



(REVIEW ARTICLE)



Comprehensive review on cosmeceuticals

B shireesha ^{1,*}, Shyamala ² and Sathoorimanasa ¹

¹ Department of pharmacy, Joginpally B R pharmacy college, Hyderabad, Telangana, India.

² Department of pharmaceutical analysis, Joginpally B R Pharmacy College, Hyderabad, Telangana, India.

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Abstract

Now days a new hot topic in the cosmetic industry is 'Cosmeceuticals', which is the fastest growing segment of the natural personal care industry. Cosmeceuticals are the future generation of skin care. They are the advances made within the world of dermatological products and the new backbone in skincare. All cosmeceuticals claim to contain functional ingredients with either therapeutic, disease-fighting or healing properties. The term Cosmeceutical was coined by Raymond Reed but the concept was further popularized by Dr. Albert Kligman in the late 1970's. Cosmeceuticals are topically applied as cosmetic- pharmaceutical hybrids, intended to enhance the beauty through ingredients that provide additional health-related function or benefit. That means they are applied topically as cosmetics, but contain ingredients that influence the skin's biological function. Today's Cosmeceuticals are serving as a bridge between personal care products and pharmaceuticals; also Cosmeceuticals are the fastest growing segment in skin care market. There is no regulatory category for Cosmeceuticals; hence this review tries to understand regulatory scenario as well the difference between drug and cosmetics is enlightened. The paper is an earnest endeavor to evaluate a Cosmeceutical product that claims a beneficial physiologic effect. This review paper is to give recent knowledge about the latest trend of cosmetic industry- Cosmeceuticals.

Keywords: Classification of cosmeceuticals; Skin cosmeceuticals; Commonly used skin cosmeceuticals; Cosmeceutical chemistry.

1. Introduction

Cosmeceuticals are future generation of skin care. They are the advances made within the world of dermatological products and the new backbone in skincare. Cosmeceutical are typically cosmetic-pharmaceutical hybrids intended to enhance the health and beauty of skin. Some cosmeceuticals are naturally-derived while others are synthetic, but all contain functional ingredients with either therapeutic, disease-fighting or healing properties. Raymond Reed, Founder of U.S. Society of cosmetic chemist, created the concept of "cosmeceutical" was popularized by American dermatologist. Albert Kligman in the late 1970's. However the Egyptians were the first to recognize the health-giving properties of cosmetics. The "Ebers" a medical papyrus wrote in 1600 BC, made frequent to several cosmeceutical-type products. A favorite formulation was using honey and milk that claimed to help cure skin diseases.

For many medieval Arab physicians and their European counterparts, there were no distinctions among cosmetics, fragrance and herbal medicines. Their research and development work covered all these disciplines simultaneously. Separation of the cosmetic and toiletries, industry from medicines, and pharmacy was 19th century. This phenomenon occurred when the modern pharmaceutical industry was first developed and the first government statue regulation the sale of drugs was drafted. The role of cosmetic as a positive healing aid ignored until its revival in the late 1970's and early 1980's Kligman rekindled interest by developing formulations to improve the appearance of UV- damaged and wrinkled skin using retinoic acid as the active ingredient [1].

*Corresponding author: B shireesha

The concept of beautifying is not restricted to women alone, even men have become aware about their look. Now day's advertisements of many anti-wrinkle and fairness cream are aimed at men. Key cosmeceuticals used by men include hair growth products, anti-aging, antiperspirant, athlete's foot and astringents. Cosmeceutical most commonly used by women include anti-wrinkles, anti-cellulite, hair removal, tanning skin whitening, antioxidants, and cell recovery products [1].

2. Classification of cosmeceuticals

The term Cosmeceuticals can be used with different terms. For all the terms the definition remains the same i.e. Cosmeceuticals formulations which are neither pure cosmetics, like lipsticks, nor pure drug, like corticosteroids. It is a hybrid category of products lying on the spectrum between drugs and cosmetics. The various terms by which Cosmeceuticals can be substituted are active cosmetics, nutricosmetics, performance cosmetics, functional cosmetics, and dermaceuticals. Cosmeceuticals basically can be classified into following categories:

- Skin cosmeceutical product- Antiaging creams, Moisturizers, Facial products and Lotions.
- Hair cosmeceutical product- Gel and creams, Hair colorants and Dyes, Shampoos, Growth Stimulators and Conditioners.
- Others- Lipstick, Nail polish, Toothpaste and Powders.

2.1. Skin cosmeceuticals

Cosmeceuticals are the cosmetic products that have medicinal or drug-like benefits are able to affect the biological functioning of skin owing to type of functional ingredients they contain. These are skin-care products that go beyond coloring and adorning the skin. Such products improve the functioning/texture of the skin by encouraging collagen growth by combating harmful effects of free radicals, thus maintaining keratin structure in good condition and making the skin healthier. Olay vitamin line, which includes vitamins A, C, D, E, selenium, and lycopene, pycnogenol plus zinc and copper, is a well-known skin care line. The treatment of aging skin with a cream containing a hormone such as estrogen results in a fresh appearance with a rejuvenating effect. Kuno and Matsumoto had patented an external agent for the skin comprising an extract prepared from olive plants as a skin-beautifying component, in particular, as an anti-aging component for the skin and/or a whitening component. Dry emollient preparation containing monounsaturated Jojoba esters was used for Cosmeceutical purpose. Martin utilized plant extract of genus Chrysanthemum in a cosmetic composition for stimulating skin and/or hair pigmentation [2].

2.2. Commonly used skin cosmeceuticals

- Hydroxy Acid: Hydroxy acid also referred to as fruit acids; they are a common ingredient found in many cosmeceutical products. Examples include citric acid, malic acid, and lactic acid. AHAs improve skin texture and reduce the signs of aging by promoting cell seeding in the outer layers of the epidermis and by restoring hydration. One hypothesis suggests that AHAs reduce the calcium ion concentration in the epidermis and, through chelation, remove the ions from the cell adhesions, which are thereby disrupted, resulting in desquamation. This is enhanced by cleavage of the endogenous stratum corneum chymotryptic enzyme on the catherins, which are otherwise protected from proteolysis by conjugation with calcium ions. The resulting reduction of the calcium ion levels tends to promote cell growth and slow cell differentiation, thus giving rise to younger looking [3].
- Botanicals: Botanicals comprise the largest category of cosmeceutical additives found into the market place today. Some botanicals that may benefit the skin include green tea extract, ferulic acid, and grape seed extract.
- Ferulic acid: This compound, which is derived from plants, is considered to be a potent antioxidant, and has been shown to provide photo protection to skin. Furthermore, when ferulic acid is combined with vitamins C and E, the product has been shown to provide substantial UV protection for human skin. Moreover, Murray et al. reported that because its mechanism of action is different from sunscreens, ferulic acid could be expected to supplement the sun protection provided by sunscreens. Grape Seed Extract: This botanical has been established as a potent antioxidant and has been shown to speed wound contraction and closure. Topical application of grape seed extract has also been shown to enhance the sun protection factor in humans [3].
- Depigmenting Agent: Skin-lightening agents added to product formulations have become increasingly popular and such products are in demand. Common depigmenting ingredients include hydroquinone, ascorbic acid (vitamin C), kojic acid, and licorice extract (glabridin). Hydroquinone: Hydroquinone has been the popular agent of choice for skin lightening. The US FDA has proposed concentrations between 1.5% and 2% in skin lighteners. A recent study suggests that this concern has been based mainly on studies with animal models

utilizing long-term exposure at high dosages are carcinogenic. Routine topical application may pose no greater risk than that from levels present in common foods.

- **Exfoliants:** Exfoliants promote skin turnover by removing adherent cells in the stratum corneum. Common exfoliants found in cosmeceutical preparations include salicylic acid (SA), lactic acid, and glycolic acid. There are concerns that repeated use of SA and AHAs could cause the dermis and epidermis to be more vulnerable to penetration by UV radiation.
- **Moisturizers:** Moisturizers restore water content to the epidermis, and provide a soothing protective film. They improve the appearance and tactile properties of dry and aging skin, restore the normal barrier function of the skin, and reduce the release of inflammatory cytokines. Moisturizers comprise an important therapeutic component in the management of various skin conditions (e.g. eczema, psoriasis, pruritus, and aged skin).
- **Topical Peptides:** Topical peptides are regarded as cellular messengers that are formed from amino acids and are designed to mimic peptide fragments with endogenous biologic activity. These pentapeptides (e.g. KTTKS) are comprised of a subfragment of type I collagen propeptide, and play a role in signalling fibroblasts to produce collagen in the skin, which can improve the appearance of wrinkles.
- **Retinoids:** Retinoids are among the most common ingredients found in cosmeceuticals. In fact, they are the most studied and have the most data behind them. They consist of natural and synthetic derivatives of vitamin A that reduce hyperpigmentation and inhibit enzymes from breaking down collagen [3].
- **Sunscreen:** Sunscreens are the single most important cosmeceutical, because they protect skin against solar radiation, which is the most important damaging environmental agent. As a result, they help to prevent the signs of aging. To be effective, sunscreens should provide broad spectrum coverage that includes both UVA and UVB blocking agents to inhibit photoaging and be part of a daily skin care regimen. Sunscreens contain active ingredients that act as ultraviolet filters
- **Antioxidants:** Antioxidants reduce free-radical damage, thereby preventing impairment at the cellular level. They inhibit inflammation, which leads to collagen depletion, and they offer protection against photodamage and skin cancer. Common antioxidants include alpha-lipoic acid (ALA), L-ascorbic acid (vitamin C), niacinamide (vitamin B3), N-acetyl-glucosamine (NAG), α -tocopherol, and ubiquinone [3].

2.3. Cosmeceutical chemistry

When asked to evaluate a new Cosmeceutical product that claims a beneficial physiologic effect, it is important to ask three questions:

- Can the active ingredient penetrate the stratum corneum and be delivered in sufficient concentrations to its intended target in the skin over a time course consistent with its mechanism of action?
- Does the active ingredient have a specific biochemical mechanism of action in the target cell or tissue in human skin?
- Are there published peer-reviewed, double-blinded, placebo-controlled, statistically significant clinical trials to substantiate the efficacy claims? [4]

2.3.1. Can the active ingredient penetrate the stratum corneum and be delivered in sufficient concentrations to its intended target in the skin over a time course consistent with its mechanism of action?

The stratum corneum is an effective barrier to transepidermal water loss and to penetration of exogenous substances. One need not progress to the stage of clinical trials to suspect that these active ingredient marketing claims have little basis in scientific reality. For example, topically applied hyaluronic acid is found in many cosmeceutical moisturizers. It has not been shown that hyaluronic acid penetrates through the stratum corneum. It increases cutaneous water-holding capacity; but does not have any other pharmacologic effects in human skin? This situation awaits further research [5].

2.3.2. Does the active ingredient have a specific biochemical mechanism of action in the target cell or tissue in human skin?

If the agent can meet the first criterion (penetration of the stratum corneum), the second question must be: Is there a feasible biochemical or pharmacologic mechanism of action for this active ingredient to substantiate the efficacy of the marketing claim? If a feasible biochemical or pharmacologic mechanism of action exists, and the product can reach its target at sufficient concentrations for sustained times, the product is deserving of further clinical experimentation. It is possible that some of these products have mechanisms that are currently unknown, requiring future research. For example, vitamin K (phytonadione) has a known biochemical mechanism of action in liver it is a cofactor in the enzymatic carboxylation of glutamate residues on a variety of hepatic enzymes that affect blood clotting. Vitamin K is now being marketed topically as a substance that speeds the resolution of endogenous purpura (solar purpura) and iatrogenic purpura (after cosmetic procedures such as laser procedures) [6]. Purpura refers to extravagated red blood cells and their associated hemoglobin breakdown products deposited in the dermis. What is the mechanism of action of

vitamin K for this claim in skin? This question should raise a specter of doubt until evidence is presented explaining the mechanism of action.

One of the largest areas of interest in Cosmeceuticals is topical vitamins and antioxidants.

These include derivatives of vitamin A (retinol), vitamin C (ascorbic acid), and vitamin E (d- α -tocopherol). Vitamin C has a dual role as an antioxidant and an enzymatic cofactor. It is accepted in the field of aging research that oxidative stress is important in the aging process. UV light generates free radicals, reactive oxygen species that result in tissue damage and subsequent inflammatory responses [7], in the skin. A few articles have been published on them effects of topically applied vitamins C and E on UV-induced erythema; however, more research is needed." [8-12] Numerous topical vitamin C products are marketed; formulation is difficult, however, because the molecule is oxidized rapidly. The questions a dermatologist must ask regarding topical vitamin C therapy are: How often does it need to be applied to the skin, is there a reservoir within the stratum corneum, and does it penetrate rapidly into the dermis and stay there in sufficient concentration? Can it prevent some of the negative effects of UVA damage on elastin and collagen? Topical applications probably would not provide increased concentrations of vitamins to the dermis greater than what can be supplied orally; however, they may supply increased epidermal concentrations. These areas warrant further research on a basic science and clinical level.

2.3.3. Are there published peer reviewed, double-blinded, placebo-controlled, statistically significant clinical trials to substantiate the efficacy claims?

If a Cosmeceutical can meet the first two criteria-the penetration of the stratum corneum and a feasible biochemical mechanism of action-it is important to undertake a double- blinded, placebo- controlled, statistically significant clinical trial to show the efficacy claims. Human clinical trials are expensive and difficult to design. Promising agents usually are tested on mouse skin before proceeding to human trials. It should be possible to go to the scientific literature and review trials of these products tested first on animal (mouse) skin. Most published studies on Cosmeceuticals in human skin are uncontrolled and are performed on small study groups. Manufacturers need to fund well-controlled, double-blinded clinical trials to show the efficacy of these products (as has been done for retinoic acid) if they want to make claims on reversal of photo aging.

3. Regulatory aspects

There is no regulatory category for cosmeceuticals. In fact, FDA does not even recognize the word as an official product type. However, it regulates cosmetics under the Federal Food, Drug and Cosmetics Act (FDCA), which define cosmetics as "intended to be rubbed, poured, sprinkled, or spray on, introduced into, or otherwise applied to the human body for cleansing, beautifying, promoting attractiveness or altering the appearance". To avoid drug regulation, cosmeceuticals must not be intended to diagnose, cure, mitigate, treat or prevent disease. FDA has stated marketing claims, consumer's perception of a products intentions and incorporation of certain ingredients well know to the public as therapeutic can all trigger drug regulations. This leaves cosmeceuticals in a similar situation to that of functional foods and dietary supplements, so the same amount of marketing and formulation care will be required [13]. The claims made about drugs are subject to high scrutiny by the Food and Drug Administration (FDA) review and approval process, but cosmetics are not subject to mandatory FDA review. Much confusion exists regarding the status of 'cosmeceuticals.' Although there is no legal class called cosmeceuticals, this term has found application and recognition to designate the products at the borderline between cosmetics and pharmaceuticals. Cosmeceuticals are not subject to FDA review and the Federal Food, Drug and Cosmetic Act do not recognize the term itself. It is also often difficult for consumers to determine whether 'claims' about the actions or efficacies of cosmeceuticals are in fact valid unless the product has been approved by the FDA or equivalent agency. Some experts are calling for increased regulation of cosmeceuticals that would require only proof of safety, which is not mandatory for cosmetics. Some countries have the classes of products that fall between the two categories of cosmetics and drugs: for example, Japan has 'Quasi-drugs'; Thailand has 'controlled cosmetics' and Hong Kong has 'cosmetic-type drugs.' The regulations of cosmeceuticals have not been harmonized between the USA, European, Asian and other countries [3].

3.1. Indian regulatory scenario

Key issues with the current Indian cosmetic regulations include the following:

- Multiple and complex regulations under different bodies.
- Indian cosmetic definition is narrow & restrictive.
- Lack of implementation guidelines of the D & C Act for regulators for issues related to cosmetics such as-

- Non uniform licensing approvals across various states.
- Inconsistent approach across authorities in interpretation of a particular issue.
- Absence of guidelines on product claim interpretation as well as illustrative list of cosmetics, cause difference in interpretation between licensing authorities on product classification and hence delaying the process of product licensing and product trade cycle
- Pace of BIS Standards development/ revision are not in line with technological progress thus deterring innovation and growth. Drugs and Cosmetics Act, 1940 governs the provisions relating to manufacture, sale, storage, distribution and import of Drugs as well as cosmetics in India. Whereas the said Act clearly defines the terms "Drug" and "Cosmetic" as under, there is no term as "Cosmeceutical" in the Act. As such nobody has a legal or statutory right to use the term for drawing benefits of any sort. For all intents and purposes either "drug" or "cosmetic" terms have to be used and usage of any other term to replace or substitute either of these two terms is simply illegal, there is no rationale. However the term "Cosmeceuticals" may be used for purposes other than legal/statutory/ drawing benefits/ seeking relaxations or concessions etc [3].

4. Conclusion

The usage of cosmeceuticals has drastically hiked in recent years, which in turn has increased the spectrum of the physician to broaden their range of products to enhance the comeliness of the patients associated with dermal problems. However, at times, where generations are keenly worried for their beauty, lots of manufacturing companies are competing and working hard to provide convincing results to meet requirements of the patients. Claims of effectiveness lack convincing evidence, thus the industry is challenged to provide evidence on the effectiveness of these compounds. Cosmeceuticals like vitamins, sunscreens, hydroxyl acids & many more have proved their efficacy in treating skin diseases thus enhancing the skin texture. Clinical trials of cosmeceuticals are important to know the interaction between skin and cosmeceuticals which could even be influenced by environmental fact. The global trend in the cosmetic industry towards developing 'medicinally' active cosmetics, and in the pharmaceutical industry towards 'cosmetically' oriented medicinal products as part of a current 'life-style' ideology. The future promises increasingly sophisticated formulations for cosmetics and skin-care products. Cosmetic companies are finding ways to deliver small-dose ingredients that do not require medical regulations and to introduce steroids and hormones into lip balms, which would result in production of cosmeceuticals that could help to improve body mass, nail, and hair growth. New challenges will also be presented to government regulatory agencies as more chemicals with true biological activity are invented and tested. Claim substantiation and premarketing testing must also evolve to accurately assess efficacy and safety issues with important implications for total body health. The new vehicles and delivery systems combined with established ingredients will alter percutaneous absorption, requiring re- evaluation of substances with an assumed good safety profile . Biotechnology will also compete directly with the pharmaceuticals and cosmetic businesses. The most influential angle over the coming 5 years will be the links between internal health, beauty, and anti-aging. The next big beauty trend will include skin gestibles that will promote beauty from the inside out, borrowing of pharmaceutical terms for cosmetic applications, amino peptides to make the skin more elastic, neuron mediators which are chemicals to tell the brain to be happy and the blurring of boundaries between surgeries.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest.

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