DEPARTMENT OF PHYSICS AND NANOTECHNOLOGY
SRM INSTITUTE OF SCIENCE AND TECHNOLOGY

Nanocosmetics

- The applications of nanotechnology and nanomaterials can be found in many cosmetic products including moisturisers, hair care products, make up and sunscreen.

- Almost all the major cosmetic manufacturers use nanomaterials in their products. L'Oréal has a number of nanotechnology-related products in the market and ranks 6th in US in the number of nanotech related patents in US.

- The European Commission estimated in 2006, that 5 % of cosmetic products contained nanoparticles.

- The application of nanomaterials in cosmetic products has been the subject of continuous discussion in the media, scientific circles and among policy makers for the past few years.

- Toxicity issues have been raised due to conflicting research papers about the safety of nanomaterials and lack of agreement between researchers on whether the nanomaterials are safe for dermal use.

- There are a number of classes of nanoparticles used, or proposed for use, in cosmetic applications.

- In cosmetics there are currently two main uses for nanotechnology. The first of these is the use of nanoparticles as UV filters. Titanium dioxide (TiO2) and zinc oxide (ZnO) are the main compounds used in these applications. Organic alternatives to these have also been developed.

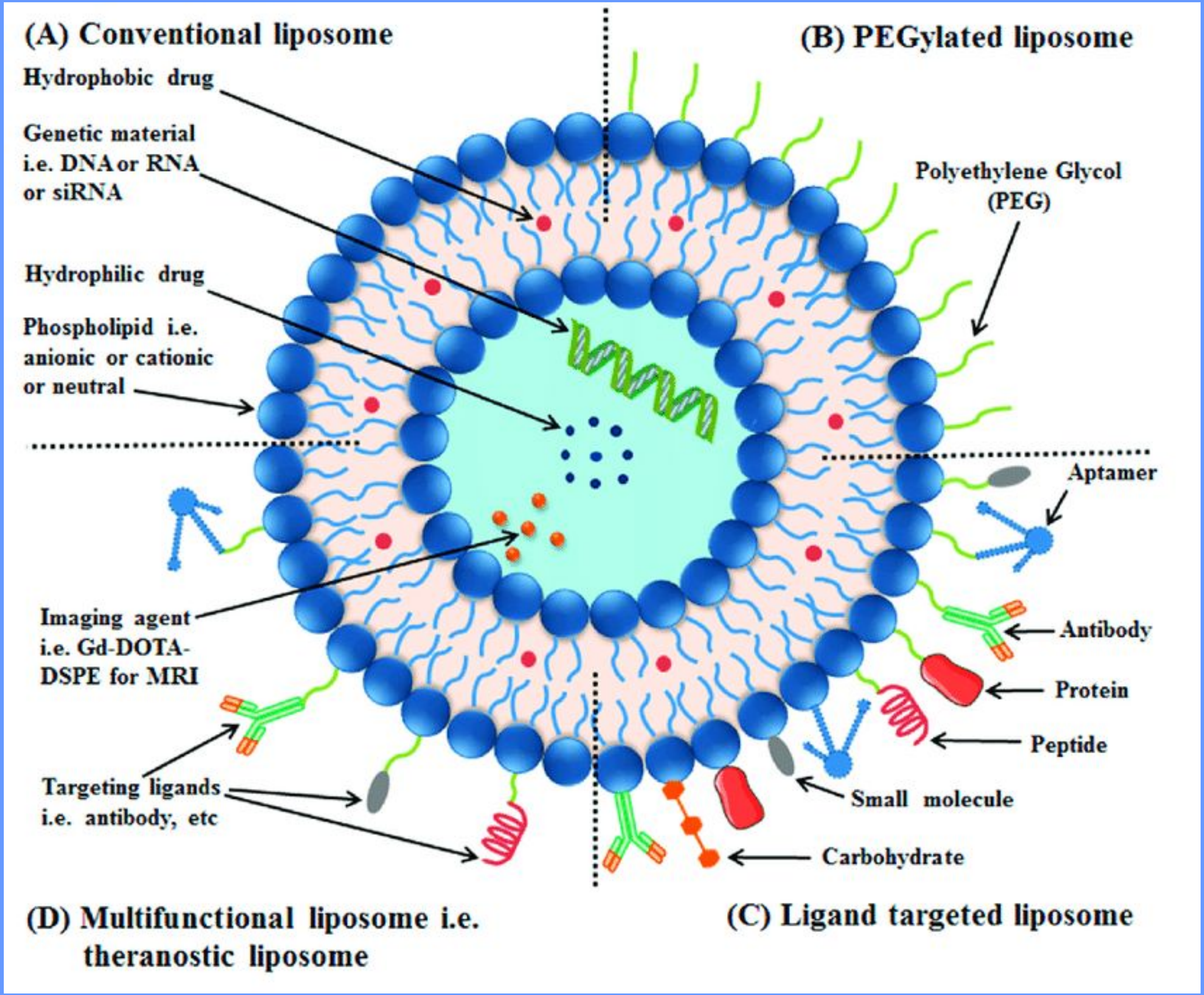
- The second use is nanotechnology for delivery. Liposomes and niosomes are used in the cosmetic industry as delivery vehicles. Newer structures such as solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) have been found to be better performers than liposomes.

- In particular, NLCs have been identified as a potential next generation cosmetic delivery agent that can provide enhanced skin hydration, bioavailability, stability of the agent and controlled occlusion.

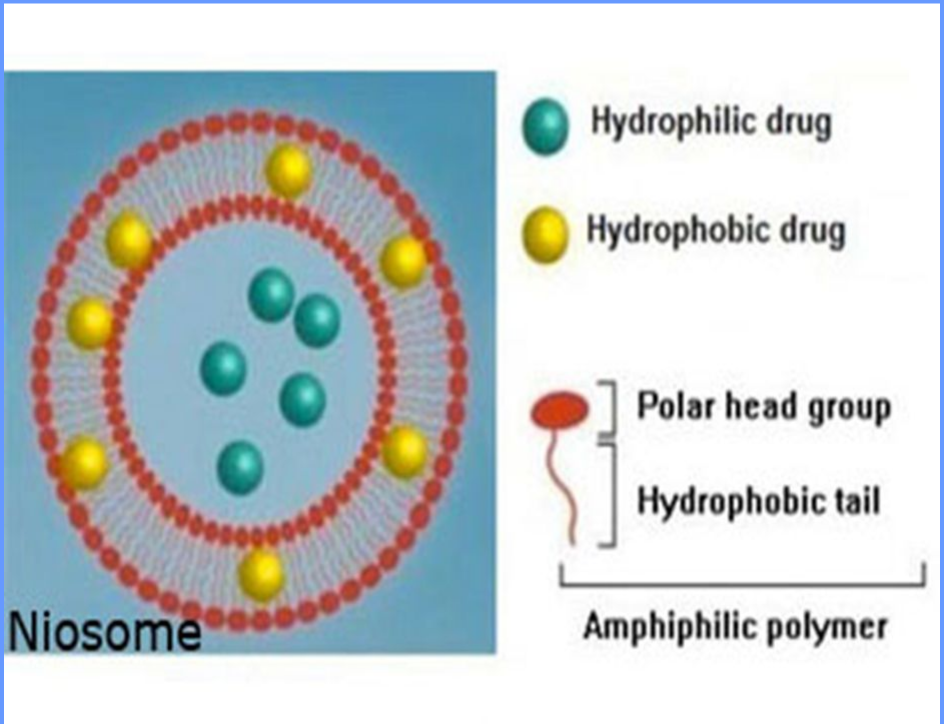
- Encapsulation techniques have been proposed for carrying cosmetic actives.

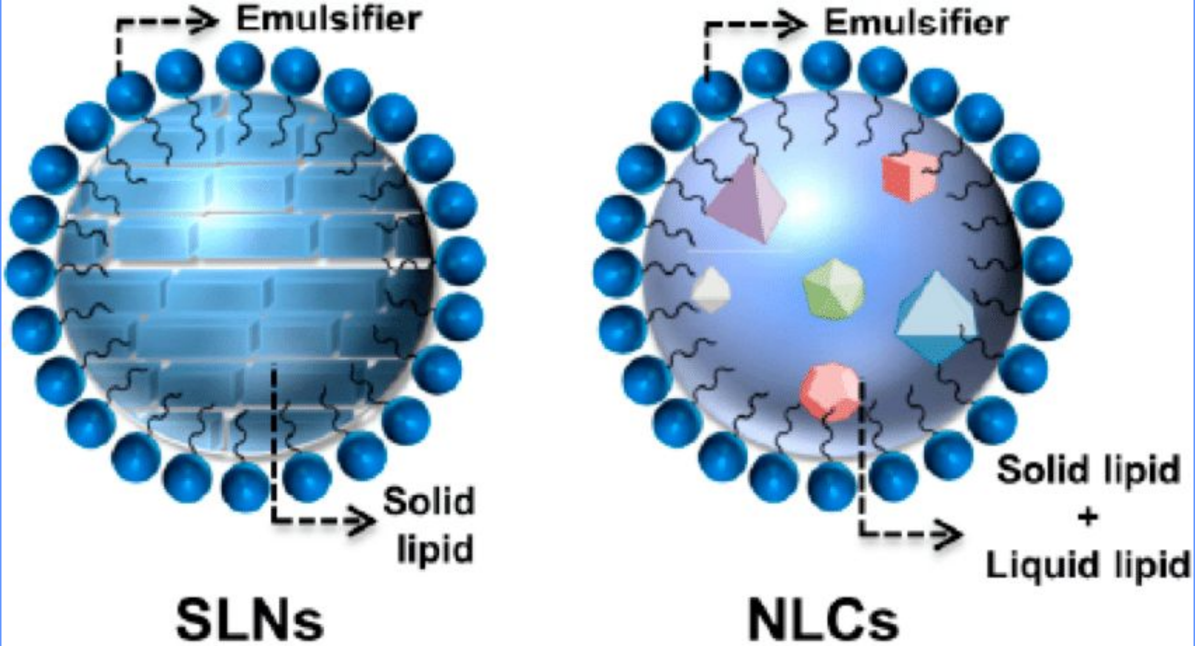
- Nanocrystals and nanoemulsions are also being investigated for cosmetic applications.

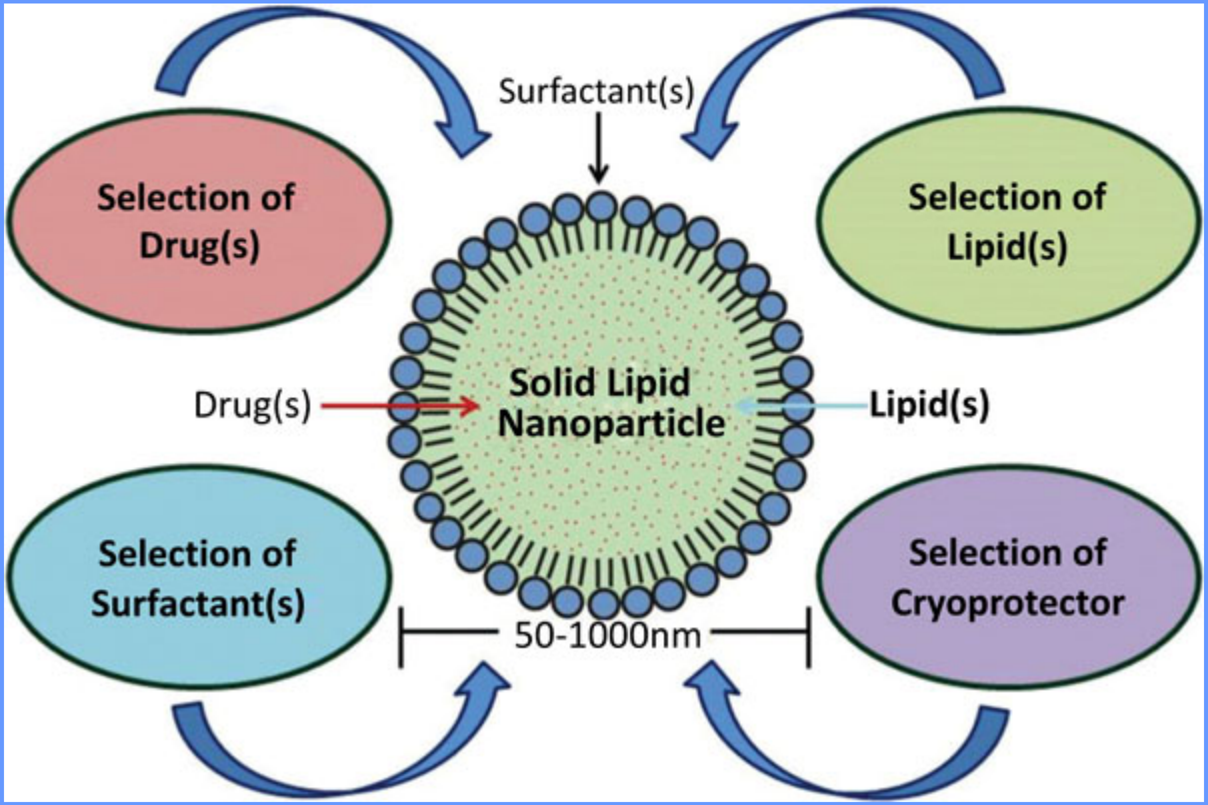
- Patents have been filed for the application of dendrimers in the cosmetics industry.
- Other novel materials, such as fullerene, have also appeared in a small number of beauty products.



(A) Conventional liposome
Hydrophobic drug
Genetic material
i.e. DNA or RNA
or siRNA
Hydrophilic drug
Phospholipid i.e.
anionic or cationic
or neutral
(B) PEGylated liposome
Polyethylene Glycol
(PEG)
Aptamer
Antibody
Protein
Peptide
Small molecule
Carbohydrate
Imaging agent
i.e. Gd-DOTA-
DSPE for MRI
Targeting ligands
i.e. antibody, etc
(D) Multifunctional liposome i.e.
theranostic liposome
(C) Ligand targeted liposome


Hydrophilic drug
Hydrophobic drug
Polar head group
Hydrophobic tail
Amphiphilic polymer
Niosome


Emulsifier
Solid lipid
SLNs
Emulsifier
Solid lipid
+
Liquid lipid
NLCs


Surfactant(s)
Selection of Drug(s)
Selection of Lipid(s)
Drug(s)
Solid Lipid Nanoparticle
Lipid(s)
Selection of Surfactant(s)
Selection of Cryoprotector
50-1000nm

The loading of active pharmaceutical ingredients (APIs) within nano-sized drug delivery systems is being currently exploited to promote product innovation by developing nanoproducts.

Nanoproducts used for the delivery of APIs to the skin (e.g., nanopharmaceuticals, nanocosmeceuticals) have already proven their efficacy as several products are already available on the market for the treatment of skin injuries (e.g., atopic dermatitis, skin cancer, skin burns, wound healing, and protection from ultraviolet (UV) radiations.

A successful example is the formulation of sunscreens into nanoproducts. This approach was found to decrease the adverse side-effects of UV inorganic filters (e.g., titanium dioxide (TiO_2), zinc oxide (ZnO)) and of chemical filters (benzophenone-3), improving the safety to consumers.

Besides, it has also been demonstrated that the loading of sunscreen into solid nanoparticles can offer a synergistic effect, as nanoparticles can themselves have a sun-blocking effect.

In the past years, dierent types of nanoparticles have been proposed to load sunscreens, antioxidants and vitamins for skin care formulations.

The first cosmetic products manufactured using nanotechnology were the liposomes-containing moisturizing creams, launched 40 years ago.

Since then, several other types of biocompatible nanomaterials have been proposed, being nanoemulsions, solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC) of special interest due to their lipid composition.

Besides, lipid nanoparticles also improve skin hydration because of the formation of a thin lipidic film onto the surface of the skin, retaining its moisture for longer time

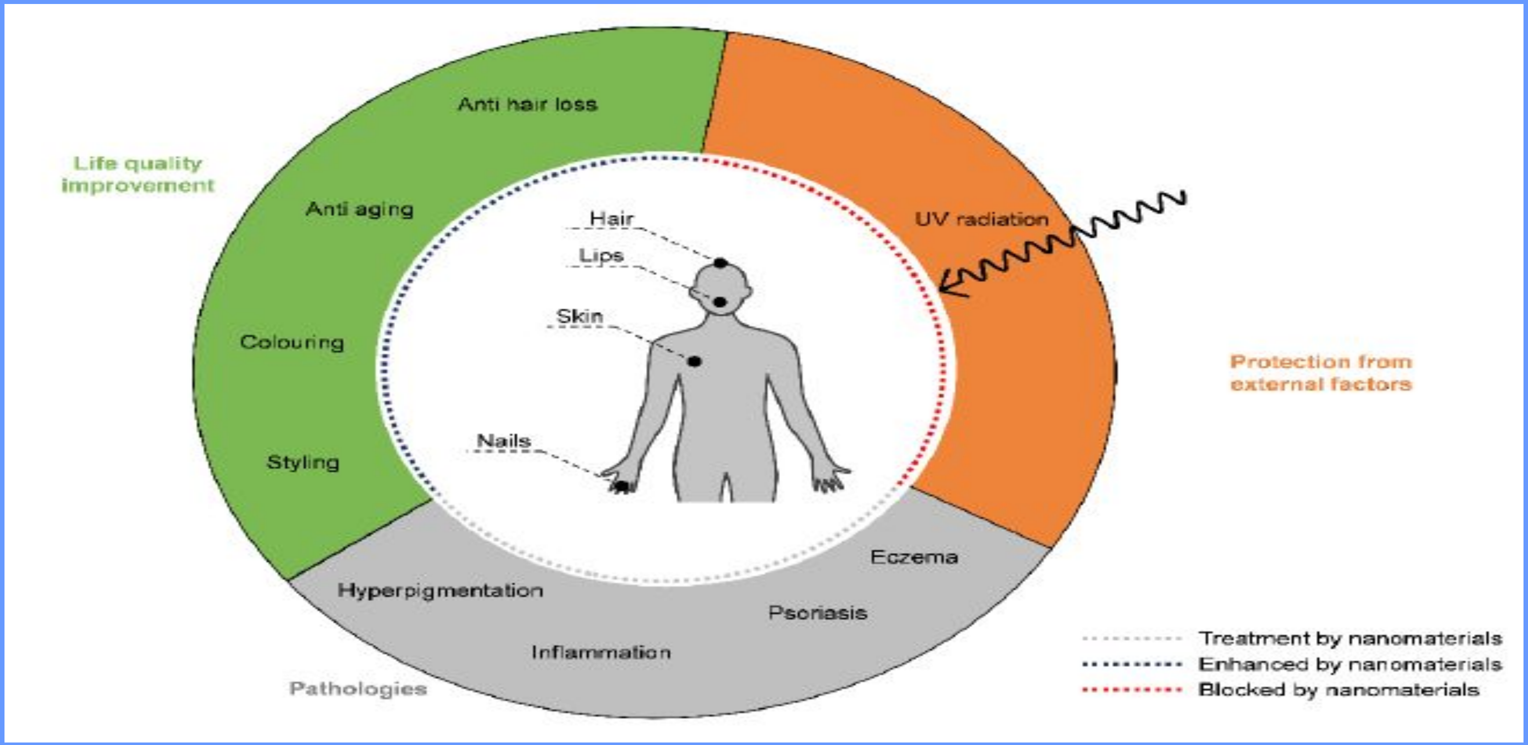
Over the course of the 20th century, cosmetics raised their popularity as daily products with a substantial marketed increase.

Various cosmeceutical formulations for skin, body, and hair applications are being proposed for the treatment of a range of problems, such as hair damage and/or loss, wrinkles, hyperpigmentation, and photo-aging.

The main advantages of nanocosmeceuticals include the controlled release of APIs site-specific targeting, occlusive properties with enhanced hydration, which contribute to increase skin permeation to the API

Cosmeceuticals are used for a variety of applications, e.g., to improve skin texture by stimulating collagen growth, as anti-aging formulations as their antioxidants neutralize reactive oxygen species and protect the structure of keratin, which results in a healthier skin.

Marketed antiaging nanocosmeceuticals as hair care products (e.g., shampoos, conditioners, hair growth stimulants, coloring and styling products) may be composed of nanotubes, poly(lactic-co-glycolic acid (PLGA) nanospheres, fullerenes, gold nanoparticles, niosomes, microemulsions, nanoemulsions, liposomes, with the purpose of sealing the moisture around the cuticles and optimizing the contact time with the scalp and the follicles, by forming a protective film



Types of Nanomaterials Used in Cosmetic Formulations

Due to its large surface area, the skin is an interesting administration route for several APIs.

The advantages of topical drug delivery include the possibility to overcome the risk associated with the parenteral administration (e.g., pain, infection), avoidance of first pass metabolism associated with the oral administration of drugs, possibility to extend the treatment for longer timeframe which allows the use of drugs with small biological half-lives, and consequently reduce the gastrointestinal irritation promoted by the systemic administration.

The major challenge encountered in the delivery of APIs through the skin is to overcome the different physiological layers of distinct polarity.

Skin is known to protect the body from xenobiotics, which can be not only toxic agents and pathogens, but also drugs while ensuring the expulsion of physiological fluids for homeostasis.

Nanoemulsions

They are defined as oil droplets stabilized by a combination of surfactant and co-surfactant in aqueous dispersion, preserving both the lightness and transparency.

Nanoemulsions are a common delivery system for the control release of nutraceuticals and APIs into deeper skin layers.

Their lipophilic core makes nanoemulsions appropriate for the delivery of lipophilic compounds.

Another advantage is their small droplet size (<200 nm), which provides a large surface area in contact with the skin.

Nanoemulsions contribute also for the reduction of transepidermal water loss (TEWL) keeping the skin hydrated and thus more permeable to APIs.

Among the most popular cosmetic formulations used in e.g., sun care products, anti-aging or in moisturizing creams, are the nanogels obtained from concentrated o/w nanoemulsions which generate a continuous network, useful to form a film onto the skin, avoiding TEWL, and increasing skin permeation to APIs.

Several other marketed products (foams, creams, sprays, and liquids) are obtained from nanoemulsions e.g., deodorants, sunscreens, shampoos, lotions, nail polishers, conditioners, and hair care.

Liposomes

Liposomes are concentric phospholipid bilayers enclosing an aqueous core, making them suitable to load hydrophilic, lipophilic, and amphiphilic compounds.

Their use has been described for a set of administration routes, among which the topical delivery of APIs has been successfully exploited.

Their lipid composition makes liposomes biocompatible and biodegradable, with low risk of toxicity acting as penetration enhancers for the delivery of APIs into deeper skin layers (e.g., dermis).

The risk of undergoing oxidation and/or hydrolysis, or even suering drug leakage, are pointed out as the main disadvantages of liposomes.

The main component of liposomes is phosphatidyl choline, but several other lipids (e.g., glycerophospholipids, glycerolipids, phingophospholipids, ceramides, and cholesterol) can also be included in their composition.

Cholesterol is commonly used to increase the rigidity of the vesicles and their encapsulation eciency. Other compounds, e.g., tetracationic gemini Dabco-surfactants, have also been proposed for transdermal drug delivery.

As happens with lipid nanoparticles, when liposomes are applied onto the skin, a thin lipid film is formed which can offer occlusive properties while avoiding water evaporation from the skin, keeping it moist and permeable to APIs.

Liposomes have been produced with lipids from stratum corneum for the treatment of atopic dry skin. Several anti-oxidants (e.g., superoxide dismutase, catalase, glutathione, N-acetylcysteine, Coenzyme Q10, curcumin, resveratrol, tocopherols, retinoids, ascorbic acid, carotenoids) have been formulated in liposomes for anti-aging.

The antioxidants are also used to increase the physical and chemical stability of the vesicles when dispersed in water. In addition, the antioxidant agents in their composition improve the stability of formulation also prevent the action of free radicals, pollution and oxidative stress, and improves skin health.

The liposomal anti-aging and antioxidant creams reduce the water loss of the skin, which reduces wrinkles and lines of expression, restoring the normal balance of the skin. Another clinical study has shown that flexible liposomes help in wrinkle reduction, have decreased the efforescence in the treatment of acne and increase skin smoothness

Liposomes have been formulated with chemical (benzophenone-3,octyl methoxy cinnamate [87]) and physical (ZnO and TiO2 [88]) sunscreens to oer UV protection in cosmetic formulations. Liposomes are reported for the delivery of vitamins, mainly in anti-aging creams, moisturizing cream, sunscreens, and for the treatment of hair loss.

Natural marine lipid-containing polyunsaturated fatty acids have anti-inflammatory properties, which is beneficial in inflammatory skin disorders, and promote the hydration and softening of the skin.

The combination of plant extracts, and/or isolated natural compounds, with liposomes created a new class of healthcare products, becoming commonly used in the production of sunscreen formulations, anti-aging and moisturizing products, as they have antioxidant, anti-cellulite, and antimicrobial effects .

Sunscreens with zinc oxide and titanium dioxide in their composition are the most eective in skin protection, originating less greasy products, with less smell and transparent aspect.

Given that SLN, nanoemulsions, liposomes, and niosomes have the ability to keep the skin hydrated, due to the formation of a film of humectants that retain moisture for a longer period, they are widely used in moisturizing formulations.

In the case of anti-aging cosmetics, the main products that are available consist in the use of nanocapsules, liposomes, nanosomes, and nanospheres for the loading of skin cosmeceuticals.

Nanoformulations used in shampoos retain the moist within he cuticles increasing the contact time with scalp and hair follicles due to a formation of a protective film.

Conditioning nanocosmetic agents were created to increase the softness, shine, silkiness, gloss, and disentangling of hair.

The newest developments in hair care use niosomes, microemulsion, nanoemulsion, nanospheres, and liposomes, aiming the repair of damaged cuticles, restoration of hair texture and gloss, and to keep the hair shinier, less greasy, and less brittle.

The aging processes occur intrinsically at dierent rates and dier among individuals. It depends on genetic regulation, metabolism, lifestyle, and the formation of toxic products as part of metabolism processes.

The major factors that influence the aging process are basically split into:

(i)the biological factors, that are intrinsically determined by the genetic and are unchangeable and by metabolism;

(ii)the environmental factors, that depend on lifestyle (e.g., time of exposure to the sunlight; nicotine habits, etc.); the environment pollution;

(iii) the mechanical aging, which is the response to the muscle movements;

(iv) miscellaneous factors, such as diet, sleeping habits, mental health, and so on.

Aging is a process that starts with a decrease of cell renewal together with alterations in external matrix protein integrity.

Therefore, as intrinsic aging progresses, a decrease in subdermal fat tissues is promoted together with elastolysis and modest changes in collagen organization, which leads to the loss of support, causing sagging of the skin.

On the other hand, extrinsic aging occurs due to environmental factors, stress episodes and the use of products that compromise skin integrity.

Environmental factors are essentially climate conditions, e.g., sun exposure, air pollution, the nicotine habits, and so on.

By promoting the formation of free radicals, UV radiation is deleterious to collagenous tissues and also to elastin.

The decrease of cell turnover, of water content, the hyperpigmentation and the occurrence of wrinkles are signals of skin aging.

As strategies against photo-damage cascade episodes, the most common actions block UV-radiation penetration using sunscreens, both physical or chemical, decreasing and/or preventing inflammation by using anti-inflammatory products and promoting the removal of reactive oxygen species using antioxidants.

Ultraviolet radiation and its effects on human skin

There are three main categories of ultraviolet radiation including UVA, UVB, and UVC radiation. UVC radiation (100–280 nm)1 will not be emphasized as this form of radiation does not generally reach the earth's surface to a significant degree.

The earth's atmosphere blocks most UVC rays, and therefore, they are not thought to be important contributors to the biological effects on human skin.

UVB radiation (280–315 nm), has been implicated in three major adverse effects in human beings: sunburn (inflammation of the skin), skin cancer, and immunosuppression.

However, it should be noted that UVB does play a beneficial role in human health and wellness as it is important in the conversion of vitamin D in the skin to useable forms for human metabolism.

UVA radiation (315– 400 nm) was previously regarded as having insignificant carcinogenic potential and mainly implicated as a cause of aging and wrinkling.

However, recent evidence has suggested that it too has an important role in carcinogenesis and immunosuppression. Although, the major source of human exposure to UVA is still natural sunlight, tanning beds have had an increasing role in UVA exposure during recent year

The molecular effects of UV radiation on human skin can be broadly separated into shortterm (acute) effects, and long-term, continuous effects.

When the skin is acutely exposed to UV radiation, DNA damage in the form of pyrimidine dimers occur.

Furthermore, when individual cells recognize that too much damage has ensued and normal DNA repair processes will not suffice, cells engage in active, purposeful cell death to prevent the cell from multiplying and propagating mutagenic DNA which would lead clinically to cancer.

On a physical level, acute UV radiation exposure can lead to two main changes: sunburn and tanning.
Sunburn describes the phenomenon thickening of the outer skin layer (stratum corneum) and swelling in the layers of the skin containing blood vessels.

This clinically appears as swollen, red skin that is painful to the touch. In addition to sunburn, tanning is a known side effect of UV radiation exposure as the cells in the skin responsible for pigment production (melanocytes) are stimulated to produce more pigment for unclear physiological reasons.

Long-term effects of sunlight exposure include both photoaging and increased risk of skin cancer including both non-melanoma type as well as melanoma.

Photoaging results from thickening of outer skin layers and breakdown in the support structure proteins of the skin, mainly collagen and elastin.

The clinical manifestations of photoaging include freckles, dryness, hyperpigmentation, wrinkling, and dilated blood vessels.

Efficacy of titanium dioxide sunscreens

The efficacy of sunscreens is determined by the ability to protect against both UVB radiation and UVA radiation. As discussed in previous paragraphs, titanium dioxide sunscreens are effective broad-spectrum agents, meaning that they are capable of protection against both types of radiation.

A sunscreen's efficacy in protecting against UVB radiation is assessed based on two values: the sun protection factor (otherwise known as SPF) and substantivity.

The SPF is calculated as a ratio of the amount of ultraviolet radiation needed to cause sunburn when the skin is protected with a certain sunscreen to the amount of ultraviolet radiation needed to cause sunburn when the skin is left unprotected.

Therefore, if a product is SPF 30, then 30 times the UV radiation is needed to cause sunburn if the patient is wearing the sunscreen with that SPF value.

Generally, in order to be considered broad spectrum, a sunscreen must be at least SPF 30 or greater.