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Cosmeceuticals: Boon for human dermal care

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Abstract

The use of cosmeceuticals has radically risen in recent years. This considerably increases the armamentarium of the clinician in humanizing the treatment of skin, hair, and other circumstances. They are at the point in time where wellness meets beauty and growing use by consumers is analytic of their popularity. This chapter focuses on skin, hair, and other cosmeceuticals and their regulatory aspects.

Keywords: Cosmetics, skin, safety, packing.

1. Introduction

The concept of beauty and cosmetics dates back to ancient mankind and civilization. Generally herbal cosmetics are also referred to as natural cosmetics. Herbal cosmetics are formulated, using different cosmetic ingredients to form the base in which one or more herbal ingredients are used to cure various skin ailments. Plants are highly used for development of new drug products for cosmeceuticals and pharmaceutical applications [1].

Herbal Cosmetics, referred as Products, are formulated, using various permissible cosmetic ingredients to form the base in which one or more herbal ingredients are used to provide defined cosmetic benefits only, shall be called as “Herbal Cosmetics”. Herbs do not produce instant cures. They offer a way to put the body in proper tune with nature [2,3].

A huge number of cosmetic and toiletry formulations have been designed and developed based upon Indian Herbs recently. Other than traditionally documented applications, some modern trials have also been using the utility of Indian herbs in Personal Care products. The demand of herbal medicines is increasing rapidly due to their skin friendliness and lack of side effects. The natural content in the herbs does not have any side effects on the human body; instead provide the body with nutrients and other useful minerals [4].

The term Cosmeceuticals was first used by Raymond Reed founding member of U.S Society of Cosmetics Chemist in 1961. He actually used the word to brief the active and science based cosmetics. [5]. Cosmeceuticals are cosmetic-pharmaceutical hybrids intended to enhance health and beauty through ingredients that influence the skin's biological texture and function [6].

The largest organ of the human body is the skin. It protects our bodies from the environment, maintains body temperature, excretes waste matter, gives sensory information to the brain and regulates body moisture. We think about our skin more than any other part of our bodies, and we manifest that attention by investing our emotions and about 6 to 20 % of our disposable income into our skin [7].

In this article the psycho-social impact of cosmetics will be examined as well as why cosmetics are deemed necessary. The physiology of skin, how cosmetics affect skin function and the effects of synthetic and natural cosmetic ingredients on the skin will also be considered.

2. The Psycho-Social Impact of Cosmetics

Our society is preoccupied with the "culture of beauty"[7] which includes the notion that our skin must always look young and appear free from blemish. Our psychological well-being is often closely enmeshed with perceptions of how our skin appears to ourselves and others. We define our self-image to include the visible representation of our skin to others; so as a result, it has become the "primary canvas on which our cultural and personal identity is drawn". Cosmetic companies set aside concepts of natural beauty so that flaws such as large pores, fine lines and wrinkles are brought to the fore, influencing our spending habits in pursuit of flawless skin. In the animal kingdom, most male species are endowed with colourful physical attributes so that a less colourful, but wisely camouflaged female mate will be attracted to it.

3. The Need for Cosmetics

A cosmetic is any substance which, when applied, results in a temporary, superficial change [8]. We use a myriad of cosmetics on our skin, from moisturizers to lipstick. Make-up alters our visual appearance by enhancing our facial features through the artistic application of colour. It can beautify the face and be used to express our sense of self to others. Make-up can hide blemishes, scars, under-eye circles or even out our skin tone. Skin care cosmetics treat the surface layer of the skin by providing better protection against the environment than skin left untreated. Creams treat the skin's surface by imparting moisture to the skin cells on the outermost layer of the skin. It also forms a thin barrier which traps moisture underneath, thereby preventing the evaporation of water from the skin's surface. Creams also accelerate the hydration of skin cells on the outer layer, giving the skin a temporarily smooth, plump appearance. Exfoliants improve the appearance of the skin by sloughing away flaky skin, blackheads and some dead skin cells. Astringents improve skin tone and texture by swelling the pore walls so dirt and debris do not collect within. Soaps loosen particles of dirt and grime by dissolving the greasy residue left on the skin from natural skin oils, creams and make-up.

4. The Physiology of the Skin and How Cosmetics Affect Skin Function

Skin is made up of three main layers: the epidermis, the dermis and the hypodermis (Figure 1).

The epidermis is the only layer we can see with our eyes and as we age, remarkable changes occur which are hidden from our view. For instance, the skin gradually thins over time, especially around the eyes. Some cosmeceuticals can minimally re-thicken the skin, but the process of thinning is inevitable. Elastin and collagen, located in the dermis keep the skin resilient and moist, but with ageing these fibres break down to create lines and wrinkles. Exposure to ultraviolet radiation accelerates this process, and since few cosmetics can actually reach the dermis, the idea that a cosmetic can reverse this process is unfounded. The best way to prevent fine lines and wrinkles is to limit our exposure to the sun and ultraviolet radiation. The skin is a highly complex, dynamic tissue system. One square inch of the skin is composed of 19 million cells, 625 sweat glands, 90 oil glands, 65 hair follicles, 19 000 sensory cells and 4 metres of blood vessels [7]. The outermost layer of the epidermis is called the cornified layer, and is made of sheets of keratin, a protein, and squames, dead, flat skin cells. It is our barrier against dehydration from the environment. It receives its primary supply of moisture from the underlying tissue, since constant contact from the external environment tends to dry out the skin's surface. When the skin is exposed to dry conditions, the cornified layer can become dry, brittle, firm and if untreated, it can crack and lead to infection. Creams create a waxy barrier to prevent dehydration and keep the skin moist and supple. Underneath the cornified layer lie six more layers of the epidermis responsible for cell generation. The life cycle of skin cells within this layer takes approximately 28 days, so it may take three to four weeks to observe any changes at the skin's surface from using a new cosmetic.

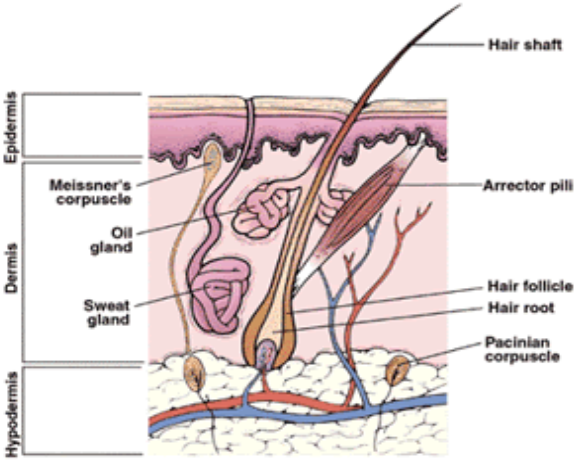

Figure 1: Skin Cross section

The skin surface is also home to millions of healthy micro-organisms which increase our immunity to pathogenic, or disease-causing bacteria. Thus, our desire to sterilize the skin also destroys beneficial bacteria, such as streptococcus mutans, and micrococcus luteus.

5. The Effect of Natural and Synthetic Cosmetic Ingredients on the Skin

A natural substance is any plant or animal extract, rock or mineral which is obtained from the earth. An

artificial or synthetic substance is a substance which has been modified through chemical reactions in an industrial process [8]. We use a myriad of cosmetics on our skin, but before we use these beauty aids, three essential questions should be asked:

- What is the composition of the cosmetic?
- Why is each ingredient used?
- Do the ingredients have positive or negative effects on the skin and body?

The health of the skin is dependent on sound nutritional practices, healthy living and effective, safe protection on its surface. The organic make-up company can help you achieve healthy, radiant skin by offering a complete line of cosmetics and makeup composed of all natural ingredients, with no animal, synthetic or petroleum-based ingredients. Our products are made fresh for you once we receive your order, and contain preservatives such as d-alpha tocopherol (*vitamin E*), ascorbic acid (*vitamin C*) and other plant oils with anti-microbial properties.

6. Hairs and there physiology

Hormone and hair follicles the effects of neurohormones on hair follicle growth are very complex and strongly dependent of hair cycle stage. A close localization of sensory and autonomic nerve fibers and bulge area support the possibility that neuropeptides and neurotransmitters may influence stem cells and modulate hair cycle. However, it is now clear that human hair follicles are not only a target of neuromediators, but they are also a non-classic production site for neurohormones, which are synthesized by keratinocytes, melanocytes, and fibroblasts[10] Several studies in humans showed the expression of a neuroendocrine system in the human hair follicle[11-12] In particular, the expression of corticotropin-releasing hormone (CRH), urocortin, and CRH receptors, the propiomelanocortin-derived neuropeptides (a-MSH, b-endorphin, ACTH, thyrotropin-releasing hormone, melatonin) and their associated receptors, has been previously reported. The role of neurohormones and neuropeptides in human hair follicle pigmentation extends far beyond the control of melanin synthesis by a-MSH and ACTH and includes melanoblast differentiation, reactive oxygen species scavenging, maintenance of hair follicle IP, and remodeling of the hair follicle pigmentary unit. There are several clinical evidences about the involvement of neurohormones in hair pathologies. In humans, an overproduction of ACTH is a well-recognized cause of acquired hypertrichosis, which is a process in which nonpigmented vellus hair follicles are converted into large terminal hair follicles with a strong and pigmented hair shaft. This induction of hypertrichosis by ACTH suggests evidence that the neuropeptide may stimulate and/or prolong the anagen phase [13]. Other data suggest that severe psycho-emotional stress may cause the onset of AA. This effect may be mediated by CRH release that acts as a direct proinflammatory peptide or through activation of mast cells leading to the destruction of the hair root[14] More recently, another study confirmed the enhanced expression of CRH, ACTH, and a-MSH in AA[15]. Aging is associated with progressive decreases in the maximal function and reserve capacity of all organs in the body, including the skin. The most common phenomenon of aging in hair is graying. It occurs in the fourth decade regardless of gender, even if some clinical differences are noted between men and women: the temporal and occipital areas are more involved in men than in women and, usually, graying starts in the temporal area in men and in the frontal area in women [16]. Maintenance of hair pigmentation is dependent on the presence and function of melanocytes, which are maintained by the stem cells of the bulge area of the hair follicle. Loss of melanocytes and melanocyte stem cells is associated with the loss of hair pigmentation seen with human aging. In particular, studies for pMel17 and microphthalmia-associated transcription factor demonstrated a decreasing number of unpigmented melanocytes in the bulge region of the hair follicle [17].

7. Eye and its physiology in relation to cosmetics

Eye cosmetics are part of everyday life around many parts of the world. Women and men judge eye cosmetic use as a factor in facial attractiveness and the psychosocial and even economic impact of cosmetics use is well documented [18]. The cosmetics market is certainly large, with UK sales ranking fourth in Europe, exceeding €8.5 billion.3 Indeed, Mintel have reported a 38% increase in eye cosmetic sales since 2004[19]. Lead toxicity and changes in conjunctival and periocular pigmentation are documented complications arising from the use of kohl, commonly used in Indian and Middle Eastern cultures, but there is little published literature that reviews the long term side effects of Western eye cosmetic use. All cosmetic products manufactured for sale in Europe must undergo rigorous safety assessments to comply with the European Cosmetics directive (76/768/EEC) to ensure that the product does not cause harm to human health. There are several reported cases where the use of Western formulations of mascara and eyeliner have caused increased conjunctival pigmentation, ranging from diffuse pigmentation of the tarsal conjunctiva and conjunctival fornices to discrete, punctate deposits[20]. However these publications are dated in light of modern cosmetic product formulations. More recently, there have been case studies reporting the accumulation of cosmetic products within the

lacrimal system and on the ocular surface which have resembled melanomas. However, the reported and published incidence of these unusual circumstances are rare compared with the incidence of allergic contact dermatitis (ACD) around the eyelids caused by cosmetics use, which is approximately 4%.15 Preservatives and fragrances added to products are the primary causative agents of cosmetic ACD and irritant contact dermatitis. If cosmetic products induce a dermatological reaction, a localised response involving redness, swelling, small vesicles/blisters and sweating may be present which may generate a range of symptoms including tingling, burning, tightness, itchiness or pain. Although regulated eye cosmetic products should cause no harm or morbidity to the ocular surface, mild undesirable effects may go undetected or unreported – presumably many consumers simply choose to omit the use of incompatible products from their daily regime.

Although the influence of external factors such as the regular use of eye cosmetics upon dry eye symptoms have been suggested to cause symptoms of dryness and discomfort [23,24] these findings are not yet well established. The mechanisms of eye irritation is unproven but potentially arises from several factors: particles and pigments from cosmetic products may cause foreign body sensations and may reduce tear film stability, the presence of preservatives and fragrances may induce toxic and allergic responses [25] and may also play a role in altering tear film pH and osmolarity. The way in which eye cosmetics are applied in the Western world is largely dictated by fashion trends and personal preference. Of particular interest is the use of kohls and eyeliners. Traditional kohl is applied within the mucocutaneous junction in many Eastern cultures as it was once believed that this reduced the effects of glare in sunny climates [26]. Alternatively, eyeliner is also commonly applied outside the eyelash line, directly onto periorbital skin. There is evidence of the migration of cosmetic products into the tear film when applied to periorbital skin, resulting in contamination of the tear film. Cosmetics such as eyeliner can be applied with even closer proximity to the ocular surface when used along the lid margin and over the meibomian glands. Meibomian gland dysfunction (MGD) is a major cause of dry eye disease [28]. However, to date, there are no published data reporting the changes in ocular comfort when such eye cosmetics are used within the mucocutaneous junction.

The fine vertically-oriented muscles lie directly beneath eyelid skin allows vertical movement of lid skin, facilitating the gradual migration of ointments over the lid margin and onto the ocular surface. Once cosmetic products are in the tear film, changes in pH and tear osmolarity may occur which may lead to reduced tear film stability, resulting in further discomfort. However, the likelihood of cosmetic product migration in this manner is likely to be productdependent. With an increasing trend of formulating 'long wear' and 'waterproof' cosmetic products, the improved residency on skin and lashes may alter or even minimize patterns of migration compared to products which may be powder-based. The addition of preservatives, surfactants and emulsifiers to cosmetic products may cause irritation to the ocular surface, in a similar way it may irritate periocular skin. Preservatives commonly used in cosmetic products include: parabens, imidazolydinil urea, diazolydinil urea, formaldehyde, benzalkonium chloride and 2-bromo-2-nitropropane-1,3-diol, all of which are cosmetics ingredients which responsible are for eyelid allergic contact dermatitis. Pigments and particles suspended in coloured eye cosmetic products, varying in particle size, may provoke foreign body sensations when in contact with the ocular surface.

Certainly, in the formulation of ophthalmic pharmaceutical preparations, it has been recommended that particle sizes are no larger than 10 lm to minimise eye irritation. Dermatologists recommend changing products or application techniques for patients with sensitive skin and eyes. The use of unpigmented (clear) mascara and restricting application to the tips of the lashes can cause less irritation for some patients. Cosmetic manufacturers may formulate hypoallergenic products which contain less sensitising ingredients, further reducing the potential for irritation which may be ideal for sensitive patients. While alternatives to daily colour cosmetics application exist (eyelash tinting, permanent make-up), these invasive procedures carry their own risks and should only be carried out by suitably trained professionals.

In this study, no trends were identified with frequency of eye cosmetics use or the type of products used in relation to OSDI scores. As previously discussed, the use of the OSDI questionnaire to detect changes in irritation for this cohort may not be suitable. However the confounding influence of multiple product usage is unknown. The results indicated that the majority of cosmetics users applied two or more products as part of their weekly routine; only a small number of users chose to apply one product only. Eyeliner use was analysed according to formulation (pencil or liquid) and the position of eyeliner application (within or outside the lash line) to explore the hypothesis that product placement closer to the lid margin may contaminate the tear film resulting in tear film changes and subsequent discomfort. MGD remains a leading cause of evaporative dry eye and obscuring these gland openings with cosmetic products might be factorial in dysfunction. A host of associated ophthalmic risk factors for the condition have been summarised by the International Workshop on

Meibomian Gland Dysfunction, but there are no published data which explore the effects of applying eye cosmetics close to, or along the meibomian glands. While the acute effects of eyeliner application due to tear film contamination might be tear film instability, long term effects of eyeliner application on meibomian gland morphology or meibum lipid profiles are unknown. Conversely the application, and particularly removal, of eye cosmetics inevitably involves digital manipulation of the lids which also may encourage expression of meibum into the tear film. Increased meibum in the tear film will increase tear film lipid layer thickness which, in turn, can retard tear film evaporation. Indeed digital expression of meibomian glands is a recognised therapy for MGD37 which has been shown to significantly reduce tear evaporation rates[29].

8. Nail

A nail is a horn-like envelope covering the tips of the fingers and toes in most primates and a few other mammals. Nails are similar to claws in other animals. Fingernails and toenails are made of a tough protective protein called keratin. This protein is also found in the hooves and horns of different animals. A healthy fingernail has the function of protecting the distal phalanx, the fingertip, and the surrounding soft tissues from injuries. It also serves to enhance precise delicate movements of the distal digits through counter-pressure exerted on the pulp of the finger.[1]

8.1 Growth

The growing part of the nail is under the skin at the nail's proximal end under the epidermis, which is the only living part of a nail.

In mammals, the growth rate of nails is related to the length of the terminal phalanges (outermost finger bones). Thus, in humans, the nail of the index finger grows faster than that of the little finger; and fingernails grow up to four times faster than toenails [31].

In humans, nails grow at an average rate of 3 mm (0.12 in) a month. The longest female nails to ever exist measure a total of 601.9 cm. Fingernails require three to six months to regrow completely and toenails require twelve to eighteen months. Actual growth rate is dependent upon age, sex, season, exercise level, diet, and hereditary factors. Contrary to popular belief, nails do not continue to grow after death; the skin dehydrates and tightens, making the nails (and hair) appears to grow.

8.2 Permeability

The nail is often considered an impermeable barrier, but this is not true. In fact, it is much more permeable than the skin, and the composition of the nail includes 7–12% water. This permeability has implications for penetration by harmful and medicinal substances; in particular cosmetics applied to the nails can pose a risk. Water can penetrate the nail as can many other substances including paraquat, a fast acting herbicide that is harmful to humans, urea which is often an ingredient in creams and lotions meant for use on hands and fingers, and several fungicidal agents such as salicylic acid, miconazole branded Monistat, natamycin; and sodium hypochlorite which is the active ingredient in common household bleach (but usually only in 2–3% concentration).

9. Rheology [32-35]

Cosmetics and pharmaceuticals are developed for external application, for example in the form of lotions, gels, creams, or for oral application, for example as pills or syrups. Since they occur as liquids, semi-solids and solids, they present the whole scope of rheology. These materials' rheological characteristics are important for production, packaging, filling and storage.

Why measure the rheological characteristics of cosmetics and pharmaceuticals?

- To control the quality of raw materials, final products, and manufacturing processes (mixing, pumping, packaging, and filling)
- To gain knowledge of the effect of different parameters such as formulation, storage time and temperature to the quality and acceptability of a final product
- To investigate and understand the fundamental nature of a system for research and development

Rheology is widely used in the cosmetic and pharmaceutical industry to test a variety of products. The fields of application range from very common tests like measuring the stability of a cream at different temperatures to very challenging measurements of small sample quantities like antibodies and injectable hydrogels, which may be very expensive and time-consuming. In this case the instrumentation required to test such kind of materials must be extremely sensitive and precise to generate reproducible analytical results, for example at ambient and body temperatures.

10. Typically measured cosmetics and pharmaceuticals:

10.1 Hair Gel

Hair is of particular importance to us. It is an expression of beauty and individuality, but can also show affiliation to a culture or group. To keep the hair in shape, there are certain auxiliary means to make sure that the hairstyle is perfect and will stay that way for a certain time. Besides hairspray, hair gel is certainly one of the most important products to achieve this goal. Modern hair gel must meet high requirements. On the one hand it has to be extremely strong, moisture-resistant and should provide

long-lasting hold; on the other hand it should not lead to sticky hands or sticky hair.

10.2 Hair gel and rheometry:

Gel is an abbreviation of "gelatin" and has the same Latin root as "jelly" (thickened fruit or meat juice). It is frequently a finely dispersed system consisting of at least a solid and a liquid phase, forming a three-dimensional network. Its consistence is viscoealstic and can be tested with a rheometer. Constantly checking a product's viscosity and yield point guarantees a consistently high quality. Whereas the viscosity of a hair gel is a particularly important parameter during production and for product evaluation during the development, the yield point is particularly important for the customer's evaluation of the end product. The yield point corresponds directly with the elastic properties of the sample at rest. Gels with a high yield point or a strong gel character are perceived by the customer as having "more volume". A strong gel character gives the impression of a high-quality product to a majority of customers.

10.3 Nail Polish

Nail polish is a material that needs to satisfy various rheological demands. On the one hand it should be thick enough to stick to the brush, on the other hand it has to be thin enough when transferred from the brush to the nail. Furthermore, the material should flow enough in order to level out any brush marks after the application. Finally, it has to dry fast enough for the customers to go about their business.

10.4 Nail polish and rheometry:

A very important factor with regard to nail polish is its thixotropic recovery. Thixotropy is a special kind of time-dependent viscosity behavior. Under constant shear, the viscosity of a thixotropic material decreases. Once shearing stops, the material will recover more or less completely. This behavior is observed in the decomposition and recovery of the inner material structure, which can be measured with rotational or oscillatory tests by performing a three-interval thixotropy step test.

10.5 Skin Cream

The feel and longtime stability of skin cream, both in cosmetic and pharmaceutical applications, are important points for the acceptance by the consumer. These properties are largely influenced by the ingredients but also by the manufacturing process. The replacement of ingredients with functional properties, such as emulsifiers or stabilizers, may be necessary since some of these are suspected to cause allergies and are therefore no longer accepted by the consumer. However, the quality of the products needs to stay the same. Likewise, an ingredient exchange – to reduce production costs, for example – should not necessarily result in a change of the physical properties typically associated with a certain product.

10.6 Skin cream and rheometry:

The characterization of the physical properties of an emulsion with a rheometer is suitable for determining and evaluating the influence on the properties of the final product when changing the composition or the manufacturing process. Additionally the mechanical stability of the final product can be tested in a relatively short time with an amplitude sweep, which is an oscillatory test performed at variable amplitudes while keeping the frequency at a constant value. Using the values of the storage modulus G' and loss modulus G" in the range of very low strain or stress values (which is the so called linear-viscoelastic or LVE-range), this kind of testing provides information about the structure strength and the viscoelastic character of a cream at rest.

10.7 Cosmetic cream making [36]

Creams can be either an oil-in-water or water-in-oil emulsion consisting of emollients and lubricants dispersed in an oil phase, and a water phase containing emulsifying and thickening agents, perfume, color and preservatives. Active ingredients are dispersed in either phase depending on the raw materials and the desired properties of the end product. A typical cream manufacturing process would be as follows:

• Flake/powder ingredients, such as cetyl alcohol and stearic acid, sometimes dry blended in advance, are dispersed into the oil phase. Heating may be required to melt some of the ingredients.

• Active ingredients are dispersed in the appropriate phase.

• The water phase, containing emulsifiers and stabilizers such as Veegum or Carbopol, is prepared separately.

• The two phases are then mixed to form an emulsion. This is aided by heating to between 45~85°C depending on the formulation and viscosity.

• Mixing is continued until the cream is homogeneous.

11. Main methodological approaches [37-39]

Depending on the intended use of the cosmetic product in course of development, it is possible to use and combine several experimental approaches: - the sensorial approach (sight, touch, olfaction) by consumers themselves or experts; - the instrumental approach which favours specific criteria measured using *in vivo*, ex-vivo or *in vitro* approaches which do not reproduce normal conditions of the use of products, but allow objective analysis of specific activities taken out of context or attempt to replicate key parts of the product use cycle under controlled conditions. Experimental design of studies is a large and complex subject and for optimal results has to rely on knowledge and

awareness of statistical principles in design and analysis of the study, including appropriate consultation with an experienced statistician. This is to ensure that the studies achieve scientifically valid conclusions with the minimum number of subjects.

11.1 Evaluation on Human volunteers

Sensorial tests these tests are based on an appreciation of product performance made through the senses of either panel lists or of experts. They give information mainly on observed or perceived parameters.

Auto Evaluations: Use tests by consumers A use test evaluates the consumers' perception of product efficacy and cosmetic properties based on parameters that they can observe or feel. They must be conducted on a sufficient number (see Statistical Guidance) of people. There are two main types of use tests: o Blind use tests are product tests without providing any information such as brand, decor, communication which could influence the consumers' judgement and alter their perception of the effect of the product alone. o Concept use tests are product tests combined with elements of communication that help to check whether the concept, the communication and the effect of the product as perceived by the consumers match up; information from concept use tests are used to complement that contained in the product efficacy dossier.

Sensorial-evaluation tests by trained expert panels: The sensorial evaluation enables a profile of the product to be drawn up according to predefined criteria. They must be conducted with the help of a panel of trained experts, following a well-defined protocol, with precise sensorial criteria. b) Evaluation by professional experts • Tests under medical supervision. These tests in relation to the cosmetic benefits of a product are performed under the control of a physician. The parameters are evaluated by clinical observation and/or scoring. They can be quantified by comparison with initial results or with an untreated control or a placebo or a reference product.

Tests under the control of other professionals: The tests can be conducted by a suitably qualified professional. Examples include: paramedical practitioners, hairdressers, aestheticians or other professional experts. The above would evaluate the performance of a product in terms of tactile and visual appreciation against a previously established scale. Auto-evaluation by volunteers themselves can be associated with these tests (evaluation by professional experts) in order to assess that they perceive the expected effects.

Instrumental tests these tests are performed with instruments that can precisely measure given parameters, according to a defined protocol, following the application of a product on human subjects.

Laboratory instrumental tests: These tests are performed under the control of a technician trained in the skilled use of the apparatus. The measurements are made on subjects in controlled laboratory conditions/environment: for example measurements of hydration, roughness, firmness, elasticity of the skin or measurements such as sun protection factors, UVA protection factors of filtering products, etc.

Instrumental measurements associated with an evaluation by professional experts. These measurements are made under the control of a suitably qualified professional and use precise criteria: e.g. trichogram analysis and its derivatives for hair formulae, measurement of hydration and of the skin's mechanical properties, measurement of cutaneous fold/crease, centimetre measurements, colorimetric tests, etc.

Ex Vivo / *In Vitro* Tests Ex Vivo (latin: "off the living"): relates to phenomena observed in the laboratory on a biological substrate taken from a living organism, without modification to the intrinsic properties of the substrate. For example ex vivo tests may correspond to instrumental tests which are conducted in the laboratory on keratin supports such as isolated hair fibres or hair tresses which have been cut from the human head in order to measure their mechanical properties, their surface properties or their colour in conditions that allow for the isolation of any effects emanating from the scalp. Other examples of ex vivo studies would include skin microflora and tape strips of skin. These tests can be generally quantified and comparative (with and without a specific ingredient, reference product, etc.). *In Vitro* (latin: "in glass"): relates to phenomena observed in the laboratory, in artificial media (e.g. in test tubes or other containers such as culture dishes). *In vitro* tests are generally made in order to give prominence to performances which can be provided by ingredients or finished products which can be best demonstrated in this way. *In vitro* tests may be used as screening instruments during product development or to illustrate an ingredient's mode of action. They may also be used to demonstrate mechanisms relating to the finished product provided that a correlation with actual product usage can be demonstrated.

11.2 General principles for all tests

Studies must be relevant and comprised of methods which are reliable and reproducible. The studies should follow a well-designed and scientifically valid methodology according to good practices. The criteria used for evaluation of product performances should be defined with accuracy and chosen in compliance with the aim of the test. Studies conducted on volunteers should naturally respect ethical rules and products tested should have previously undergone a safety investigation.

Human studies should be conducted on the target population when necessary, defined by strict inclusion/exclusion criteria. Depending on the aim of the study, tests can be open, single- or double-blind. Ex vivo/*in vitro* tests must be conducted under standardized conditions and their protocols must refer to published and/or "in house" validated methods. Clear descriptions of the methodology will be documented, as well as the statistical analysis of the data. These tests should be conducted in a controlled environment. A study protocol must be drawn up and validated by the parties involved. This is essential to enable the study manager/promoter to monitor the study and the experimenter to carry out the test in order to ensure its quality. The test laboratories must have standardized operating procedures. The equipment must be the subject of documented maintenance adapted to its use. Whatever the type of study, it is important that the person conducting the study: - has the appropriate qualifications; - has the training and experience in the field of the proposed study; and - is respected for ethical quality and professional integrity. A study monitoring system must be set up in order to ensure that the protocol and the operating procedures are correctly followed. Data processing and the interpretation of results must be fair and should not overstep the limits of the test's significance. Data recording, transformations and representation in tabular or graphical form should be transparent or clearly explained if complex. It should not be designed to overstate the effect(s) measured. Appropriate statistical analysis of the data should be performed.

11.3 Preservatives for Cosmetics [40-45]

What is preservation? When we speak as formulators about preservatives, we are referring to the protection of cosmetic products from contamination by bacteria, yeast, or mold from the time the product is manufactured up until the time the product is completely used up by the consumer. In order to understand this problem and its solutions it is necessary to first define a number of terms.

Preservatives are defined as a material that will prevent the growth of or react with and destroy microorganisms that might damage the product or create a health hazard by growing on or in the product. An antiseptic is a material that prevents the growth of and/or destroys microorganisms when applied to living tissue. An example of an antiseptic would be hydrogen peroxide. Disinfectants are materials that destroy disease-producing microorganisms on inanimate objects. Germicide is a general term used to refer to products that kill microorganisms. Two common suffixes used in microbiology are the terms cidal meaning kill and the term stasis meaning inhibition of growth. Preservatives however are not a replacement for basic good housekeeping procedures. This does not mean that the types of products that we are concerned about here must all be manufactured under sterile conditions, but a reasonable level of cleanliness is dictated by "GMP's" (Good Manufacturing Procedures). In other words, preservatives is intended to keep a clean product free of incidental contamination, not kill the overwhelming number of microorganisms that can be introduced during manufacturing in an unclean plant.

Now that we have defined preservation, it is important to understand why products need to be preserved. Microbial contamination of cosmetic products is of concern to industry, to regulatory agencies and most importantly to the consumer. Contamination of finished products may result in visible changes which may include off odor, color changes, viscosity and texture changes, gas production, degradation of active ingredients, or possibly, the most important and often invisible concern, potential health hazards. Regulatory agencies are particularly concerned about inadequately preserved topicals which may come into contact with the eye or which may be used on infants, the sick or the elderly.

Although we live in a world filled with microorganisms, these groups are particularly vulnerable to microbial attack. For example, infections caused by Pseudomonas aeruginosa, a Gram-negative bacterium, can be fatal to burn victims.

11.4 General Microbiology

The organisms that are capable of compromising both product integrity and safety are divided into 3 broad categories: bacteria, yeast and mold. For optimum growth, bacteria in general prefer neutral or slightly alkaline pH and warm temperatures of 30-37'C. Bacteria can be divided into two classes based on a differential staining procedure, which distinguishes the chemistry in the bacterial cell wall. Gram-positive bacteria retain the primary stain while Gram-negative bacteria do not retain the stain material. This distinction is very important because many of the Gram-negative bacteria are considered pathogenic or disease producing while only a very few of the Gram-positive bacteria are considered pathogenic. Gram-negative bacteria are extremely difficult to control because of the complexity of their multilayered cell walls. The genus of Gram-negative bacterium that is of greatest concern to formulators is Pseudomonas. Pseudomonas species are widely distributed in nature and can be isolated from soil, tap water, marine water, and even from the skin. Many Pseudomonas species are noted for their nutritional versatility and adaptability. Pseudomonas can be found which can degrade a wide variety of organic compounds such as starch, cellulose, hydrocarbons, and resins. They are resistant to most antimicrobials and are often severe health hazards. Pseudomonas aeruginosa is often responsible for

bum and wound infections, urinary tract infections, and severe eye infections, which can result in conjunctivitis or loss of sight. Yeast usually prefer an acidic pH and room temperature for optimal growth. They are of concern due more to their effects on the aesthetics of the formulation than to health hazards. Candida albicans is the most common representative of this group. Mold, like yeast, also prefer an acidic pH and room temperature. They reproduce by spore formation and the spores can continue to survive indefinitely under favorable conditions. Spores are difficult to control as they can remain dormant in a hostile environment and can then become activated when the circumstances become conducive to their growth. A typical member of the group is *Aspergillus niger*, a widely distributed mold capable of product spoilage.

Microorganisms, like most other living things, normally have three basic requirements that are essential for growth: water, air (for aerobes) and nutrients.

Water is required in order to secure food and to eliminate waste products. However, even anhydrous or non water-based products should be protected by preservatives systems. During use conditions, for example in the bathroom, a film of water can form on an anhydrous product and in the high local concentration of water, microorganisms will grow.

Most microorganisms require air for survival and growth-, they are called aerobes. Air is required for the conversion of nutrients into energy. Nutrients or food are required for the synthesis of cell-building materials or as a source of energy. Practically any carbon compound can nourish one microbe or another. The list ranges from the usual growth substances such as proteins and carbohydrates to unusual nutrients such as rubber, oil or paints. Cosmetic formulations in particular are an excellent source of nutrients for microorganisms. Examples of ingredients that are especially good sources of food include: alcohols such as glycerol, sorbitol, mannitol and fatty alcohols, fatty acids and their esters, sterols including lanolin and its derivatives, proteins, vitamins, and botanical extracts. There are many variables that influence the effectiveness of a preservative system. These include concentration of the preservative, contact time, the number of microorganisms present, PK inactivation or enhancement by other ingredients in the formulation, and packaging. We will explore each of these in greater detail. In general, the higher the concentration of the preservative, the more effective it will be. Often preservatives are cidal, which are they kill, at high concentrations and exhibit stasis, that is prevent growth, at low concentrations. There is sometimes a tendency to want to "over preserve" products. This is not advised because high levels of preservatives activity are often associated with toxic or irritant properties on animal tissues. One must remember that preservatives are specifically designed to kill living cells. Therefore, at some concentration they will undoubtedly begin to affect the skin. On the other hand, too low a concentration of preservative may be ineffective or may even stimulate microbial growth.

A second factor is contact time between preservatives and the formulation. This is important since the longer the contact time the greater the number of organisms killed. Theoretically, microorganisms are killed at a logarithmic rate. Under a specific set of conditions, the same percentage of a microbial population should be killed with each unit of time. The third factor regulating preservatives activity is the number of microorganisms challenging the system. Obviously, the greater the number the longer it takes for the preservative system to drop the count to some acceptable level. Too many organisms can overwhelm the preservative system.

The pH of the formulation is a fourth factor, as some preservatives, such as benzoic acid or parabens are only active in their acidic form. One must also consider the interaction between the preservative and other ingredients in the formulation. This interaction can result in either inactivation or enhancement of the preservative depending on the chemical reaction taking place. For example, anionic surfactants usually inactivate preservatives that are cationics. Proteins inactivate quats, parabens and phenolics. Alternatively, enhancement of the preservative can occur when using raw materials such as alcohols, aldehydes, and acids because they often have some antimicrobial activity of their own. Another example of preservative enhancement is the use of EDTA (ethylenediamine tetraacetic acid) in a formulation. EDTA can be used to increase the permeability of the cell wall by chelating the metal ions that are part of its composition, thus increasing the organism's sensitivity to a wide variety of preservatives. In addition, EDTA’s chelating ability allows it to tie up metal ions in the organism's surroundings, depriving it of essential mineral nutrients. A related problem is the potential interaction with packaging. The finished product packaging should be designed to prevent access of contaminants into the container, but also must be made of materials that will not cause inactivation of the preservative due to adsorption or complexation. Low density polyethylene, for example, may adsorb parabens from a product.

11.5 Testing Preservatives

Preservatives efficacy testing is an essential part of substantiating the safety of a product. Most large personal care manufacturers have a microbiology staff that performs preservative testing. Smaller companies may use the services of an outside micro lab for testing. The goal of efficacy testing is to determine, not only which preservatives system to use against the strains of

microorganisms to which the product may be exposed, but also that concentration of preservatives that will preserve the product during manufacturing and under use conditions.

The microbiologist's most important procedure for testing if a sample is contaminated is the Aerobic Plate Count or APC. The APC is used to determine the number of viable organisms present in a sample. This is carried out on agar plates that contain materials that support microbial growth. Each colony is assumed to represent growth from a single organism. Preservative testing is often lengthy and time consuming. Therefore, there are a number of fairly rapid screening methods that are used by microbiologists. The most common of these is called the Minimum Inhibitory Concentration or MIC test. This test determines the lowest concentration of the preservative system that will retard microbial growth. It uses inoculations of standard organisms that are representative of both Gram-positive and Gram-negative bacteria, yeast and mold. In light of the previous discussion of all of the factors that may influence the activity of a preservative, it is essential to test the preservative system in the actual finished formulation. This is done by means of an Adequacy of Preservation Challenge Test or Challenge Test. For this test, the preservatives are generally incorporated into a product base and "challenged" or inoculated with a large number of standard organisms along with various "house" organisms. "House" organisms are organisms that have adapted to a particular product or environment and whose metabolic activity is varied from the norm of its particular strain. They are often unique to a manufacturing plant. Assays are performed over a predetermined period of time, typically 4 to 8 weeks, sometimes with a rechallenge at 3 or 4 weeks.

11.6 The "Ideal" Preservatives

Before we can discuss the chemistry and function of preservatives, it is important to review the proper-ties of the so-called "ideal" preservative system. Please keep in mind that the "ideal" preservative does not exist and probably cannot exist in a single chemical entity. An ideal cosmetic preservative would have broad spectrum activity, which is the ability of the preservative to kill a wide range of microorganisms. Such a product would be effective against both Gram-negative and Gram-positive bacteria, yeast and mold. Usually, a multiple preservative system is needed to accomplish this goal.

Cosmetic preservatives should be effective at low concentrations in order to reduce costs, minimize toxicity effects and not adversely affect the physical properties of the finished product. Preservatives should be stable under whatever conditions it may encounter in the manufacture of the finished product (i.e. temperature, pH, etc.). It should not affect either the color or the odor of the product and it should be compatible with the wide range of ingredients that may be found in the formulation. The ideal cosmetic preservative should offer protection during manufacturing and should maintain activity throughout the intended life of the product in the hands of the consumer. It should be easy to analyze in the finished product. This is more difficult than it sounds since determining the concentration present does not necessarily indicate that it is all available to preserve the product. For example, some of the preservative may be bound to other chemicals or even the packaging, as mentioned previously, and therefore not be active. The material should be easy to handle and safe to both the environment and to humans. This is also not easy since a chemical that will kill microorganisms is biologically toxic, and therefore has the potential to adversely affect the environment and mammalian tissue.

12. Safety of cosmetics [46-50]

The role of the National Health Surveillance Agency is to regulate, control and supervise the processes, products, supplies and services that can potentially be harmful to the population's healthand quality products, ANVISA is responsible for authorizing the marketing of toiletries, cosmetic and fragrance products, by granting the manufacturer the product registration or notification. ANVISA also supervises and sets standards for the manufacturing companies, by checking the production process, the techniques and methods used until the final consumption. Thus, both the production and the marketing process of cosmetic products in Brazil are regulated by ANVISA and, therefore, subjected to its supervision. According to the Guide for the Safety Evaluation of Cosmetic Products of ANVISA, cosmetics, fragrances and toiletries are formulations constituted by natural or synthetic substances for external use on several parts of the human body: skin, hair, nails, lips, external genital organs, teeth and mucous membranes of the oral cavity, aiming exclusively to clean, scent, change the aspect and/ or correct body odors and/or protect or keep them in good condition (ANVISA, 2003). Cosmetics, as well as toiletries and fragrance products are classified according to the degree of risk they offer, in which grade 1 represents the products with minimal risk and grade 2 products with potential risk (RDC 211, 2005). The criteria for this classification were defined by ANVISA according to the intended product use, body areas covered, use directions and any special care to be observed during use (Leonardi, 2008). For marketing products rated as Risk Level 1, a notification must be sent 30 days prior to their marketing. For submitting the notification, it is not necessary to submit studies to prove its safety and efficacy. However, the National Health Surveillance Agency may require the manufacturer to present at any time, the safety tests

performed. Thus, it is important for the manufacturer to properly evaluate the safety of the product and maintain all study records. Products rated as Risk Level 2 are those with specific recommendations, which characteristics require safety and/or efficacy support, as well as information and special care concerning the use directions and restrictions, in that it is mandatory to present this information when requesting the product registration (RDC 343, 2005). The safety evaluation of cosmetic products before marketing is extremely important for preserving consumer's health. The first exposure to a new cosmetic product must occur in a controlled and monitored way, in clinical studies monitored by expert physicians, and not in a large scale, in the consumer market. It is a way to prevent the occurrence of unexpected reactions directly to the consumers, preserving the health and wellbeing of the population. Despite the existence of different processes for products registration and notification, the importance must be directed to the conduction of an appropriate safety evaluation of the products. Resolution No. 79 of August 28th, 2000 updates the list of allowed, allowed with use restricted to certain conditions or prohibited substances in cosmetic products, and updates the standards and procedures contained in Resolution 71/96 concerning the registration of toiletries, cosmetic and fragrance products and others included in this context. Products categories not existing in Resolution 71/96 were also created. A cream for cellulite or stretch marks, for example, that had no specific category before, with the publication of Resolution 79, enters the category "cellulite/stretch marks cream" and is rated as a product of risk level 2. The same occurs with body products containing SPF that are now rated as products of risk level 2 (RDC 79, 2000). As a consequence, besides using safe raw materials covered by the conditions outlined in the lists of substances made available by the Regulatory Agency, the industry should have the results proving the safety of every marketed cosmetic product. When submitting their products for clinical trials, the company must ensure they do not offer foreseeable risks for the subjects and that the raw materials used are consecrated and do not represent health risk

In vitro non-clinical assays are important today for replacing the tests performed in animals, with some alternative methods already internationally validated. Initially developed to properly meet the needs of the pharmacology studies, alternative methods were also used to evaluate the toxicological effects (ANVISA, 2012). They are of a great importance to evaluate new raw materials. After running pre-clinical tests, the product safety when in human use should be evidenced by clinical studies results (ANVISA, 2012).

The clinical trials aim to confirm the safety of the finished product, taking into account possible interactions between the ingredients, which are required for products registration (ANVISA, 2003). The clinical and non-clinical studies may prove the safety of components or finished products, by evaluating the potential for skin irritation, photoallergy and phototoxicity, ocular irritation, acnegenicity, comedogenicity, sensitization, among others. The ocular irritation studies are not required for registration, unless the manufacturer wishes to explore as product claims expressions like "Ophthalmologically Tested" or "Tear-free", for example. However, it is important to highlight that if any consumer reports any unwanted effect in the eyes, the manufacturer may be required to present tests confirming the product safety in this area. Therefore, although mandatory only in cases in which special claims are used on the product labels, tests in the ocular area are extremely important, since toxic profile products may cause injury when in contact with the eyes (Azevedo, 2003), as occurred in the 30s in the United States with Lash Lure® cosmetics, which made at least 12 individuals go blind. These cosmetics were used in beauty salons as permanent colorant for eyelashes and eyebrows. Its composition comprised amine paraphenylene, a substance with high dermal-sensitizing potential, causing, weeks after use, severe corneal damages to its consumers

The criteria and procedures for validating methods have been developed and implemented in Europe by the ECVAM - European Centre for the Validation of Alternative Methods and its independent Committee ESAC - European Scientific Advisory Committee, in the United States by the ICCVAM - Interagency Coordinating Committee on the Validation of Alternative Methods, in Japan by the JaCVAM - Japanese Centre for the Validation of Alternative Methods and internationally by the OECD - Organization for Economic Co-Operation and Development. The main objective of this validation body is to promote the scientific and regulatory acceptance of alternative methods through research, development and validation of new tests, aiming to contribute for the principle of the 3Rs (Reduction, Refinement and Replacement of animal tests). Before an alternative method is officially accepted by the regulatory agencies, it is essential that the validity of the new methods be demonstrated in an independent validation and scientifically accurate program.

During the pre-validation process, the method must first become valid. Since the alternative method went through the process of pre-validation and validation, it will be analyzed by the SCCP (Scientific Committee on Consumer Products). After approval by the SCCP, it will be submitted for approval by the regulatory agencies and

written OECD guideline. That being said, it is clear that the process of validation of any alternative method for safety evaluation of chemical substances and finished products in is a factor of scientific, technological and industrial development and competitiveness for the cosmetic, sanitizing, pesticides and pharmaceutical industry.

Clinical studies Since the cosmetic products are produced with raw materials known to be safe, as per the lists of ingredients made available by the Regulatory Agency and found in the literature, and that new raw materials are incorporated in these products only after they have been extensively studied through pre-clinical tests, the clinical studies aim to prove the safety of these products in humans. These studies allow knowing the action of the product, directly into the target public, on the mucosa or on the skin from different body areas.

12.1 Manufacture and sale of cosmetic [51-53]

The manufacture and sale of cosmetic products are regulated by different governmental entities around the world. There may be different specific regulatory systems; they have a common goal of ensuring that cosmetic products are safe and properly labeled. In the industrialized countries these regulations have evolved to the point where they are rather extensive and, largely because the United States and European Union are the two largest markets in the world for cosmetic products. The cosmetics market in India is growing at 15-20% annually, twice as fast as that of Tthe United States and European market. Indian cosmetic industry is matured enough and responsible to ensure the quality and safety of its products. The cosmetic regulations in India are complex and time consuming for pre marketing approval. It is therefore important for a cosmetic manufacture to understand the difference in regulatory system in India when compare to USA and EU. Legal authority and manufacture of cosmetics for sale USA: In the US, cosmetics are regulated by Federal Food, Drug and Cosmetic Act. It is the role of the FDA to oversee the compliance with these regulations. However, as opposed to drugs, cosmetic products do not require verifiable, mandatory compliance (such as FDA approval) before they can be marketed. The Voluntary Cosmetic Registration Program (VCRP) is an FDA post-market reporting system for use by manufacturers, packers, and distributors of cosmetic products that are in commercial distribution in the United States.The VCRP applies only to cosmetic products being sold to consumers in the United States. It does not apply to cosmetic products for professional use only, such as products used in beauty salons, spas, or skin care clinics. It also does not apply to hotel samples or free gifts or cosmetic products you make in your home to sell to your friends. EU: EU cosmetic legislations are based on Council Directive 76/768/EEC of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products (Cosmetics Directive). As in the U.S., manufacturers are responsible for ensuring that cosmetic products comply with the law before they are marketed. The manufacturer or importer of cosmetics is responsible for demonstrating that the product is safe for its intended use. Regulations are enforced at the national level, and each country in the EU has an authoritative body that is responsible for upholding compliance. INDIA: In India the Drugs and Cosmetic Act (1940) operates the regulations of cosmetics. For the manufacture of cosmetics for sale or distribution the manufacturer should build the factory premises according to the Schedule M-II and application for license in the form 31 and along with license fee of Rs. 2500/- and an inspection fee of Rs.1000/- for every inspection to the licensing authority of the state government where in the manufacturing unit is located. And the information is reviewed by (local state) licensing authority and shall be granted in the form 32. Labeling Aspects USA: The regulations for labeling of cosmetics in United States are controlled by FDA under the authority of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and the Fair Packaging and Labeling Act (FP&L Act). The label statements required under the authority of the FD&C Act must appear on the inside as well as any outside container or wrapper. Ingredient labeling and statement of the net quantity of contents on the principal display panel, only apply to the label of the outer container. The labeling requirements of principal display panel (the part of the label most likely displayed or examined under customary conditions of display for sale) must state the name of the product, identify by descriptive name or illustration the nature or use of the product, and bear an accurate statement of the net quantity of contents of the cosmetic in the package in terms of weight, measure, numerical count, or a combination of numerical count and weight or measure. The declaration must be distinct, placed in the bottom area of the panel in line generally parallel to the base on which the package rests, and in a type size commensurate with the size of the container as prescribed by regulation. The net quantity of contents statement of a solid, semisolid or viscous cosmetic must be in terms of the avoirdupois pound and ounce, and a statement of liquid measure must be in terms of the U.S. gallon of 231 cubic inches and the quart, pint, and fluid ounce subdivisions thereof. If the net quantity of contents is one pound or one pint or more, it must be expressed in ounces, followed in parenthesis by a declaration of the largest whole units (i.e., pounds and ounces or quarts and pints and ounces). The net quantity of contents may additionally be stated in terms of the metric system of weights or measures. The name and place of business of the firm marketing the product must be stated

on an information panel of the label. And the information must be in the English language. Declaration of Ingredients: The declaration of ingredients must be in descending order of predominance. Color additives and ingredients present at ≤1% may be declared without regard for predominance. The ingredients must be identified by the names established or adopted by regulation those accepted by the FDA as exempt from public disclosure may be stated as "and other ingredients". Cosmetics which are also drugs must first identify the drug ingredient as active ingredient before listing the cosmetic ingredients. Label Warnings Cosmetics which may be hazardous to consumers when misused must bear appropriate label warnings and adequate directions for safe use. The statements must be prominent and conspicuous. Law Enforcement Authority According to the enforcement of the law, the FDA may conduct examinations and investigations of products, inspect establishments in which products are manufactured or held, and seize adulterated (harmful) or misbranded (incorrectly or deceptively labeled or filled) cosmetics. EU: The requirements of cosmetic labeling under 76/768/EEC directive are: It should carry the name or trade name and address or registered office of the manufacturer or of the person responsible for marketing the cosmetic product within the Community and weight or volume of product and any precautions and a distinctive identification of the batch number or product reference number.

Summary of cosmetic regulations

CONTENTS	 USA	 EU	 INDIA
AUTHORITY	FDA	EMEA	CDSCO
RULES AND REGULATIONS	FOOD,DRUG AND COSMETIC Act	COUNCIL DIRECTIVE 76/768/EEC	DRUGS AND COSMETICS Act
PRE-MARKET APPROVAL	Not required	Not required by Cosmetic Directive	Required under state government licensing
LABELLING	Should comply with the FD&C and FP&L	Based on Council Directive 76/768/EEC	Should comply with part XV of D&C rules 1945
EXPIRY DATE	No date required	Date of minimum durability if durability is <30 months. Period after opening if durability is >30 months	Indicated as "Use before date"
POST MARKETING REPORTING SYSTEM	Yes. (Voluntary Cosmetic Registration Program)	N/A	N/A

13. Advantages of Herbal Cosmetics over Synthetic [54-69]

Herbal cosmetics are the modern trend in the field of beauty and fashion. These agents are gaining popularity as nowadays most women prefer natural products over chemicals for their personal care to enhance their beauty as these products supply the body with nutrients and enhance health and provide satisfaction as these are free from synthetic chemicals and have relatively less side-effects compared to the synthetic cosmetics. Following are some of the advantages of using natural cosmetics which make them a better choice over the synthetic ones: Natural products The name itself suggests that herbal cosmetics are natural and free from all the harmful synthetic chemicals which otherwise may prove to be toxic to the skin. Instead of traditional synthetic products different plant parts and plant extracts are used in these products, e.g. aloe-vera gel and coconut oil. They also consist of natural nutrients like Vitamin E that keeps skin healthy, glowing and beautiful. For example, Aloevera is a herbal plant species belonging to liliaceae family and is naturally and easily available. There are a rising number of consumers concerned about ingredients such as synthetic chemicals, mineral oils who demand more natural products with traceable and more natural ingredients, free from harmful chemicals and with an emphasis on the properties of botanicals . Safe to use Compared to other beauty products, natural cosmetics are safe to use. They are hypo-allergenic and tested and proven by dermatologists to be safe to use anytime, anywhere. Since they are made of natural ingredients, people don't have to worry about getting skin rashes or experience skin itchiness. Example - BHA (Butylated Hydroxyanisole) and BHT (Butylated Hydroxytoluene) are closely related synthetic antioxidants and are used as preservatives in lipsticks and moisturizers. BHA and BHT can induce allergic reactions in the skin. The international Agency for Research on Cancer classifies BHA asa possible human carcinogen. Herbal cosmetics contain natural antioxidants like vitamin C. Compatible with all skin types Natural cosmetics are suiTable for all

skin types. No matter if you are dark or fair, you will find natural cosmetics like foundation, eye shadow, and lipstick which are appropriate irrespective of your skin tone. Women with oily or sensitive skin can also use them and never have to worry about degrading their skin condition. Coal tar-derived colors are used extensively in cosmetics, Coal tar is recognized as a human carcinogen and the main concern with individual coal tar a color (whether produced from coal tar or synthetically) is they can cause cancer. But natural colors that are obtained from herbs are safer. Wide selection to choose from Natural cosmetics may still be a new type in the beauty industry but they already offer a variety of beauty products for all make up crazy people out there to choose from. One will find a variety of foundation, eye shadow, lipstick, blush, mascara, concealer and many more which are all naturally formulated. Furthermore, one will find locally made natural cosmetics or those made by famous designers worldwide. There exist a large variety of herbal extracts, to name a few *Andrographis Paniculata* (Kalmegh), *Asparagus Racemosus* (Shatawari), *Boswellia Serrata* (Salai Guggal), Asphalt (Shilajit) etc. Fits your budget Natural cosmetics are not that expensive. In fact, some of these products are more affordable than synthetic ones. They are offered at discounted prices and are sold for a cheap price during sales. Just need to survey enough to look for great deals. An estimate of WHO demonstrates about 80% of world population depends on natural products for their health care, because of side effects inflicted and rising cost of modern medicine. World Health Organization currently recommends and encourages traditional herbal cures in natural health care programs as these drugs are easily available at low cost and are comparatively safe. Not tested on animals Some cosmetics are initially tested on animals to ensure that they are safe and effective to use for human. However, natural cosmetics need not be tested on animals. These natural formulations are tested by experts in laboratories using state of the art equipment with no animals involved. No side effects The synthetic beauty products can irritate your skin, and cause pimples. They might block your pores and make your skin dry or oily. With natural cosmetics, one need not worry about these. The natural ingredients used assure no side effects; one can apply them anytime, anywhere. For example herbal cosmetics are free from parabens that are the most widely used preservative in cosmetics and can penetrate the skin.

14. Regulatory status of cosmeceuticals Cosmeceuticals - cosmetics or drugs?

The legal difference between a cosmetic and a drug is determined by a product's intended use. Under present concept, the boundary at which a cosmetic product becomes drug is not well-defined and different laws and regulations apply to each type of product. The drugs and cosmetic Act 1940 defines a drug and a cosmetic as; Drug-" All medicines for internal or external use of human beings or animals and all substances intended to be used for ; or in the diagnosis, treatment, mitigation or prevention of any disease or disorder in humans or animals".

Cosmetic-"Any article intended to be rubbed, poured, sprinkled or sprayed on or introduced into or applied to any part of the human body for cleansing, beautifying, promoting attractiveness or altering the appearance and includes any article intended for use as a component of cosmetic". Cosmetic and drug: Some products meet the definitions of both cosmetics and drugs. This may happen when a product has more than one intended uses. For example, a shampoo is a cosmetic because its intended use is to clean the hair. An antidandruff shampoo is a drug because its intended use is to treat dandruff. Among the cosmetic/drug combinations are toothpastes that contain fluoride, deodorants that are antiperspirants and moisturizers with sun-protection claims. The claims made about drugs are subject to detailed analysis by the Food and Drug Administration (FDA) review and approval process, but cosmetics are not subject to mandatory FDA review. Although there is no legal category called cosmeceuticals, the term has found application to designate the products at the borderline between cosmetics and pharmaceuticals. 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 efficiency of cosmeceuticals are valid unless the product has been approved by the FDA or equivalent agency. 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. Herbs Used in Cosmetics/Cosmeceuticals There are numerous herbs available naturally having different uses in cosmetic preparations for skincare, hair care and as antioxidants, fragrant etc. Some of the important examples are as follows: Skincare Coconut oil: It is produced by crushing copra, the dried kernel, which contains about 60-65% of the oil.

Coconut oil contains a high amount of glycerides of lower chain fatty acids. Coconut oil is derived from the fruit or seed of the coconut palm tree *Cocos nucifera*, family Arecaceae. The melting point of coconut oil is 24 to 25°C (75-76ºF) and thus can be used easily in liquid or solid forms and is often used in cooking and baking. Coconut oil is excellent as a skin moisturizer and softener.

Sunflower oil: It is the non-volatile oil extracted from sunflower seeds obtained from Helianthus annuus, family Asteraceae. Sunflower oil contains lecithin, tocopherols, carotenoids and waxes. It has smoothing properties and is considered non-comedogenic.

Jojoba oil: It is a mixture of long chain, linear liquid wax esters extracted from the seeds of the desert shrub simmondsia chinenesis, family simmondsiaceae. Jojoba oil is easily refined to remove any odor, color it is oxidatively stable, and is often used in cosmetics as a moisturizer and as carrier oil for exotic fragrances. Human sebum and jojoba oil are virtually identical. Sebum protects and moisturizes the skin and hair but is stripped away by chemicals, pollutants, sun and the aging process, resulting in dry skin and hair. Jojoba oil replenishes what skin and hair lose and restores them to their natural pH balance.

Olive oil: This oil is a fixed oil extracted from the fruits of olea europaea, family oleaceae. The major constituents are triolein, tripalmitin, trilinolein, tristearate, monosterate, triarachidin, squalene, β-sitosterol and tocopherol. It is used as skin and hair conditioner in cosmetics like lotions, shampoos etc. It is a potent fatty acid penetration enhancer

Aloe vera: Aloevera is a herbal plant species belonging to liliaceae family that is found only in cultivation, having no naturally occurring populations, although closely related aloes do have presence in northern Africa

15. Packing of cosmetics

Before going into various aspects of Packaging in general, let us understand uniqueness of Cosmetics packaging. The primary aim of packaging is the protection of the product from all hazards it can be exposed to during transport and handling. A cosmetic package, in addition, is also required to be attractive and unique in its features so to trigger “impulse buying” in the end user. Many a times we all have encountered this situation that instead of purchasing medicine from a chemist’s shop, we land in purchasing a Cosmetic that immediately drew our attention. The role of packaging for Cosmetics is not only the prime role of containing but also to enhance aesthetics. In fact it acts as a silent salesman, acting as an advertisement for the product it contains and influencing consumer’s purchasing choices. It is meant to seduce the consumer and transform products into objects of desire. Cosmetics packaging are attractive and eye-catching as they are extensively decorated. Cosmetic packaging contains everything from the logo of the cosmetic company to the ingredients that the cosmetic contains. It is what gives the consumer their initial opinion about the product. There are various reasons as to why the graphics on the packaging is important to the consumer. Packaging contributes to the overall feel and image of a brand; high quality packaging signals to consumers that the product inside is high quality. As in other industries, “cosmetics companies try not only to sell a brand to consumers but an image that is associated with certain characteristics or qualities. Even if the products themselves are relatively similar, the packaging can be what sets them apart. With cosmetics, there is a direct relationship between quality (or perceived quality) of packaging and the perceived price and quality of a product.

Package: A package is a manufactured article which partially or totally encloses a quantity of products.

Purpose of packaging: Products are packed in a suitable package for the following purpose:

1) To facilitate transportation and storage.
2) To guard against contamination.
3) To prevent accidental spoilage.
4) To prevent from pilferage.
5) To minimize spoilage.
6) To identify the products contained and the quality.
7) To proclaim the manufacturer of the product contained.
8) To explain how the product should be used.
9) To attract the shopper’s attention and
10) To convince the customers to buy.
11) To add convenience in distribution, handling, stacking, display, sale, opening, reclosing, use, dispensing, reuse, recycling, and ease of disposal.
12) To have portion control– Single serving or single dosage packaging has a precise amount of contents to control usage. e.g. Sachet

Package classification: Packages may be classified according to function, to a common property, to the materials they are made up of, or to their contents.

It is sometimes convenient to categorize packages by layer or function: "primary", "secondary", etc.

- Primary packaging is the material that first envelops the product and holds it. This usually is the smallest unit of distribution or use and is the package which is in direct contact with the contents.
- Secondary packaging is outside the primary packaging, perhaps used to group primary packages together.
- Tertiary packaging is used for bulk handling, warehouse storage and transport shipping. The most common form is a palletized unit load that packs tightly into containers.

Classification according to contents: Beverage packaging, Food packaging, Hardware packaging, Drugs and Cosmetics packaging.

Classification according to common property: Flexible, Semi-rigid or rigid packages; Breakable or Non-breakable packages; Transparent or Opaque packages; Liquid-Tight or gas tight packages.

Classification according to materials : Glass Bottles, Metal Cans, Paperboard Cartons, Wooden Crates, Paper Labels, Plastic Bottles, Laminated Tubes etc.

The packaging function: The package is merely a part of the system by which a product is Marketed and distributed. The packaging function is to bring together the product and its package in the desired way with the desired end result in the quantities needed in a given time. In most packaging operations the product is formulated first and then brought to the package. Each and every step in the packaging must be carefully controlled, if good final package performance is to be achieved. Improperly made packages will interfere with opening, filling or closing operations. It is important in the development of a package, that it not only perform the static duty of containing and protecting the product but also that it perform the dynamic duty of surviving and efficiently moving through the packaging operations. This must also include warehouse stacking and transportation.

The only way this performance can be assured is for the packaged product to be submitted to extensive testing both simulated abuse testing in the laboratory and actual performance tests in the plant, in the warehouse and in the transportation system.

Packaging materials: Glass has served Cosmetics industries as an efficient container for many centuries as glass is economical, can be handled at high speed on production lines, and is inert thus giving excellent product pack compatibility. It provides good product presentation (clarity, sparkle, design and shades) and good product identification. Glass is completely impermeable to all gases, solutions or solvents.

If a product is sensitive to light, amber glass or cartoning can be used. Glass can be moulded into very attractive designs and provides excellent brand or product image.

Glass is manufactured in many different formulations but the most common in packaging is soda lime glass. Soda lime glass contains Silica (from sand), Calcium Carbonate (Limestone), Sodium Carbonate (soda ash), Aluminium oxide and Trace oxides. It is trace oxide that provide colour to glass. The only disadvantage which glass has is that it is fragile and it has weight.

The technology of glass making is thousands of years old but it is only in recent years that fully automatic methods have been developed for manufacture of glass components. There is various glass moulding processes like. The suction process, Press and blow flow process or Blow and blow flow process.

Metals were first used as containers at least as early as 4000 B.C. and probably before that. Today steel, tinplate and aluminium are used for packaging. Metal containers are strong, relatively unbreakable, opaque and impervious to moisture-vapour, gases, odours, bacteria; provided they are pinhole free. They are resistant to both high and low temperature. However, metals require the application of coatings and lacquers to prevent chemical reaction and corrosion from the inside or outside. Special coatings and coating techniques have therefore been developed for this purpose. Metal containers are available in a variety of shapes, sizes and styles ranging from small elongated collapsible tubes and shallow drawn containers to large built-up containers including steel-drums. It is in the field of aerosols that metal containers have predominantly been used. Another area in which metal containers have found a specialised usage is for cosmetics items such as Lipstick cases. The use of collapsible aluminium tubes is extremely widespread and almost all varieties of semi-solid products, including emulsions, pastes and gel are marketed in collapsible tubes.

Plastics: The use of plastic for producing primary components and point-of-sale material now dominates packaging technology. There are two main groups that are used – Thermoplastic resin and thermosetting resin Thermoplastics Resins can be extruded at their melt temperature and then blow moulded or injection moulded. After cooling the resin can be remelted by heating to the limits of thermal fatigue and oxidation. Polyvinyl Chloride (PVC), Low density polyethylene (LDPE), High Density polyethylene (HDPE), Polypropylene and Polystyrene are thermoplastic. Thermosetting resin are moulded using an irreversible chemical reaction and the resins tend to be rigid, hard, insoluble and unaffected by heat up to decomposition temperature Generic term “amino plastics” is used for plastics produced by reacting formaldehyde with amino compounds. Their applications range from electrical equipment such as switch plates, sockets or circuit breakers, work surface laminates, etc. It is generally processed by compression moulding

Paper and Board: It is mainly used for Secondary and Tertiary packaging. Rigid and semi-rigid paper board packages e.g. Cartons, Box, Corrugated Shippers are widely used in cosmetics industries. Varieties of rigid plastic materials like plastic bottles, boxes, vials, trays, sleeves and closures are used for the packaging of cosmetics products.

Printing, foiling and decoration: All packaging components can be printed to give a wide range of decorative effects. Different processes are used depending on the application. It could be Screen printing, Letterpress, Flexography, Offset lithography or Gravure printing.

Package Development and Design: In the development of New Product, Packaging must be considered as early as possible to allow time to ensure that pack and product are compatible. The pack must be suitable for the product and

its market. The development process begins with a detailed analysis of the product so that a pack can be designed to give protection. Graphics and aesthetic design should also be considered at this stage.

Testing for product compatibility: Compatibility testing is performed when the final product formulation and packaging system has been decided. The general compatibility of the pack and product needs to be checked by storage testing which will enable as assessment to be made of the effect of the pack on the product as well as that of the product on the pack. The first step in selecting a package system for a given product is a compilation of the characteristics of the product itself. Package - product interaction can result either in a weakening of the package, a partial destruction of the product or both. These undesired results can occur from permeation, sorption, leaching, photochemical reaction or chemical reaction. Thus checking of behavior of product while in contact with package and vice versa must be done and studied to avoid any possible interaction. Effect of spillage on the outside of pack and Shelf life testing must also be done. Even convenience of the pack must also be tested by in-use tests as well as by laboratory tests and local customs and the climate of the country in which the product is to be marketed. That means one must ascertain all aspects that can affect product-pack interaction to ensure no problem in future.

Security Features in Cosmetics Packaging:

Product counterfeiting is an Intellectual Property (IP) crime, which is a deliberate attempt to deceive consumers by copying and marketing goods bearing well-known trademarks. Product counterfeits look like those made by a reputable manufacturer when they are, in fact, inferior illegal copies that can have a serious impact on the health and safety of the consumer. I myself have experience to have witnessed hundreds of counterfeit of brand leaders in the market. Preventing the counterfeiting of sensitive and vulnerable products is a big business globally and one in which packaging plays a crucial role on the front lines in thwarting crime that causes economic damage and risks the health--and potentially the lives--of consumers.

Following methods are adopted to prevent counterfeiting.

-Hologram
-Ultra-violet fluorescent ink
-Thermal reactive ink
-colour shifting ink
-RFID

The counterfeiting of cosmetics products, particularly at the higher-end and luxury segments of the market has continued to be a significant issue, especially for manufacture of prestige brands.

Let us update ourselves on what is New in Cosmetics Packaging

-Marc Jacobs Lipstick is designed in the shape of stylized pencil, made of sublime metallic materials.

-Airless compact for higher viscosity and high-coverage foundation formula is available with foam cushion and without.

-Foil pillow pouch is introduced by Unit Pack, which is foil unit pack having metering channel and an iris tip to control flow of dispensed liquid without it spilling all over. The high barrier foil ensures stability and prevents contamination. It also tears easily, allowing neat discharge of product.

Environment Friendly Packaging

Growing awareness about environmental crisis and eco-friendly options are fueling innovation in design, manufacture and material used for Packaging.

-Bamboo packaging is eco friendly and bio-degradable. Beauty products with a bamboo packaging are more attractive thus triggering impulse purchase.

-Paper from Stone: Limestone or calcium carbonate is the material being used by some companies to create TREE-FREE paper. Terra Skin, a paper made from limestone starts to degrade six to nine months after direct exposure to sunlight. Limestone for it is collected as waste material from construction industry.

-Bio-based Jars are made with a hybrid resin comprising of tapioca and potato blended with traditional petroleum based PP.

"Packaging plays a very important role as Packaging will ultimately make Cosmetics and Personal care products stand out from the crowd and seduce the consumer. Often the first impression of a product and its value are based on the quality of the design and manufacturing of pack components, so the pack can help contribute to the purchasing decision of consumer.

Science behind hi-tech skincare

Ingredients must not only be employed in the correct combinations, they have to be presented in a way that ensures they can penetrate the skin and get to where they are needed. According to Frauke Neuser, principal scientist at Olay, new technologies have taken the guesswork out of formulation.

"The future of ingredient identification lies in connectivity mapping," she says. "This means that, now we know which genes are expressed in healthy young skin and how ageing or disease affects that gene expression, we can look at the genetic profile of various ingredients and find one that does the opposite.

"So if, say, there are 1,000 genes involved and 300 are up-regulated, that is they work harder, while 700 are down-regulated and work less efficiently, using a bank of

ingredients whose genetic profiles we know, along with algorithms and data crunching, we can find an ingredient that will down-regulate those 300 and up-regulate the 700." And once an ingredient is identified, it has to be packaged in a way that the skin can use and sometimes this takes time. In the case of a molecule called LR2412, the key ingredient in Lancôme's Visionnaire, it took more than a decade, as L'Oréal UK's director of scientific affairs Katriona Methven explains.

Inspired by nature

In many ways LR2412 typifies the sort of ingredients that are increasingly at the forefront of cosmetic chemistry – derived from, or inspired by, nature and synthesised in such a way that they are highly effective in humans. Because, whatever the "nature's best" brigade might argue, the line between "natural" and "synthetic" is very fine.

Salicylic acid, long heralded as a gold standard in the treatment of acne, is originally derived from willow bark, while star anti-ageing ingredients, retinoids, are found in cod liver oil. The focus on ingredients reflects an increased consumer appetite for knowledge about the contents of their cosmetics. In 2011, Mintel's *Facial Skincare – UK* report showed only 7 per cent of consumers were interested in ingredients, while just a year later, that figure had increased by more than a quarter to 9 per cent. But a little knowledge can be a dangerous thing, as exemplified by the parabens story. Parabens, natural preservatives found in fruit such as raspberries, were demonised by a combination of scaremongering celebrities and a widely reported, yet potentially flawed, piece of research linking them with breast cancer. Rather than educating consumers about the science, most manufacturers bowed to public pressure and started going "paraben free". But as Sam Farmer, whose range of toiletries for young people does include parabens, explains this caused problems of its own.

"When companies moved away from parabens, they needed another inexpensive and effective preservative. Methylisothiazolinone (MI) had long been used in shampoos and other wash-off products, but formulators knew it was not advisable to use it in leave-on products, such as moisturisers and sun cream. However, in the rush to replace parabens, this seems to have been forgotten," he says. The result is consumers buying paraben-free products are leaving MI on their skin and getting sensitivity reactions, so they can no longer use any products that contain MI. But new technologies should make such problems a thing of the past. Computer modelling is so sophisticated it can show not only how safe and effective a product might be, but also if the active ingredient will penetrate to where it needs to get. This means it will take less time to develop molecules like LR2412. And, according to Dr Neuser, future wonder ingredients could replicate natural mechanisms, such as hormones, but with modifications to avoid the accompanying systemic effects. "We know what the gold standard is in existing ingredients," she says. "Now it's about finding something just as good, but without side effects."

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