate them as an exothermic reaction. These ingredients in sunscreens may also be a cause of photodermatitis.<sup>[19,20]</sup> Avobenzene is broad spectrum, but photo-unstable thus degrading the sunscreen function. Benzophenones are photostable, give less protection but are lipid soluble and hence have greater bioavailability.<sup>[21]</sup>

## MOISTURISERS

Humectants, occlusives, and emollients are all used as ingredients. Glycerin, pyrrolidine, carboxylic acid, and urea are humectants, which absorb moisture from the environment as well as the dermis. Petrolatum, waxes, butters, silicones, and oils are occlusive, which tend to seal the moisture in the epidermis. Esters and oils are emollients, which improve the texture of the skin. They are used as anti-aging agents, as they smoothen the skin, keep it supple, hydrated, and maintain the skin barrier. Different vehicles and techniques are used to give esthetically appealing end products which are also longer lasting.<sup>[22]</sup>

## RETINOIDS

The largest number of evidence-based studies has been done on this stand-alone cosmeceutical.<sup>[23-26]</sup> It is the second most important cosmeceutical after a sunscreen.

Kligman and Willis, the father of cosmeceuticals,<sup>[27]</sup> propagated this molecule for anti-aging. Tretinoin is the most widely studied and potent molecule among this class as a wrinkle and fine line reducer. Retinaldehyde, retinol esters, and other derivatives are the other retinoids in use.

The threshold concentration of retinol and retinaldehyde to be effective is 0.025%. Any less as in common cosmeceuticals is ineffective.<sup>[28,29]</sup> However, they are most widely used because of their fewer irritating effects on the skin and in lower concentrations, they are non-prescription drugs. They are also dispensed in moisturizers and hair care cosmeceuticals.<sup>[30]</sup> Side effects are directly proportionate to the concentration of the retinoids, skin dryness being the most common.<sup>[31]</sup>

## PROVITAMINS

Niacinamide, pantothenol, and many botanicals fall in this category.

They are photoprotective and anti-aging. They also enhance barrier properties. Niacinamide in the concentration of 2–5% is used as a cosmeceutical and prevents the transfer of melanosomes to the keratinocytes. It tightens pores, is anti-inflammatory, antioxidant, and improves barrier function. It is well tolerated with fewer side effects.<sup>[32]</sup> Vitamin B5 and D (dexa) pantothenol have better penetration than Vitamin B5 alone. They have all the above functions except depigmentation and have been reported comparable to tretinoin in wrinkle treatment.<sup>[33]</sup>

## ANTIOXIDANTS

They prevent free radical damage by quenching nascent oxygen, superoxide, and hydroxyl ions and may be topical

or systemic. They act to maintain the barrier function, are photoprotective, and lighten the skin color.<sup>[32]</sup>

Some of the potent antioxidants are polyphenols like genistein in soy which is a flavonoid. Catechins like proanthocyanidin in grape seed extract and epigallocatechin 3-gallate in green tea extract are also potent antioxidants. Proanthocyanidin inhibits xanthine oxidase which generates oxygen radicals. Pycnogenol present in pine bark extract is depigmenting, antioxidant, anti-inflammatory, and an anticancer agent. Lycopene present in tomatoes and red carrots is also a strong antioxidant.<sup>[34]</sup> Coenzyme Q10, idebenone, Vitamin C, ferulic acid, and glutathione are some oral and topical antioxidants. Ferulic acid when combined with Vitamins C and E gives a 4-fold increase in photoprotection.<sup>[35]</sup>

### HYDROXY ACIDS<sup>[36,37]</sup>

They are fruit acids and are either alpha hydroxy acids such as lactic acid and glycolic acid, beta hydroxy acids such as salicylic acid, or polyhydroxy acids such as gluconolactone. They cause chelation of calcium ions, promote desquamation, and hence retain moisture in the epidermis. They are also antioxidants and textural improvers, as they act as humectants. They also increase glycosaminoglycans and collagen. Glycolic and lactic acids have the smallest size and penetrate the most. Polyhydroxy acids rectify the irritating potential of the alpha hydroxy acids on the skin. They are dispensed in 5–12% concentration,<sup>[38]</sup> whereas, concentrations up to 20% are considered safe for self-application.<sup>[39]</sup>

### DEPIGMENTING AGENTS

Hydroquinone is one of the most potent depigmenting agents, which prevents conversion of tyrosine to melanin. It is used in the strength of 2% as an OTC product.<sup>[37]</sup> Prescription strengths of hydroquinone can go up to 3–4% or beyond in special compounding.<sup>[40]</sup> Side effects are irritation, contact dermatitis, and exogenous ochronosis.

Arbutin is a glucopyranoside derivative of hydroquinone. It is a naturally occurring compound found in the dried leaves of plants including bearberry, blueberry, cranberry, and pear trees. It inhibits tyrosinase as well as melanosome maturation.<sup>[23]</sup>

Glabridin, also known as licorice root extract, is used in the concentration of 10–40% and has skin lightening effects 16 times greater than hydroquinone. It is also faster acting, with onset of action within 7 days.<sup>[41]</sup>

Other ingredients used are N-acetyl glucosamine a precursor of hyaluronic acid which is a tyrosinase inhibitor, kojic acid which is derived from a fungus and chelates copper used in 1–4% concentration and azelaic acid, a dicarboxylic acid

derived from *Pityrosporon ovale* which is well-tolerated. Mequinol is a chemically derived ingredient, which is also a depigmenting agent.<sup>[37]</sup> Soy and Vitamin C inhibit the PAR-2 pathway. These are used for melasma, solar lentigines, freckles, and post-inflammatory hyperpigmentation.<sup>[42]</sup>

### GROWTH FACTORS

Epidermal growth factors stimulate epidermal healing and reepithelialization post-burns or resurfacing procedures.<sup>[43]</sup> Their larger molecular weight (usually >15,000 Da) inhibits their absorption through the stratum corneum, hence the use of lipophilic preparations for adnexal penetration or use of dermarollers and lasers for percutaneous drug delivery are used.<sup>[44]</sup>

Transforming growth factor like TGF Beta 1 stimulates normal skin growth, repair, and angiogenesis. It is extracted from neonate dermal skin.<sup>[45]</sup>

### TOPICAL PEPTIDES

These are signal, carrier, or neurotransmitter inhibiting.<sup>[46]</sup> They act in response to fragmented collagen and elastin fibers. Peptides are usually attached to palmitic acid moieties to enhance penetration through the skin.

There is evidence to show that twice daily application shows histological and ultrastructural evidence of thickening of epidermis and increase in collagenesis and hence improvement in texture and skin lightening.<sup>[47,48]</sup>

### MALE-SPECIFIC COSMECEUTICALS

Several male-specific cosmeceuticals have been propagated in the market.<sup>[49]</sup> These are basically made taking the male physiology into account.<sup>[50]</sup> The unique practice of shaving in men is also exploited to introduce male-oriented cosmeceuticals.<sup>[51]</sup> However, till date, all studies about cosmeceuticals are done on women. Male cosmeceuticals are usually related to hair growth, antiperspirants, moisturizers, sunscreens, barrier repair creams, and hair styling products.

### NAIL CARE COSMECEUTICALS

Several cosmeceuticals are now being used for nail care. Many of these are added to nail varnish or are used as stand-alone products. Some important ingredients of these products are keratin, hyaluronic acid, green tea, pentavitin, shea butter, and Vitamin C. These are used for nail shine or to improve brittle nails. Anti-aging nail polishes and professional manicures also have these ingredients. Silver nanoparticles are being added to nail polishes for their antibacterial and antifungal effects.<sup>[52]</sup>

## HAIR CARE COSMECEUTICALS

Zinc pyrithione, caffeine in shampoos, yarrow extract, and saw palmetto are some of the ingredients used in hair care cosmeceuticals.<sup>[53]</sup>

Yarrow extract is a botanical, used for oily hair. Caffeine relaxes smooth muscle fibers around the hair and inhibits 5-alpha reductase, hence is proposed to be useful in androgenetic alopecia.<sup>[54]</sup> Sericin is an important cosmeceutical ingredient, which seals the cuticle and prevents damage to the hair shaft.<sup>[55]</sup>

Nanotechnology is used to prepare some of these cosmeceuticals, to prevent damage to the cuticle. Hair care cosmeceuticals are used to prevent hair loss, promote hair growth, silkiness, shine, and for overall hair care.

## COSMECEUTICALS FOR PERIORBITAL CONCERNS

Periorbital hyperpigmentation, under eye puffiness, periorbital fine lines and wrinkles, and thin skin with visible vasculature are all concerns for which cosmeceuticals are used.<sup>[40]</sup> Under eye creams, gel serums and patches are the different formulations used. The ingredients that are most commonly used are green tea extracts which contain caffeine which acts as a decongestant and tannins which promote lymphatic drainage.<sup>[56]</sup> Vitamin K creams also help with congested vasculature in the under-eye area, which help to reduce the bluish discoloration in the area.<sup>[57]</sup> Hyaluronic acid serums help with moisturization and thin skin. Peptide serums may help with hyperpigmentation, fine lines, and wrinkles. Vitamins C, E, and ferulic acid used in formulations help with hyperpigmentation.<sup>[58,59]</sup> Azelaic acid containing formulations help with hyperpigmentation.<sup>[60]</sup>

## SNAIL MUCOUS AND MARINE PRODUCTS

Snail mucin called “Snail filtrate” and jellyfish mucin is rich in glycoproteins, pseudopterosins, mycosporine, and phlorotannins which retain moisture, absorb ultraviolet radiation, and are antioxidants. They are used to improve texture, for anti-aging, acne, rosacea, and stretch marks.<sup>[61]</sup> Studies report their antibacterial and wound healing properties with or without honey.<sup>[62]</sup> Many used as nutricosmetics are now nutraceuticals.<sup>[61]</sup> Seaweeds, wild or cultivated crops, algae, corals, fish scales and salmon, collagen gold from fish scales, and salmon, which are a rich source of pyridoxine, are used as anti-aging molecules.<sup>[62]</sup>

## SIDE EFFECTS

Active ingredients in cosmeceuticals are not just bland or inert and may exhibit side effects associated with them, which come under

the realm of a topical applicant.<sup>[29]</sup> Phototoxic and photoallergic reactions, contact dermatitis, skin irritation, and cosmetic intolerance syndrome<sup>[63]</sup> are all seen with cosmeceuticals. Even though many of the ingredients are botanicals, yet they can cause severe reactions. The term botanicals and herbals, hence, do not make the cosmeceutical inert.

Some specific side effects include severe allergic reactions with angioedema, contact urticaria, and conjunctivitis with tea rinses and compresses, interactions with warfarin and cyclosporine metabolism which need to be given in higher doses caused by chamomile, hydroquinone-induced irritant contact dermatitis and exogenous ochronosis, and post-inflammatory hyperpigmentation by repeated use of lower strengths of glycolic acid.

## REGULATORY ASPECTS

The US Federal Food Drug and Cosmetic Act recognizes the term “cosmetic,” but not “cosmeceutical.” In the present time, there exist no statutory and very few regulatory laws that allow for their entry into the market with their claims regarding their functional benefits.<sup>[5]</sup>

In the US, entrants into the market must be careful, as any claim or a consumer’s perception of a product being one with a therapeutic indication, will attract scrutiny under the FDA with the strict laws. To prevent scrutiny, they are called “quasi drugs,” “controlled cosmetics,” or “cosmetic-type drugs” in different countries.<sup>[64]</sup>

Another aspect that should be considered here is the concentration of the ingredients of a cosmeceutical that is used. Therapeutic concentrations would classify them as drugs and attract scrutiny that goes along with the introduction of a drug in market. Side effect avoidance may further push companies to reduce ingredients to suboptimal concentrations, thus negating any therapeutic effect these may possibly have on the skin.<sup>[65]</sup>

So, what is the standing of all the claims made about cosmeceuticals? A lot needs to be settled on this aspect.

## A DERMATOLOGIST’S ROLE IN COSMECEUTICAL USE

Dermatologists are an interface between cosmeceuticals and consumers.

Various panel discussions and lectures at dermatology forums discussing various aspects of cosmeceuticals in recent times are evidence to the fact that that these are important skin care products.

As dermatologists, we must be aware of the various cosmeceutical ingredients, their uses, their therapeutic concentrations, and side effects, to guide patients to make

a right choice regarding these. Awareness about the active ingredients, synergistic and antagonistic actions between multiple actives in a product, and layering, should be done in various forums including social media. Accurate advice is a challenge requiring knowledge of human skin and scientific data coupled with the fact that individuals have different skin types.

## FUTURE OF COSMECEUTICALS

Biotechnology, nanotechnology, genomic studies, botanical research, and research into long-term safety are needed.

Nanotechnology using nanoparticles, 50–5000 nm in diameter, is being used to produce elegant, longer-lasting, and more efficient cosmeceuticals,<sup>[52]</sup> with smaller sized particles, which can penetrate the stratum corneum. Nano silver and gold particles are used as nail cosmeceuticals, which act as antibacterial and antifungal molecules. Specific genes being mapped to pinpoint which one is responsible for wrinkling, texture, skin pigmentation, and then use these to target concerns at a molecular level.

Research into hair and nail cosmeceuticals will form an important topic for future research.

## CONCLUSION

The future is all in all exciting for this brilliant category of skin care medical cosmetics. Biotechnology, nanotechnology, genomic studies, botanical research, and research into long-term safety will all be exploited to produce elegant and acceptable end products. Cosmeceuticals are here to stay. These “Jokers in the dermatologists armamentarium” may indeed be the bridges between internal health, beauty, and anti-aging. They shall be more acceptable if further peer-reviewed evidence-based, statistically significant studies are conducted to cement the place of cosmeceuticals in the prescription regime of a dermatologist. Treatment of most skin conditions requires a holistic approach with proper skin care as an adjunct to prescription medication.<sup>[66]</sup> Preventive skin care is also being promoted to delay extrinsic aging and for rejuvenation.

### Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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### Conflicts of interest

There are no conflicts of interest.

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