

## **Introduction**

Cosmeceuticals are future generation of skin care. They are the advances made within the world of dermatological products and the new beckon in skin care. Cosmeceuticals are topical 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.

The concept propounded by Dr. Albert Kligman states that “The cosmeceuticals are topical agents distributed across a broad spectrum of materials lying somewhere among pure cosmetics (lipstick and rouge) and pure drugs (antibiotics, corticosteroids). They partake of both categories”[1].

Cosmeceuticals improve appearance, but they do so by delivering nutrients necessary for healthy skin. This chapter focuses on classification of cosmeceuticals, promising ingredients, their mechanism of action and future area of cosmeceutical skin care research.

## **How does the law define a cosmetic?**

The Federal Food, Drug, and Cosmetic Act (FD&C Act) defines cosmetics by their intended use, as "articles 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".

## **How does the law define a drug?**

The FD&C Act defines drugs, in part, by their intended use, as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" and "articles (other than food) intended to affect the structure or any function of the body of man or other animals".

## **How can a product be both a cosmetic and a drug?**

Some products meet the definitions of both cosmetics and drugs. This may happen when a product has two intended uses.

For example, a shampoo is a cosmetic because its intended use is to cleanse the hair. An antidandruff treatment is a drug because its intended use is to treat dandruff. Consequently, an antidandruff shampoo is both a cosmetic and a drug.

Among other cosmetic/drug combinations are toothpastes that contain fluoride, deodorants that are also antiperspirants, and moisturizers and makeup marketed with sun-protection claims. Such products must comply with the requirements of both.

## **Difference between “cosmetics” & “cosmeceuticals”**

Cosmeceuticals typically contain levels of active ingredients including phytochemicals, vitamins etc.

Like cosmetics, cosmeceuticals are topically applied, but contain ingredients that influence the biological function of the skin.

Cosmeceutical products are intended to improve appearance from a functional standpoint whereas Cosmetics are used just to color and adorn the body in a stylish fashion, leaving the real problem unaddressed.

## **History of cosmeceuticals**

Raymond Reed, founder of the U.S. Society of cosmetic chemists, created the concept of "cosmeceutical" in 1961. Further the term “cosmeceutical” was popularized by American dermatologist Albert Kligman in the late 1970s. 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 reference 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, fragrances and herbal medicines. Their research and development work covered all these disciplines simultaneously. Separation of the cosmetic and toiletries industry from medicine, and pharmacy was in 19th century. This phenomenon occurred when the modern pharmaceutical industry was first developed and the first government statute regulating the sale of drugs was drafted.

The role of cosmetics as a positive healing aid ignored until its revival in the late 1970s and early '80s. Kligman rekindled interest by developing formulations to improve the appearance of UV-damaged and wrinkled skin using retinoic acid as the active ingredient [2].

## **Gender specific cosmeceuticals**

The concept of beautifying is not restricted to women alone, even men have become aware about their look. Nowadays advertisements of many anti-wrinkle and fairness creams are aimed at men. Key cosmeceuticals used by men include hair growth products, anti-aging, antiperspirant, athlete’s foot and astringents. Cosmeceuticals most commonly used by women include anti-wrinkles, anti-cellulite, hair removal, tanning, skin whitening, antioxidants, and cell recovery products [2].

## Mechanism of action of cosmeceuticals

The modern cosmeceutical products act functionally. To what extent and how they work is important to know for a researcher. Evidence to support the claims or use of cosmeceutical ingredients are often lacking in literature. However ten basic mechanism of action of cosmeceuticals are enlisted in below Table. [3]

**Table: Ten basic cosmeceutical mechanisms of action**

Sr. No.	Mechanism of action	Cosmeceutical example
1	Activate a receptor	Retinoids: Tretinoin, Retinol,
2	Enhance barrier function	Moisturizers based on: Petrolatum, Silicone, Mineral oil glycerin
3	Increase exfoliation	Salicylic acid
4	Normalize cellular repair	Copper peptides
5	Decrease inflammation	Green tea
6	Inhibit oxidation	Lactobionic acid, Vit E
7	Provide a cellular messenger	Pentapeptides
8	Regulate cellular communication	Hexapeptides
9	Modulate pigmentation	Avobenzone, micronized titanium dioxide
10	Deliver photo protection	Avobenzone, micronized titanium dioxide & microfine zinc oxide

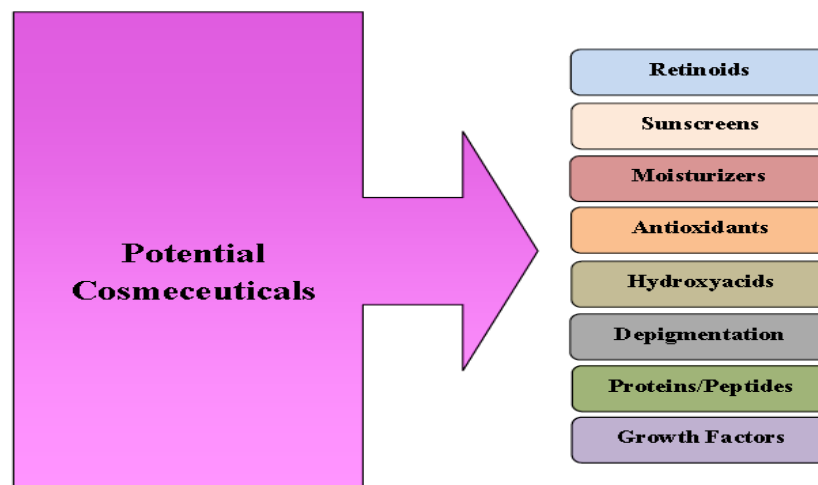
## Characterization of Cosmaceuticals

Cosmeceuticals could be characterized as follows:

1. The product has pharmaceutical activity and can be used on normal or near-normal skin.
2. The product should have a defined benefit for minor skin disorders (cosmetic indication).
3. As the skin disorder is mild the product should have a very low-risk profile

## Classification of cosmeceutical products

The cosmeceuticals are divided into seven categories. Cosmeceuticals are broadly classified as shown in Figure;



### 1. Retinoids

These are the most prevalent cosmeceuticals in the market. Retinoids are natural and synthetic derivatives of vitamin A. Vitamin A generically encompasses retinol (vitamin A alcohol), retinal (vitamin A aldehyde), and retinoic acid (vitamin A acid).

Retinoids are premier evidence-based cosmeceuticals, as they function through surface cell receptor interaction to produce a clinically defined effect. Other retinoids such as pro-B vitamins (niacinamide and panthenol) function differently by physically enhancing barrier properties of stratum corneum [4].

### Clinical uses

In clinical use, retinoids have established their effectiveness in treating

- Acneiform eruptions (e.g., Isotretinoin),
- Disorders of keratinization, such as psoriasis (e.g., Acitretin)
- Neoplastic processes (e.g., Tretinoin for leukemia, isotretinoin for squamous cell carcinomas).

### Classification of Retinoids

Generation	Retinoid
First generation	Tretinoin, Isotretinoin
Second generation	Etretinate
Third generation	Arotinoid
Naturally occurring in humans	Retinol (vitamin A), Retinal (vitamin A- aldehyde) Retinoic Acid

## The Roles of Naturally Existing Retinoids

Retinoid	Role
Retinol	Growth promotion, Differentiation/ maintenance of epithelia & Reproduction
Retinal	Vision
Retinoic acid	Growth promotion, Differentiation/ maintenance of epithelia

### Role in cosmeceuticals

Different retinoid used are Isotretinoin has also been adequately documented in double-blind, vehicle controlled trials to improve the same parameters of photoaging. Adapalene has been proven effective in treatment of acne. Tazarotene, another recently studied retinoid, has been shown to be effective in psoriasis and acne will likely be effective in photoaging. Retinol, the prototypic retinoid, is the alcohol of retinoic acid and has been shown to be somewhat active in animal models of photodamage.

## 2. Sunscreens

They are regarded by dermatologists as the single most important formulation that should be applied daily. UVA and UVB radiation contribute to the disruption of the extracellular matrix, a hallmark of photoaging. Broad-spectrum UVA and UVB sunscreens are the cornerstone of photoaging therapy. Enzophenones (dioxybenzone, oxybenzone, sulisobenzone), aminobenzoic acid, titanium oxide, zinc oxide and others give protection in the UVB and UVA II range (320–340 nm) [5].

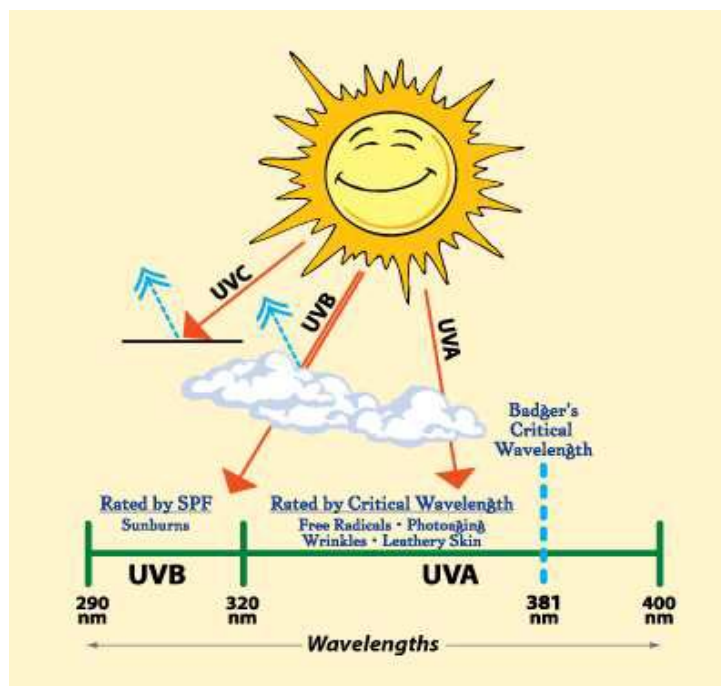
### UV damage is manifested as

- sunburn,
- skin discoloration
- texture loss.

UV rays also trigger skin aging through free radical reactions and oxidative stress, by increased activity of enzymes such as collagenase and elastase that are catalyzed by metal ions.

### The results are;

- Abnormal cross linking of Collagen fibers
- Scar tissue build up and visible wrinkles and skin discoloration
- Ravages of chronological aging are accelerated



Several natural extracts protect the skin from the damaging effects of UV rays such as Tetrahydrocurcuminoids, SabiWhite, Green tea Extract, Sesame antioxidants, Umbelliferin, Xylosin, Rosemary extract, Rosmarinic acid, Lupeol, Arjunolic acid etc.

### 3. Moisturizers

Moisturizers are most useful product for management of various skin conditions (e.g., atopic dermatitis, psoriasis, pruritus, and aging skin). These products include emollients, occlusives, and humectants.

Simple occlusion of the skin, with a “moisturizer” such as petrolatum, has definite effects on skin structure and probably on function. Older or photodamaged skin is frequently perceived as “dry,” there is substantial evidence that TEWL is actually decreased in chronologically aged skin.

Moisturizers and emollients may exert their positive effects in several ways. Simple occlusion effects may acutely allow retention of more water in the skin and acutely lead to lowered TEWL. Healing of damaged stratum corneum and replacement of intercellular lipids may re-establish normal barrier function and allow normalization of TEWL.

Moisturizers are useful for hydrated skin. Moisturizers claim to make the skin smoother, softer, more radiant, less wrinkled and firmer. Majority of moisturizers enhance skin barrier function such as petrolatum, silicon, mineral oil and glycerin enhances skin barrier functions [6].

#### 4. Antioxidants

Enhances the skin's natural antioxidant protection system with topical application. They reduce free-radical damage by blocking the oxidative processes in cells. These are used to protect skin from photo damage, cancer and photoaging. Antioxidants inhibit inflammation that causes collagen depletion. They protect against photo damage and skin cancer.

Free radicals have been shown to play a major role in sun damage as well as in aging or in pollution (tobacco, stress).

They act by degrading the skin structural fibers (collagen, elastin), cell membranes, DNA, or by creating inflammatory reactions.

#### Free radical actions can be blocked by the following.

- *Vegetable oils rich in tocopherols and tocotrienols.*
- Wheat germ oil and palm Oil are particularly rich in tocopherols and  $\alpha$ -,  $\beta$ -,  $\gamma$ -tocotrienols.
  - *Ascorbic acid*, antioxidant that is also used for many of its properties.
  - *Flavonoids*, rich extracts from *Gingko*, are used for their antioxidant and anti-free-radical properties.

Some other antioxidants include vitamins A, C, and E; alpha lipoic acid, lactobionic acid; ubiquinone (coenzyme Q-10); idebenone; polyphenols (e.g., catechins, flavonoids) [6].

#### 5. Hydroxyacids

Hydroxyacids are used worldwide and most probably for centuries as active dermatological drug and cosmetic ingredients. These include  $\alpha$ -Hydroxyacids (glycolic acid, lactic acid) and  $\beta$ -Hydroxyacids (salicylic acid). The exact mechanism of action of hydroxyacid remains unknown and is largely controversial. Some experts claim that AHAs increase the synthesis of glycosaminoglycans (GAGs), which improve quality of elastic fibers, and increase density of collagen. Whereas BHAs have dermolytic properties and helps in various xerotic and ichthyotic disorders [7].

##### a) Biological activities of hydroxyacids:

Both AHAs and BHAs exert indisputable direct effects on the stratum corneum, at least when it is affected by xerosis, ichthyosis, and analogous conditions. Comedonal hyperkeratosis in acne-prone subjects might also be improved by the same compounds. In the field of tumors, benign keratoses and viral warts may also be affected by high-concentration formulations.

The efficacy is largely related to the pH-related chemical burn. Such caustic effect is also induced in order to realize AHA skin peeling. Salicylic acid is the reference BHA used since the early days of dermatology to improve xerotic conditions.

### **b) Caustic effects:**

When applied to the skin in high concentration, AHAs cause necrosis and detachment of keratinocytes leading to epidermolysis. Such injury is a chemical peeling depending primarily upon the disruption of the skin pH.

### **6. Depigmentation agents**

Hydroquinone, aloesin, arbutin, azelaic acid, glycolic acid, kojic acids are some multiple depigmentation agents. Hydroquinone is effective and widely used for treatment of melasma, post inflammatory hyperpigmentation. It acts by inhibiting conversion of tyrosine to melanin [8].

### **7. Protein and peptides**

Cosmeceutical peptides have the potential to improve the appearance of aging skin. There are various types of cosmeceutical peptides such as signal peptides, carrier peptides, and neurotransmitter inhibiting peptides. Overall cosmeceutical peptides trigger wound-healing mechanism that activates fibroblasts in response to fragmented chains of elastin and collagen. Peptides increase collagen production to improve skin appearance, resulting in smoother skin [9].

### **8. Growth factors**

Epidermal growth factor (EGF) stimulates epidermal growth and is used in the treatment of burns and excision wounds, where it accelerates re-epithelization. Transforming growth factor (TGF) stimulates normal skin growth and cellular growth and repair. TGF exerts positive regulatory effects on the accumulation of the body's extracellular matrix proteins. TGF is also a mediator of fibrosis (repair tissue formation) and angiogenesis (development of new blood cells) and it promotes the healing of wounds [7].

### **9. Botanical Extracts**

Natural extracts, whether from animal, botanical, or mineral origin, have been used as "active ingredients" of drugs or cosmetics for as long as human history can go. Oils, butter, honey, beeswax, lead, and lemon juice were common ingredients of the beauty recipes from ancient Egypt.



In the cosmetic industry, the botanical extract *is* the active ingredient. It may contain hundreds of chemical structures and it has a proven activity.

### **Origin of botanical extracts**

Botanical extracts have been used for centuries and are present in today's products. There are plant powders for hair coloring (Henne), scrubs (apricot kernel, corn), or masks (oat flour).

### **Use of Extracts**

They can be topically applied, ingested, or injected, depending on the intended use and provided absence of toxicity has been shown. Botanicals are playing an increasingly important role in the activity and safety of cosmetics; they allow for a renewal of the source of active ingredients in drugs.

## Modern herbal cosmeceuticals [10]

Use of herbal cosmeceuticals is not new concept to India. The cosmeceutical approach towards health and beauty dates back, to centuries where vaidyas were practicing integrated holistic health incorporating botanicals, oils and massage into whole body. In ancient Greece and Rome, countless ointments and tonics were recommended for beautification of hair, skin as well as remedies for the treatment of scalp and skin diseases.

Recently herbal cosmeceuticals have gained much recognition and became popular among Indian people as well as abroad. Cosmeceutically active ingredients are now being used by large and small manufacturers engaged in cosmetics, pharmaceuticals, biotechnology and natural extracts in cosmetic formulations. A wide range of plant extracts used in skin cosmetics and toiletry preparations as cosmeceuticals are described in Table.

**Table. Plants used in skin cosmetics and toiletries as cosmeceuticals**

Sr. No.	Name of plant	Active constituent	Cosmetic use
1	<i>Areca Catechu</i>	Catechin	Antioxidant
2	<i>Crocus Sativus</i>	Crocetin	Protective
3	<i>Curcuma Longa</i>	Curcumin	Antibacterial
4	<i>Glycyrrhiza Glabra</i>	Glycyrrhizin	Skin whitner
5	<i>Green Tea</i>	Chammomile	Photoprotective
6	<i>Crataevea Murula</i>	Lupenol	Antiaging
7	<i>Rosemarinus Officinalis</i>	Rosemary	Antiaging
8	<i>Buckwheet Seeds</i>	Rutin	Antiwrinkle
9	<i>Embillica Officinale</i>	Ascorbic Acid, tannins	Protective
10	<i>Ginko Biloba</i>	Ginki	Skin tonic
11	<i>Centella Asiatica</i>	Centella	Skin firming/ Conditioning skin staining
12	<i>Psorolia Corlifolia</i>	Psorolin	Pigmenting agent
13	<i>Citrus Limonus</i>	Hesperedin	Fungal Infection of skin
14	<i>Aloe Vera</i>	Aloin	Antidermatitis
15	<i>Aricaria Recutita</i>	Chammomile, gallic acid	Antiphlogistic
16	<i>Thea Viridis</i>	Catechin and Rutin	Antioxidant
17	<i>Vitis Vinifera</i>	Carotene	Eczema
18	<i>Daucus Carota</i>	Beta Corotene	UV Protection
19	<i>Lycopericon Esculantum</i>	Tamotine and Tamotidine	Potent Bacteriostatic
20	<i>Allium Sativum</i>	Alliin and Allicin	Antioxidant
21	<i>Haemamalis Virginiana</i>	Gallic Acid	Cooling Agent

## **Future area of research in skin care cosmeceuticals**

Cosmeceuticals are destined to play an important role in future therapeutic developments but their success will be governed by control of purity, safety, and efficacy without hindering innovation. Future area of research in skin care cosmeceuticals is discussed below.

### **1. Genomics in cosmetic industry**

The role of genomics is not only limited to pharmaceutical industry. It has made mark in cosmetic industry too. Researchers are trying to find key genes in biological processes such as aging through a method called gene expression profiling. In future, cosmetic products in market may be more customized with the help of genetic technology. Cosmetic companies may find specific skin qualities like skin texture, pigmentation, hydration and wrinkles to meet individual skin needs.

### **2. Nanotechnology in cosmetic industry**

Nanotechnology is the new technology used in personal care industry. Use of nanotechnology in cosmeceutical preparations aimed to make fragrances last longer, sunscreens more effective and anti-ageing creams fight back the years[11]. Further, the technology being used to optimize manufacturing conditions for skin care formulations, a multicomponent system. The technology is so immense in skin care that some companies have decided to merge it into the hair care product-line as well. The technology uses extremely tiny (or nano) particles to penetrate the skin, far more than traditional anti-ageing treatments. Some of the nanotechnology-based innovations are nano-emulsions which are transparent and have unique tactile and texture properties, nano-capsules which are used in skin-care products, nano-pigments which transparent and increase efficiency of sunscreen products, and liposome formulations which contain small vesicles (range: 50–5000 nm) consisting of traditional cosmetic materials that protect light or oxygen-sensitive cosmetic ingredients. Some companies are also using nanotechnology in hair-care products; research is ongoing to find ways to use nano particles to prevent hair from turning grey and for prevention of hair loss [12].

### **3. Nutricosmetics**

From two decades, cosmeceutical and nutraceutical products are widely used worldwide. However as the science in beauty and health are making rapid advancements, new terminologies for different products in healthcare market are evolving. These products are termed “nutricosmetics” combination of “nutraceuticals” and “cosmeceuticals”. They incorporate nutraceutical ingredients in topical delivery systems with the elegance and ancillary benefits of cosmetics. These products are formulated to beautify the skin through

anti-aging or anti-wrinkle, reduce inflammation after UV exposure and beautify the hair or prevent hair loss.

Nutricosmetic products generally focus on three areas: skin, hair and beauty. These products are taken orally, either as pills or liquids. The major ingredients used in nutricosmetics are soy isoflavone proteins, lutein, lycopene, vitamins (A, B6, E), omega-3 fatty acids, beta- carotene probiotics, sterol esters; chondroitin and coenzyme Q10 [13].

### **Conclusion**

Cosmeceuticals are currently driving force in the field of skin care research. Ability of cosmeceutical ingredients to enhance skin functioning varies on how they formulated into creams, lotions etc. It is important for cosmeceutical ingredients to deliver it in biologically active form to the skin, reach the target site in sufficient quantity to exert an effect. Research focusing on how cosmeceutical ingredients work and better understanding of mechanism of action, will help researchers to create enhanced application systems and verify the benefits of a variety of ingredients. Cosmeceuticals will be valuable contributions to dermatology in future and skin care, if clinical efficacy can be established by controlled human clinical with the finished marketed product. The cosmeceuticals may have scientific reliability in future, if the ingredients are stable, of therapeutic concentrations, and can be adequately deliver the results to satisfy the consumers need.

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