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COSMECEUTICALS: REGULATORY SCENARIO IN US, EUROPE & INDIA

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Introduction

Cosmetics are substances used to enhance the appearance or odour of the human body. Cosmetics include skin-care creams, lotions, powders, perfumes, lipsticks, fingernail and toe nail polish, eye and facial makeup, towelettes, permanent waves, colored contact lenses, hair colours, hair sprays and gels, deodorants, hand sanitizer, baby products, bath oils, bubble baths, bath salts, butters and many other types of products. A subset of cosmetics is called "make-up," which refers primarily to colored products intended to alter the user's appearance.¹

'Cosmeceuticals', 'performance cosmetics', 'functional cosmetics', 'dermaceuticals',

'Active cosmetics' and 'nutricosmetics' are buzzwords in personal care industry.²

Cosmeceuticals refers to the combination of cosmetics and pharmaceuticals. Cosmeceuticals are cosmetic products with biologically active ingredients purporting to have medical or drug-like benefits.³

Cosmeceuticals represent a marriage between cosmetics and pharmaceuticals. Like cosmetics, cosmeceuticals are topically applied, but they contain ingredients that influence the biological function of the skin.

Cosmeceuticals improve appearance, but they do so by delivering nutrients necessary for healthy skin.

Cosmeceuticals typically claim to improve skin tone, texture, and radiance, while reducing wrinkling.

Cosmeceuticals are the fastest-growing segment of the natural personal care industry.⁴

Cosmeceuticals as a Subclass of Cosmetics (Europe and Japan) and as a Subclass of Drugs (U.S.)⁵

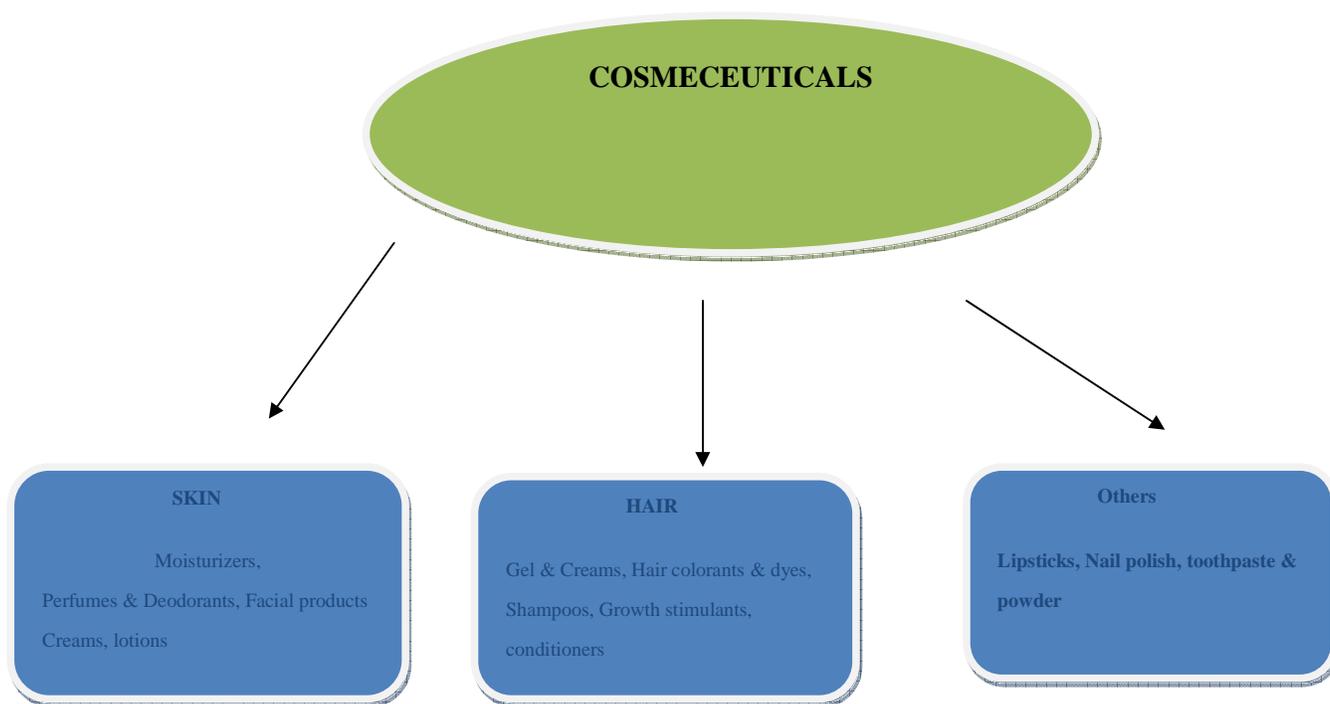
Cosmetic

Cosmeceuticals

Drug

Pharmaceutical activity	+	+	+
Intended effect in skin disease	-	(+)	+
Intended effect in mild skin disorder	-	+	(+)
Side effects	-	(±)	-

The term cosmeceuticals was introduced by Albert Kligman in 1984 to refer to substances that exerted both cosmetic and therapeutic benefits. Many contain biologically active ingredients, and in general, cosmeceuticals undergo tests to determine safety, but claims of efficacy are largely unsubstantiated. Efforts have only recently been initiated to address the issues surrounding quality control and to establish industry standards and regulations. Demonstrating the skin effect of a cosmeceuticals can be difficult; there are no placebos because anything that is applied to the skin will have an effect.⁶



Every day there seem to be more and more terms describing what we are referring to as cosmeceuticals. These include:

- Beauty supplements
- Active cosmetics
- Bio-active cosmetics
- Performance cosmetics

- Phytocosmetics
- Functional cosmetics
- Dermaceuticals
- Skinceuticals
- Cosmetic drugs
- Therapeutic cosmetics⁷

History: The Egyptians were the first to recognise the health-giving properties of cosmetics. Archaeologists have unearthed several cosmetic jars whose hieroglyphics say "good for sight" and "stops bleeding." The "Ebers," a medical papyrus written in 1600 BC, makes frequent reference to a number of cosmeceuticals-type products. A favourite was a formulation using honey and milk that claimed to help cure skin diseases, while another product mentioned in the Ebers, claiming to "expel wrinkles from the face," was made from frankincense, balantine oil, rush oil and wax, in equal proportions.⁸

Kohl was a dark powder, which was applied in an almond shape around the eyes with a stick. Kohl was made of ochre, lead, ash, burnt almonds, oxidized copper, and different colors of copper ore. For the cheeks and lips, red clay mixed with water was the makeup of choice. Even fingernails were painted yellow or orange by use of henna. In ancient China, gum Arabic, egg whites, gelatin and beeswax were used to create nail colour.

As time went on, cultures merged, and the Greeks began to move into cosmetics history and adopt the use of Egyptian cosmetics. They did not do so for spiritual purposes, but simply to look good. Centuries later, the Romans moved in, and their use for cosmetic formulas began to evolve into other purposes, such as creating aphrodisiacs. They used sheep fat mixed with blood for nail polish and, instead of just using the traditional body oils created by Egyptians, took baths in crocodile excrement and mud.⁹

Market:

Pharma and cosmetics market in India is valued at about Rs.35000 crores, and growing at 10 % per year. Carving out a niche of Rs. 50 crores in this market is fairly easy if the products chosen can catch the fancy of the consumer.

This is a specialty product market. Different marketing strategies are used for the products. Brand building and direct selling are the most widely used. Brand building is very expensive. Direct selling in a well defined geographic area is a low cost option but the gestation period is high.

It will be prudent to take up contract manufacturing work for 50 % capacity, and

Introduce own products in a phased manner¹⁰.

Total cosmeceuticals sales by country (US\$M), 2001-2011.

US\$	2001	2006	2011	CAGR 01-06	CAGR 06-11
France	672	904	1,161	6.1%	5.1%
Germany	538	698	865	5.4%	4.4%
Italy	497	655	805	5.7%	4.2%
Netherlands	106	131	157	4.3%	3.7%
Spain	234	329	423	7.0%	5.2%
Sweden	111	127	144	2.7%	2.6%
UK	421	526	637	4.6%	3.9%
Rest of Europe	511	671	839	5.6%	4.6%
Europe Total	3,090	4,041	5,031	5.5%	4.5%
US	3,003	4,150	5,386	6.7%	5.4%
Europe and United States	6,093	8,191	10,417	6.1%	4.9%

Source: Data monitor analysis¹¹

Cosmeceuticals in us:

Cosmeceuticals represent the fastest growth segment in the skin-care market, and a number of topical cosmeceuticals treatments for conditions such as photo aging, hyper pigmentation and wrinkles have come into widespread use.[2, 3] In 2005, the U.S. cosmeceuticals market was estimated to be \$12.5 billion and projected to grow to over \$16 billion by 2010. Demand for cosmeceuticals products is expected to increase 8.5 percent per year to over \$8 billion in 2010.¹²

After China, India is the most bio-diverse country. Despite the global economic downturn, India remains one of the fastest-growing beauty markets globally, growing at 13 percent per annum and valued at \$6.3 billion. The global organic cosmetics industry is valued at \$7 billion. The market offers extensive opportunities for domestic and international players. In spite of the recession period all these companies have seen an 18 percent growth this year.¹³

The EU market is estimated at approximately \$1.1 billion, and manufacturers continue developing UV absorbers with broad-spectrum protection. Given that almost all cosmeceutical formulations are focused in the skin and hair care segment of the market (perhaps 15 per cent of the former and five per cent of the latter), we can safely estimate the EU market for cosmeceuticals at approximately \$1.5-\$1.75 billion.

The Basics of Skin Care:

1. Prime

There is a difference between cleansing and exfoliating. Cleansing should be done daily to remove makeup and oil build up, and to prime the skin for the maximum absorption of skin care products including cosmeceuticals. Exfoliation is a technique used to remove the dead epidermal cells on the outer surface of the skin and to expose fresher, living cells. Exfoliation may be performed daily, but two or three times a week is sufficient as it can be abrasive. Popular exfoliation methods include alpha-hydroxy acids (glycolic and lactic), beta hydroxy acids (salicylic acid), enzyme peels and microdermabrasion. The potential benefits of exfoliation include a brighter complexion, even skin tone and better penetration of active ingredients found in cosmeceuticals, all of which can reduce the appearance of fine lines. An effective daily cleanser is Accelerating Cleanser by Skin Doctors Cosmeceuticals, an Australian skin science company with a complete line of patented cosmeceuticals designed to bridge the gap between clinical skin care and cosmetic surgery. This cleanser is gentle enough for daily use and has been specifically formulated to prepare the skin for any of the Skin Doctors treatments. Loaded with lactic acid and avocado extract, it removes dead cells and unclogs pores to allow cosmeceutical treatments to penetrate the skin deeper and more effectively.

2. Treat

once you've identified your problem area, speak to a Rexall pharmacist about selecting a cosmeceutical solution that fits your specific need. For a porcelain complexion, Skin Doctors SD White is a silky cream that can help reduce the appearance of sunspots, liver spots and freckles. It also gradually brightens darker complexions for a soft, ivory finish. Derived from natural skin brightening ingredients, SD White is suitable for all nationalities and skin shades. Some people have seen a marked difference in as little as six weeks.

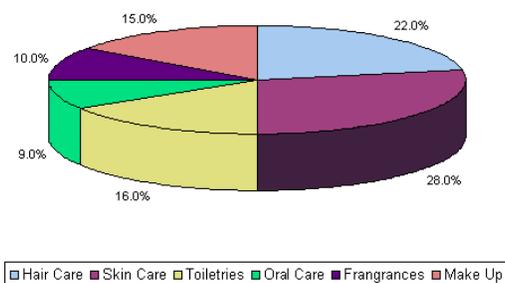
Superceutical by Skin Doctors is a great option if you're looking to reduce the appearance of wrinkles and crow's feet. Containing ProDEJine™, an anti-sagging technology that strengthens the connection between the epidermis and the dermis, this treatment works to improve elasticity. It also contains encapsulated Retinol that improves the cell renewal process and increases collagen elastin to help tone, firm and moisturize the skin.

3. Accelerate

Maximize your treatment by choosing daily care products that deliver faster results. Take years off your eyes with Eye Smooth by Skin Doctors. This creamy, eye treatment contains revolutionary peptide technology to reduce the depth of wrinkles, tighten and lift the skin to create a smoother, more uniformed appearance. Super moist Face by Skin Doctors is more than a moisturizer; it's a 24-hour hydrator, skin illuminator and skin protector. Formulated with Tamarind, vitamin E and Resurrection plant, this moisturizer is rich in antioxidants and helpful for oxidative changes caused by UV exposure.¹⁴

Some of the other medication applications of the cosmeceutical products are:

- Anti-fungal & Anti-Bacterial
- Skin-Whitening Agent
- Anti-acne Agents
- Soothing, Smoothing, Moisturizing or Protective Agents (such as calamine)
- Under eye dark circle
- Anti-Ageing & Anti-Wrinkle¹⁵



Some Common Types of Cosmeceuticals Ingredients

Alpha Hydroxy Acids
Peptides
Retinoids
Sunscreens
Exfoliants

Moisturizers
Antioxidants
Botanicals
Depigmenting Agents¹⁶

Moisturizers

The cutaneous permeability barrier is localized in the stratum corneum interstices, and it is mediated by the lamellar bilayers enriched in cholesterol, free fatty acids, and ceramides. Formulations containing skin-identical lipids have been suggested to facilitate a cascade of physiologic events in keratinocytes, normalizing damaged skin. When applied to the skin for an extended period, water can cause the excretion of cytokines. These pro-inflammatory molecules induce edema, vasodilatation, and frank inflammation; therefore, water alone may alter both the structure and the function of the skin under some conditions. By the same token, moisturizers that make the stratum corneum softer and more pliant by increasing its hydration could be considered cosmeceuticals.

A multilamellar vesicular emulsion ceramide – containing liquid cleanser and moisturizing cream plus fluocinonide cream 0.05% was found to reduce eczema duration, clearance time, and symptoms compared with a bar cleanser plus fluocinonide cream 0.05% in the treatment of mild-to-moderate eczema.¹⁷

Alpha Hydroxy Acids (AHAs)

Also referred to as fruit acids, they are a common ingredient found in cosmeceutical products. Examples include:

<ul style="list-style-type: none">• Citric acid• Glycolic acid• Lactic acid	<ul style="list-style-type: none">• Malic acid• Pyruvic acid• Tartaric acid
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AHAs improve skin texture and reduce the signs of aging by promoting cell shedding in the outer layers of the epidermis and by restoring hydration. The mechanism of action is not completely understood. 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 cadherins, 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 skin.¹⁸

Antioxidants:

Antioxidants fight against free radicals that cause damage. Antioxidants should be present in our skin abundantly in order to prevent the harmful effects of free radicals. Our skin is vulnerable to the many factors of the environment which promotes free radical damage to skin cells by causing oxidation, similar to rust on metal.¹⁹

Vitamin A

The primary benefit of vitamin A and its derivatives in cosmetics is their ability to normalize keratinisation (horny layers) by regulating skin cell growth and differentiation. These results in the derivatives, however, are more stable and the decreased efficacy can easily be overcome by increasing the dosage.

Retinol (a Vitamin A derivative) has been shown to improve the effects of photo-damage and stimulate the production of collagen²⁰

Vitamin C

Interest in vitamin C as a cosmetic ingredient is mainly a result of its ability to quench UV induced free radicals and to regenerate vitamin E, another potent antioxidant. There are three forms commonly used in cosmetics: ascorbyl palmitate, magnesium ascorbyl phosphate, and L-ascorbic acid. Ascorbyl palmitate, a fat soluble synthetic ester of vitamin C, is stable in cosmetic formulas at neutral pH. L-ascorbic acid is the most active form of vitamin C and has numerous benefits for the skin. L-ascorbic acid is water soluble and must be formulated at low pH to stay active. In clinical studies vitamin C has been found to act as an antioxidant and anti-inflammatory agent. When applied after UV burning, vitamin C reduces redness

50% sooner than untreated areas. Other inflammatory conditions as psoriasis and eczema have also shown clinical improvement with vitamin C. In addition, vitamin C has been found to stimulate collagen synthesis and to reduce dark pigmentation of the skin (e.g. age spots). Thus, vitamin C is also considered an Anti-aging ingredient.²¹

Vitamin B5, also known as pantothenic acid aids in the production of the lipoproteins of the skin, hastening its healing time. Other B vitamins also nourish the skin.

Vitamin P comprises bioflavonoid, which aren't vitamins but they are nutritional supplements that contain antioxidants like grape seed, ginkgo biloba and citrus derivatives. These function as antioxidants to eliminate free radicals that can damage skin cells. They remove the redness and irritation in skin.

Vitamins are very good for the body. Practice the habit of taking vitamins everyday for a more healthy body and mind.²²

Vitamin E

Source: Vitamin E is found naturally in some foods, added to others, and available as a dietary supplement.

"Vitamin E" is the collective name for a group of fat-soluble compounds with distinctive antioxidant activities

Function: Vitamin E is a fat-soluble antioxidant that stops the production of ROS formed when fat undergoes oxidation. Scientists are investigating whether, by limiting free-radical production and possibly through other mechanisms, vitamin E might help prevent or delay the chronic diseases associated with free radicals.

Vitamin E is involved in immune function and, as shown primarily by in vitro studies of cells, cell signaling, regulation of gene expression, and other metabolic processes²³

Botanicals

Botanicals comprise the largest category of cosmeceuticals additives found in the marketplace today. Their use is unregulated and often unsupported by science and their purported therapeutic properties remain largely unexplored.

Some botanicals that may benefit the skin include: green tea extract, ferulic acid, and grape seed extract.

Green Tea Extract: Research has shown that green tea (*Cammelia sinensis*) poly phenols are potent suppressors of carcinogenic activity from UV radiation and can exert broad protection against other UV-mediated responses, such as sunburn, immunosuppressant, and photoaging.²⁴

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.^{17, 18} Furthermore, when ferulic acid is combined with vitamins C and E, the

product has been shown to provide substantial UV protection for human skin.^{19, 20} Moreover, Murray et al. report that because its mechanism of action is different from sunscreens, ferulic acid could be expected to supplement the sun protection provided by sunscreens.²⁵

Grape Seed Extract

This botanical has been established as a potent antioxidant and has been shown to speed wound contraction and closure.²¹ Topical application of grape seed extract has also been shown to enhance the sun protection factor in humans.²⁶

Depigmenting Agents

Hyper pigmentation, the most common and distressing condition afflicting a large subset of the population, requires dermatologists to familiarize themselves with cosmeceuticals skin-lightening agents and corrective camouflage formulations.²⁷

Combination agents with sunscreen are often the most effective treatment available.

Hyper pigmentation is the result of an increased amount of melanin in the epidermis, the dermis, or both. This pigmentary change can be divided into 2 path physiologic processes: melanocytosis (increased number of melanocytes) and melanosis (increased amount of melanin). Depigmenting agents work best when melanosis or melanocytosis is restricted to the epidermis. Other methods of depigmentation being used are chemical peels.

Patients with Fitzpatrick skin types I-III benefit from local pigment lightening for the treatment of hormonally induced melasma and post inflammatory hyper pigmentation caused by acne and trauma, whereas those with Fitzpatrick skin types IV and darker may also seek therapy for pigmentary changes that occur around the eyes, in the intertriginous areas, following dermatitis, or with acne and trauma²⁸

Depigmenting agents can be divided into several groups:

Phenolic compounds include the following:

- Hydroquinone
- Monobenzylether of hydroquinone
- 4-Methoxyphenol
- 4-Isopropylcatechol

- 4-Hydroxyanisol
- N -acetyl-4-S-cysteaminylphenol

Non phenolic compounds include the following:

- Corticosteroids
- Tretinoin
- Azelaic acid
- N -acetylcystein
- L-ascorbyl-2-phosphate
- Kojic acid

Combination formulas include the following:

- Kligman's formula
- Pathak's formula
- Westerhof's formula²⁹

Regenerating Agents

There are a variety of ingredients that have mild anti-inflammatory properties able to soothe irritated and stressed skin. Typical examples include are aloe Vera, allantoin and rose hip oil which all are widely used in skin care preparations for sensitive or irritated skin. Many of these agents like provitamin B5 and hyaluronic acid have also effective regenerating properties promoting the growth of new skin cells and supporting wound healing. Both provitamin B5 and hyaluronic acid are thus often used in after-peeling treatments, anti-aging formulations and in all treatments aiming to provide smoothness & softening to the skin³⁰

Skin whitening

Skin whitening, skin lightening and skin bleaching refers to the practice of using chemical substances in an attempt to lighten skin tone or provide an even skin complexion by lessen the concentration of melanin. Several chemicals have been shown to be effective in skin whitening.

Homemade treatments

Many^[quantify] people the world over^[weasel words] use homemade treatments for a white skin, rather than buy commercial skin lighteners.^[citation needed] These homemade treatments include extracts of lemon juice, milk, lime, liquorice and other herbs³¹

Mercury

Many skin whiteners contain toxic mercury such as mercury (II) chloride or ammoniated mercury as the active ingredient. However mercury has been banned in most countries (Europe 1976)(USA 1990) for use in skin whitening because it accumulates on skin and it can have the opposite results in the long term. Some studies suggest that long-term use could cause systemic absorption that leads to tissue accumulation of the substance.

"Skin lightening products"

Hydroquinone

In medical literature, hydroquinone is considered the primary topical ingredient for inhibiting melanin production.¹ Its components have potent antioxidant abilities. Topical hydroquinone comes in 2% (available in cosmetics) to 4% (or more) concentrations (available from a physician or by prescription), alone or in combination with tretinoin 0.05% to 0.1%. Research has shown hydroquinone and tretinoin to prevent sun- or hormone-induced melasma.³²

Arbutin

Arbutin is derived from the leaves of bearberry, cranberry, mulberry or blueberry shrubs, and also is present in most types of pears. It can have melanin-inhibiting properties.^[16] Arbutin and other plant extracts are considered safe alternatives to commonly used depigmenting agents to make the skin fairer. Medical studies have shown the efficiency of Arbutin for skin lightening.^[17] There are patents controlling its use for skin lightening.³³

Kojic acid

Kojic acid is a by-product in the fermentation process of malting rice for use in the manufacturing of sake, the Japanese rice wine. Some research shows kojic acid to be effective for inhibiting melanin production.³⁴

Emollients

Emollients are key ingredients in moisturizers and cleansers. They are chemicals that remain in the stratum corneum to act as lubricants. They help maintain the soft, smooth, and pliable appearance of the skin. Emollients are often thought of as "filling in the crevices" between corneocytes that are in the process of desquamation (shedding). The emollient used in a moisturizer plays a key role in its "skin slip," the smooth feeling imparted to the skin after application.

Humectants (Skin Moisturizer) product types: ³⁵

L-Arginine

Carrageenan

Casein

Ceramide E

Chitosan

Chondroitin Sulphate

Citrulline

Conchiolin

Erythritol

Fucoidan

Glucosamine

Glycogen

Glycoprotein

Hyaluronic Acid

Isopropyl Palmitate (IPP)

Jaguar C-162

Lactic Acid

Laminine

Lecithin

Lentinan

L-Lysine

L-Pyrrolidone Carboxylic Acid-
Na (L-PCA-Na)

Mevalonic Acid

Mucin

Orotic Acid

Ophiopogon Japonicus
Polysaccharide

Polyethylene Glycol
400 (PEG-8)

Polyethylene Glycol
600 (PEG-12)

Propanediol

Pullulan

Panthenol

Pectic Acid

Phosvitin

Quebrachitol

Sericin

Serine

Sodium Lactate

Sorbitol

Sphingomyelin

Taurine

Transglutaminase

Trehalose

Wheat Protein

Xylitol

Preservatives

Preservatives are chemicals that kill bacteria, fungi and molds. They are commonly present in ANY product that contains water. For this reason, oil-based skin care products and anhydrous (water free) skin care products, do not need preservatives.

However, creams, lotions and any other product where water is present, require adding a preservative.

- Paraben and phenoxyethanol based liquid preservative
- non-formaldehyde releasing
- globally approved
- stable in low (acidic) pH

- effective in pH-ranges up to 8
- Broad, balanced spectrum of effect against bacteria, yeasts and mould fungi.
- effective even in low use-concentrations³⁶

Solvents: Substances like water and alcohol that are used to dissolve other ingredients.³⁷

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. Therefore, patients should be advised to use adequate sun protection. The Cosmetic Ingredient Review Expert Panel concluded that SAs are safe to use when formulated to avoid skin irritation and to be non-photosensitizing, or when directions for use include the daily application of sun protection.[28] Sufficient data is not available to establish a limit on SA concentration or to identify the minimum pH of formulations to inhibit skin irritation.³⁸

5% Inyline

Reduces Fine Lines - Wrinkles

Inyline (Hexapeptide-30 and Arginine) target the agrin/Musk post-synaptic pathway blocking the mechanism of Musk (Muscle-Specific Kinase) to minimize muscle contraction. By blocking these neurotransmitters, the formation of fine lines and wrinkles is reduced and prevented. When repetitive movements are impaired a collaborative effect is achieved - reduced depth of wrinkles and younger looking skin.³⁹

Regulatory Scenario:

Cosmeceuticals are not regulated as such in the European Union, United States or Japan. In the EU, most are considered cosmetics; in the United States, most are seen as drugs that probably have not been approved by the U.S. Food and Drug Administration (FDA). In Japan, they are regulated as quasi-drugs.

There is no recognized legal definition of a cosmeceutical, as compared to the legal definition of a cosmetic or a drug, anywhere in the world.

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 lists 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.

Us Regulatory Scenario:

The FD&C Act does not recognize any such category as "cosmeceuticals." A product can be a drug, a cosmetic, or a combination of both, but the term "cosmeceutical" has no meaning under the law.

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" [FD&C Act, sec. 201(i)].

Among the products included in this definition are skin moisturizers, perfumes, lipsticks, fingernail polishes, eye

and facial makeup preparations, shampoos, permanent waves, hair colours, toothpastes, and deodorants, as well as any material intended for use as a component of a cosmetic product.

Approval Requirements

FDA does not have a premarket approval system for cosmetic products or ingredients, with the important exception of colour additives. Drugs, however, are subject to FDA approval. Generally, drugs must either receive premarket approval by FDA or conform to final regulations specifying conditions whereby they are generally recognized as safe and effective, and not misbranded. Currently, certain -- but not all -- over-the-counter (OTC) drugs (that is, non-prescription drugs) that were marketed before the beginning of the OTC Drug Review (May 11, 1972) may be marketed without specific approval pending publication of final regulations under the ongoing OTC Drug Review. Once a regulation covering a specific class of OTC drugs is final, those drugs must either -

- Be the subject of an approved **New Drug Application (NDA)** [FD&C Act, sec. 505(a) and (b)], or
- Comply with the appropriate **monograph**, or rule, for an OTC drug.⁴⁰

Regulations specifically prohibit or restrict the use of the following ingredients in cosmetics. For complete details, refer to the relevant regulations (21 CFR, Parts 250.250 and 700.11 through 700.23):

Hexachlorophene Because of its neurotoxic effect and ability to penetrate human skin, hexachlorophene (HCP) may be used only when an alternative preservative has not been shown to be as effective. The HCP concentration of the cosmetic may not exceed 0.1%, and it may not be used in cosmetics that in normal use may be applied to mucous membranes, such as the lips.

Mercury compounds Mercury compounds are readily absorbed through the skin on topical application and tend to accumulate in the body. They may cause allergic reactions, skin irritation, or neurotoxic manifestations. The use of mercury compounds as cosmetic ingredients is limited to eye area cosmetics at concentrations not exceeding 65 parts per million (0.0065%) of mercury calculated as the metal (about 100 ppm or 0.01% phenyl mercuric acetate or nitrate) and provided no other effective and safe

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preservative is available for use. All other cosmetics containing mercury are adulterated and subject to regulatory action unless it occurs in a trace amount of less than 1 part per million (0.0001%) calculated as the metal and its presence is unavoidable under conditions of good manufacturing practice.

Chlorofluorocarbon propellants	the use of chlorofluorocarbon propellants (fully Halogenated chlorofluoroalkanes) in cosmetic aerosol products intended for domestic Consumption is prohibited.
Bithionol	Because it may cause photo-contact sensitization.
Halogenated salicylanilides (di-, Tri-, metabromsalan, and Tetrachlorosalicylanilide)	because they may cause photo contact sensitization.
Chloroform	Because of its animal carcinogenicity and likely Hazard to human health.
Vinyl chloride	as an ingredient of aerosol products, because of its Carcinogenicity.
Zirconium	containing complexes in aerosol cosmetic products, Because of their toxic effect on lungs, including the Formation of granulomas.
Methylene chloride	Because of its animal carcinogenicity and likely Hazard to human health. ⁴¹

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.

Regulation of cosmeceuticals has not been harmonized between the USA, Europe, Asia and other countries.⁴²

Some products can be both cosmetics and drugs. This may happen when a product has two uses. For example, a shampoo is a cosmetic because it's used to clean the hair.

But, an anti-dandruff treatment is a drug because it's used to treat dandruff. So an

antidandruff shampoo is both a cosmetic and a drug. Other examples are:

- Toothpastes that contain fluoride.
- Deodorants that are also antiperspirants.
- Moisturizers and make-up that provide sun protection.



These products must meet the standards for both cosmetics (colour additives) and drugs. Some cosmetic makers use the term "cosmeceutical" to refer to products that have drug-like benefits. FDA does not recognize this term.

A product can be a drug, a cosmetic, or a combination of both. But the term "cosmeceutical" has no meaning under the law. While drugs are reviewed and approved by FDA, FDA does not approve cosmetics. If a product acts like a drug, FDA must approve it as a drug.⁴³

The FDA sought to establish policy on the distinction between a cosmetic and a drug in three ways. First, FDA issued formal trade correspondence that set forth advisory opinions on the classification of products. Second, the agency published pamphlets and other educational materials with examples of product classification. Third, it brought court action to contest the legality of cosmetic products with labelling that contained what the agency concluded to be drug claims. From this body of literature and precedent has emerged, over six decades,

A number of well-developed examples:

- A suntan product is a cosmetic but a sunscreen product is a drug.
- A deodorant is a cosmetic but an antiperspirant is a drug.
- A shampoo is a cosmetic but an antidandruff shampoo is a drug.
- Toothpaste is cosmetic but anticaries toothpaste is a drug.
- A skin Exfoliants is a cosmetic but a skin peel is a drug.
- A mouthwash is a cosmetic but an ant gingivitis mouthwash is a drug.
- A hair bulking product is a cosmetic but a hair growth product is a drug.
- A skin product to hide acne is a cosmetic but an antiacne product is a drug.
- An antibacterial deodorant soap is a cosmetic but an antibacterial anti-infective
- Soap is a drug.

- A skin moisturizer is a cosmetic but a wrinkle remover is a drug.
- A lip softener is a cosmetic but a product for chapped lips is a drug.
- This list is illustrative, not exhaustive⁴⁴

How is a product's intended use established?

Intended use may be established in a number of ways. Among them are:

- Claims stated on the product labelling, in advertising, on the Internet, or in other promotional materials. Certain claims may cause a product to be considered a drug, even if the product is marketed as if it were a cosmetic. Such claims establish the product as a drug because the intended use is to treat or prevent disease or otherwise affect the structure or functions of the human body. Some examples are claims that products will restore hair growth, reduce cellulite, treat varicose veins, or revitalize cells.
- Consumer perception, which may be established through the product's reputation. This means asking why the consumer is buying it and what the consumer expects it to do.
- Ingredients that may cause a product to be considered a drug because they have a well known (to the public and industry) therapeutic use. An example is fluoride in toothpaste.

This principle also holds true for essential oils in fragrance products. A fragrance marketed for promoting attractiveness is a cosmetic. But a fragrance marketed with certain "aromatherapy" claims, such as assertions that the scent will help the consumer sleep or quit smoking, meets the definition of a drug because of its intended use.⁴⁵

EUROPEAN Regulatory Scenario:

The European cosmetics industry is frequently divided into the following sub-sectors:

- **Skin Care**, including sun care and other skin-care products
- **Hair Care**, including shampoos, conditioners and scalp-health products
- **Body Care**, including deodorants and a wide range of toiletries
- **Decorative**, including nail care, eye care and colour cosmetics⁴⁶

What about "cosmeceuticals"?

The FD&C Act does not recognize any such category as “cosmeceuticals.” A product can be a drug, a cosmetic, or a combination of both, but the term “cosmeceutical” has no meaning under the law.

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References:

1. Henry George Liddell, Robert Scott, *A Greek-English Lexicon*, on Perseus
2. <http://www.ias.ac.in/curresci/apr252007/1030a.pdf>
3. Zhou Chen, Jin Young Seo, Yeon Kyung Kim, Se Rah Lee, Kyu Han Kim, Kwang Hyun Cho, Hee Chul Eun, and Jin Ho Chung, Heat Modulation of Tropoelastin, Fibrillin-1, and MatrixMetalloproteinase-12 in Human Skin In Vivo *J Invest Dermatol* 124:70 –78, 2005
4. Draelos ZD. The cosmeceutical realm. *Clin Dermatol*. Nov-Dec 2008; 26(6):627-32. [Medline].
5. Elsner, maibach- cosmeceutical drugs vs. cosmetics
6. <http://www.medscape.com/viewarticle/587365>

7. <http://newhope360.com/cosmeceuticals-taking-root-europe>
8. <http://newhope360.com/cosmeceuticals-taking-root-europe>
9. <http://www.wisegeek.com/what-is-cosmetics-history.htm>
10. <http://www.apitco.org/Profiles/Nutraceuticals%5Br%5D.pdf>
11. <http://www.insidecosmeceuticals.com/articles/2007/06/fulfilling-consumer-needs-in-the-changing-cosmeceu.aspx>
12. <http://www.articlesbase.com/medicine-articles/cosmeceuticals-the-armamentarium-of-clinician-4721451.html#ixzz1PvV5F8o2>
13. <http://www.expresspharmaonline.com/20091115/market01.shtml>
14. <http://www.rexall.ca/healthresource/healthandwellness/33>
15. <http://www.frost.com/prod/servlet/market-insight-top.pag?docid>
16. <http://www.dermatology.ca/members/Media-Coverage/2009/SkinTherapyLetter-Cosmeceuticals.pdf>
17. Draelos ZD. The effect of ceramide-containing skin care products on eczema resolution duration. *Cutis*. Jan 2008; 81(1):87-91. [Medline].
18. Wang X. A theory for the mechanism of action of the alpha hydroxy acids applied to the skin. *Med Hypotheses* 53(5):380-2 (1999 Nov).
19. <http://www.nutralegacy.com/blog/general-healthcare/learn-about-cosmeceutical-ingredients/>
20. <http://www.facialmedispa.com.au/CosmeceuticalProducts.htm>
21. <http://www.makingcosmetics.com/articles/07-essential-role-vitamins-in-cosmetics.pdf>
22. <http://www.skincarecompany.net/vitamins-as-cosmeceuticals.html>
23. <http://www.sciphar.com/cosmetics.asp>
24. Hoppe U, Bergemann J, Diembeck W, et al. Coenzyme Q10, a cutaneous antioxidant and energizer. *Biofactors* 9(204):371-8 (1999)
25. Saija A, Tomaino A, Trombetta D, et al. In vitro and in vivo evaluation of caffeic and ferulic acids as topical photoprotective agents. *Int J Pharm* 199:39-47 (2000 Apr 10).

26. Murray JC, Burch JA, Streilein RD, et al. A topical antioxidant solution containing vitamins C and E stabilized by ferulic acid provides protection for human skin against damage caused by ultraviolet irradiation. *J Am Acad Dermatol* 59(3):481-25 (2008 Sep).\\
27. Badreshia-Bansal S, Draelos ZD. Insight into skin lightening cosmeceuticals for women of color. *J Drugs Dermatol*. Jan 2007; 6(1):32-9. [Medline].
28. Draelos ZD. Skin lightening preparations and the hydroquinone controversy. *Dermatol Ther*. Sep-Oct 2007; 20(5):308-13. [Medline].
29. <http://emedicine.medscape.com/article/1067778-overview#aw2aab6b7>
30. <http://www.makingcosmetics.com/Regenerating-Soothing-Agents-c12/>.
31. A Step By Step In Preparing A Home-Made Skin Lightening Cream
32. *Cutis*, March 2006, pages 177-184; *Journal of Drugs in Dermatology*, September–October 2005, pages 592-597; *Journal of Cosmetic*
33. *The Journal of Pharmacology and Experimental Therapeutics*, February 1996, pages 765-769
34. *Archives of Pharmacal Research*, August 2001, pages 307-311
35. <http://www.chinacosmeceutical.com/products4.asp>
36. <http://www.bulkactives.com/categories/preservatives.htm>
37. <http://www.numaderm.com/learn-about-cosmeceutical-ingredients/>
38. <http://www.dermatology.ca/members/Media-Coverage/2009/SkinTherapyLetter-Cosmeceuticals.pdf>
39. <http://www.ynsmedspa.com/ingredients.html>
40. <http://www.fda.gov/cosmetics/guidancecomplianceregulatoryinformation/ucm074201.html>
41. <http://www.unifra.br/professores/martafarm/cosmetology,%20cosmetics,%20comeceutical.pdf>
42. <http://cosmetics.indianetzone.com/1/cosmeceuticals.htm>
43. <http://cosmetics.indianetzone.com/1/cosmeceuticals.htm>
44. *Cosmeceuticals*. Marcel Dekker, Inc. New York • Basel. TM edited by. Peter Elsner. Howard I. Maibach. University of California, San Francisco, California ...
45. <http://www.fda.gov/cosmetics/guidancecomplianceregulatoryinformation/ucm074201.htm>

46. <http://newhope360.com/cosmeceuticals-taking-root-europe>.

47. <http://askanesthetician.wordpress.com/2011/01/17/what-are-cosmeceuticals>.

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