

FUTURE PROSPECT OF NANOTECHNOLOGY IN DEVELOPMENT OF ANTI-AGEING FORMULATIONS

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ABSTRACT

Consumers are nowadays more focussed on their health and appearance. As a result, there has been an increasing demand in topical antiageing formulations with natural and nutraceutical ingredients. Novel and innovative delivery systems are transforming the new product development in the cosmetic field because of consumer perceivable benefits and optimized sensory attributes. The applications of novel drug delivery systems can be found in many cosmetic products. Nanomaterials are nowadays used in almost all the major cosmetic industries. Nanotechnology has been used in novel cosmetic delivery systems to deliver the actives through various delivery vehicles. This review summarizes the use of nanomaterials in antiageing formulations for effective delivery of cosmeceutical ingredients.

Keywords: Novel delivery system, Antiageing creams, Cosmeceuticals, Skin care.

INTRODUCTION

With the advent of retirement age, there has been an increased interest in antiageing preparations, or cosmeceuticals, and their purported ability to enhance a person's more youthful appearance. Antiageing topicals, with their multiple claims, seemingly limitless key active ingredients, and complex formulations are leading the way in this huge growth industry of cosmeceuticals, especially as this segment of the population opts for less invasive, non-surgical alternatives to slow the effects of ageing on the skin.

Global Anti-Ageing Products Market to Reach \$291.9 Billion by 2015, According to New Report by Global Industry Analysts¹.

Skin is a feature that may make all the difference in how old an individual looks. If skin is leathery or wrinkly, it can make you look a decade older than you really are. By the same token, smooth and supple skin can take years off your appearance right away. It is for this reason that it's important to look after your skin. For some, it'd be too late to take preventative measures, but anti ageing skincare can work wonders in reversing the years.

ANTI-AGEING CREAMS

They are predominantly moisturiser based cosmeceutical skin care products marketed with the promise of making the consumer look younger by reducing visible wrinkles, expression lines, blemishes, pigmentation changes, discolorations and other environmentally (especially from the sun) related conditions of the skin. A comprehensive grading scale for anti-ageing of the skin has been validated and categorizes skin ageing as: laxity (sagging), rhytids (wrinkles), and the various categories of photo ageing, including erythema (redness), dyspigmentation (brown discolorations), solar elastosis (yellowing), keratoses (abnormal growths), and poor texture².

SOME COMMON TYPES OF COSMECEUTICAL INGREDIENTS

1. Hydroxy acids
2. Antioxidants
3. Botanicals
4. Depigmenting agents
5. Exfoliants
6. Moisturisers
7. Topical peptides
8. Retinoids
9. Sunscreens
10. Hyaluronic acid
11. Ceramides

1. HYDROXY ACIDS (HAs)

Hydroxy acids are organic carboxylic acids classified into alpha hydroxy acids (AHAs) and beta hydroxy acids (BHAs) according to their molecular structure. They are found in mass-marketed cosmetic formulations and are likely the second most available cosmeceutical.

AHAs are derived from natural sources and are often referred to as fruit acids.

The different AHAs include:

1: Citric acid 2: Malic acid 3: Glycolic acid 4: Lactic acid 5: Pyruvic acid 6: Tartaric acid

7: Lactobionic acid, a newer AHA, may have advantages over the others³.

AHAs improve skin texture and have shown to reduce the signs of ageing by promoting cell shedding in the outer layers of the epidermis and by restoring hydration. The mechanism of action is not completely understood. One hypothesis suggests that AHAs reduce the calcium ion concentration in the epidermis. The resulting reduction of the calcium ion levels tends to promote cell growth and slow cell differentiation, thus giving rise to younger looking skin⁴.

BHAs are aromatic compounds. The term beta hydroxy acid refers specifically to salicylic acid, which is used in some "anti-ageing" creams and acne treatments⁵.

2. ANTIOXIDANTS

Antioxidants neutralize free radicals — unstable oxygen molecules that break down skin cells and cause wrinkles, thus preventing impairment at the cellular level. They inhibit inflammation leading to collagen depletion and offer protection against photo damage and skin cancer⁶.

Common antioxidants include

- 1) Alpha-lipoic acid (ALA)⁷,
- 2) L-ascorbic acid (vitamin C)⁸, Niacinamide (vitamin B3)⁹,
- 3) N-acetyl glucosamine (NAG)¹⁰, α -Tocopherol¹¹, and Ubiquinone (CoQ10)¹².

3. BOTANICALS

The largest category of cosmeceutical additives found in the market today is "Botanicals". Their therapeutic properties remain mostly unexplored. Some botanicals that may benefit the skin include: green tea extract, grape seed extract and ferulic acid¹³.

4. DEPIGMENTING AGENTS

They are skin-lightening agents and offer corrective camouflage formulations. Their addition to the cosmetic formulations has become increasingly popular. Common depigmenting ingredients include hydroquinone, ascorbic acid (vitamin C), kojic acid, and liquorice extract (glabridin)¹⁴.

5. EXFOLIANTS

Exfoliants promote skin turnover by removing adherent cells in the stratum corneum. Salicylic acid (SA), lactic acid, and glycolic acid are few exfoliants found in cosmeceutical preparations. There have been concerns that repetitive use of SA and AHAs can make the dermis and epidermis more susceptible to penetration by UV rays. Therefore, consumers should be advised to use adequate sun protection¹⁵.

6. MOISTURISERS

Moisturisers comprise a vital therapeutic component in the management of various skin conditions (e.g., eczema, psoriasis, pruritus, and aged skin)¹⁶. In old age, dryness of skin is observed. To prevent this dryness, moisturizers are used. Water is the only material that would plasticize the outer dead layers of the epidermis, to give the much desired attribute called soft, smooth skin. If water is lost more rapidly from stratum corneum than it is received from lower layers of the epidermis, the skin becomes dehydrated and loses its flexibility. Dryness of aged skin is mainly due to UV exposure. There are three approaches to restore water content of skin i.e.: Occlusive, Humectants and Restoration of deficient materials^{17, 18, 19}.

7. TOPICAL PEPTIDES

Peptides are widely used in anti-wrinkle creams and claims to reduce fine lines and wrinkles and result in overall improved appearance of photo aged skin. Peptides include-Argireline (acetyl hexapeptide-3), Matryxil and Copper Peptides.

Argireline™ is touted as the new, safe and non-invasive alternative to Botox™ injections. Like Botox™, it is said to relax facial muscles thus reducing fine lines and wrinkles by inhibiting the nerve/muscle connection.

Matrixyl is a patented ingredient in Revitol, and it contains palmitoyl pentapeptide-3. Indeed, the results of early research on its stunning effects on wrinkled skin caused a stir at the 20th World Congress of Dermatology in Paris (Matrixyl 1999™). A six-month study revealed that it temporarily produced a significant reduction in deep and moderate wrinkles²⁰.

Copper peptides: Copper is a trace element found in every cell. In products applied to the skin, it's combined with small protein fragments called peptides. Copper peptides enhance wound healing. They also stimulate production of collagen and may enhance the action of antioxidants²¹.

8. RETINOIDS

Retinoids are amongst one of the essential ingredients found in cosmeceuticals. They are the most explored ingredients with sufficient data supporting them. They comprise of natural and synthetic derivatives of vitamin A that reduce hyper pigmentation and causes inhibition of enzymes from breaking down collagen. The beneficiary cosmeceutical claims of retinoids are mostly based on data obtained from studies on tretinoin and other classes of retinoid drugs. Some key retinoids include retinoic acid (tretinoin), retinol, and retinaldehyde²².

9. SUNSCREENS

They provide protection to skin against sun rays, which is the most important damaging environmental agent. Sunscreens include UVA and UVB blocking agents that inhibit photo ageing²³. Labelling changes proposed by the US FDA on sunscreen products are forthcoming²⁴. A high level of UVA protection is recommended as UVA radiation is associated with ageing effects such as wrinkles; thus sunscreen is a vital component of antiageing formulation²⁵.

10. HYALURONIC ACID

Hyaluronic acid, otherwise known as hyaluronan is a major component of skin, where it is involved in tissue repair. It is also important in maintaining skin firmness and structure. Photo damaged skin produces less hyaluronan, and contributes to hyaluronan deficiency, thus resulting in wrinkles. Topical application of hyaluronan has helped in maintaining healthy collagen levels and moisturises the skin²⁶.

11. CERAMIDES

Ceramide is a natural component of the human skin that is critical to the skin's good health and youthful appearance. As we grow old, skin begins to experience a natural loss of ceramide, making it more vulnerable to the signs of ageing. Ceramide-C incorporated into the antiageing formulation reduces the appearance of fine lines and wrinkles by restoring the skin's natural ceramide.

Ceramide has been added in extensive products to fight all the effects of ageing by sloughing off old skin cells making skin look fresher, more vibrant, and glowing²⁷.

VESICULAR SYSTEMS

Following are the promising vesicle delivery systems in cosmetics:

1. Liposomes
2. Silicone vesicles and matrices
3. Multi-walled delivery systems

LIPOSOMES

Liposomes are the most widely known cosmetic delivery systems. These are artificial spherical submicroscopic vesicles with diameter between 25 and 5000 nm. Vesicles are composed inevitably of amphiphilic molecules. Liposomes that have vesicles in the range of nanometres are also called nanoliposomes^{28, 29}.

Liposomes are used in a variety of skin care rejuvenation products because of their ability to encapsulate active anti-ageing ingredients and deliver them deep into the cells. Liposome acts as an efficient delivery system. When a gel or cream with liposomes is applied to the skin it is quickly absorbed and penetrates into the deep layers of the skin merging with the cell membranes and deposits the active ingredients into the cell membranes. The effects of liposomes benefit the skin in several ways, one of which is delaying the beginning signs of ageing. In addition to delaying the appearance of wrinkles and skin ageing, liposomes provide other unique qualities and benefits to the skin. A special characteristic of liposomes is the ability to adapt to water soluble and non water soluble ingredients within a product such as a cosmetic cream or gel without the use of a surfactant (an active ingredient in soap) or an emulsifier (a substance added to oil to help the oil mix with water). Not having to add these ingredients make the cosmetic product safer for the skin. Other Effects-Liposomes also improve skin hydration making the texture of the skin softer and smoother. Liposomes prevent oxidation (the combination of a substance with oxygen, an example is the rusting of iron due to oxygen).

It's non toxic, biodegradable and absorbs quickly into the skin which means other skin products may be applied soon after its application. Liposomes are nano-sized particles with a high affinity to the skin and they are highly absorbent. Liposomes are usually combined with several other anti-ageing ingredients into to one product^{30, 31}.

Dior launched the first liposome containing antiageing cream 'Capture' which combats cell ageing and helps reducing the signs of ageing³².

Marinosomes® are liposomes based on a natural marine lipid extract containing a high polyunsaturated fatty acid ratio. The characterisation studies showed Marinosomes® as promising candidates for topical application in view of the prevention and treatment of skin diseases³³.



Fig. 1: Capture Anti Ageing Cream

NIOSOMES

Niosomes are non-ionic surfactant based vesicles that have a similar structure to that of phospholipid vesicles like liposomes. They can be used to encapsulate aqueous solutes and act as drug and cosmetic carriers. They are formed by the self-assembly of non-ionic surfactants in aqueous media. The application of heat or physical agitation helps niosomes to attain a closed bilayer structure³⁴. The hydrophobic parts are shielded from the aqueous solvent while the hydrophilic head groups are in contact with it. They have been used for the delivery of anti-inflammatory agents³⁵ and anti-infective agents³⁶. They have also been used to enhance transdermal drug delivery. Niosomes were developed and patented by L'Oreal (www.loreal.com) in the 1970s and 80s^{37,38}.

The first product 'Niosome' was introduced in 1987 by Lancôme (www.lancome.com; a L'Oreal company). The advantages of using niosomes in cosmetic and skin care applications include their ability to increase the stability of entrapped drugs, improved bioavailability of poorly absorbed ingredients and enhanced skin penetration. Example of antiageing cream containing niosome is Niosome Day time skin treatment by Lancôme³⁹.



Fig. 2: Niosome Day Time Skin Treatment by Lancôme

ULTRASOMES

Ultrasomes are specialized liposomes encapsulating an endonuclease enzyme extracted from *Micrococcus luteus*; the enzyme recognizes the sun damage to the skin and initiates removal of damaged DNA. Endonuclease recognizes UV damage and is reported to accelerate its repair four-fold. Ultrasomes also protect the immune system by repairing UV-DNA damage and reducing the expression of TNF, IL-1, IL-6 and IL-8. Interestingly, Ultrasomes also stimulate the production of melanin by melanocytes in the tanning response following UV exposure. A dose-dependent response has been observed in vitro^{40,41}.



Fig. 3

The Anti-Age Night Recovery Cream "claims to moisturize, repair cellular damage, retain water, and also boost your skin's natural collagen production." In fact, the Rodan + Fields website goes further, stating that the Night Recovery Cream contains patented Ultrasomes, which are DNA anti-ageing ingredients. These ultrasomes help repair cellular damage, fight wrinkles, sagging skin and loss of tone and elasticity⁴².

PHOTOSOMES

Photosomes contain the enzyme photolyase encapsulated in a liposome structure. Photosomes are incorporated in sun-care product to protect the sun-exposed skin by releasing a photo-reactivating enzyme extracted from a marine plant, *Anacystis nidulans*⁴³. This enzyme can be activated by light and can work during the day to support the skin DNA repair process. Combined with ultrasomes, they constitute the "intelligent" DNA repair system.

365 Cellular Elixir protects the skin's DNA by + 30% and supports the skin's DNA repair process by up to 60 % - the first time ever a cosmetic formula has been proven to protect and support the natural skin DNA repair process. This DNA Action complex is made of photosomes and ultrasomes. This product has been created by Lancaster⁴⁴.



Fig. 4

TRANSFEROSOMES AND ETHOSOMES

Transfersomes are specially designed vesicular particles, composed of phospholipids, with 10-25% percent surfactant and 3-10% ethanol⁴⁵. They significantly improve photostability and skin deposition of α -tocopherol. Ethosomes are non-invasive delivery carriers composed mainly of phospholipids, with 20-50% ethanol and water, which enable drugs to reach the deep skin layers. These are soft, malleable vesicles tailored for enhanced delivery of active agents. The in vitro release rate of azelaic acid was more rapid from ethosomal systems than from liposomal systems⁴⁶.

AQUASOMES

Aquasomes are nanoparticulate carrier system but instead of being simple nanoparticles these are three layered self assembled structures, comprised of a solid phase nanocrystalline core coated with oligomeric film to which biochemically active molecules are adsorbed with or without modification. Alternatively aquasomes are called as "bodies of water", their water like properties protect and preserve fragile biological molecules, and this property of maintaining conformational integrity as well as high degree of surface exposure is exploited in targeting of bio-active molecules like peptide and protein hormones, antigens and genes to specific sites^{47,48}. Genesphere is an anti wrinkle cream with new Aquasomes. It smoothenes lines and eliminates crow's feet⁴⁹.



Fig. 5

SILICONE VESICLES

For those looking to maintain a youthful appearance, silicone science is helping provide effective alternatives to injections and surgical procedures, by improving the visual and sensory effects of anti-ageing skin care products. Silicones can help provide a powdery feel, luxuriant texture, silky smoothness, easy application, and reduced tackiness in lotions and creams. Silicone elastomers can help anti-ageing products impart a natural look. During application, they form small, soft micro particles that fill wrinkles and skin imperfections to create a more uniform appearance. These particles are held in place with other silicone ingredients designed to prolong a smoother, velvety and powdery feel for long-lasting wear. Silicone elastomer powders coated with alumina can help mask wrinkles, lessen dryness and provide a soft-focus effect to improve skin appearance.

Silicone elastomers also show their versatility as vehicles to deliver active ingredients such as moisturisers, fragrances and vitamins. Silicones can play an important role as texture and sensory modifiers, making it easier to incorporate ingredients that might otherwise have negative aesthetic effects⁵⁰.

Cross-linked silicones such as elastomers and adhesives are a relatively new class of cosmetic raw materials that have utility in delivery systems for active ingredients. Silicone elastomers are cross-linked and the interconnections between polymer chains make the elastomers solid material. Because of this structure, an active ingredient can be trapped in the matrix and will not separate even if the active ingredient is not soluble in the elastomer matrix⁵¹.

Example of anti ageing cream containing silicone vesicles is Supreme Feel Anti-Ageing Cream 414. The melting texture of this delightful, silicone based, technological innovation makes the skin delicate and young⁵².



Fig. 6

MULTI-WALLED DELIVERY SYSTEMS

The multi-walled delivery system (MDS) is based on a combination of structured vesicle-forming materials and high shear processing. It provides exceptional long-term stability to cosmetic skin treatment products. MDS is analogous to the structure of membrane lipid found in the intracellular matrix and made up of non-phospholipid amphiphilic molecules (oleic acid, derivatives of polyglycerols, amino acid residues). MDS gives stability to liposomes but by combining hydration and delivery, MDS also nourishes and protects the skin, bringing the formulator closer to optimizing product performance⁵³.

Charmzone DeAGE CRD Red-Addition is the brand new CRD system that contains rich anti-oxidants found in red food: red grapes, red wine, pomegranate and tomato. Multi-Walled Delivery System (MDS) enables rapid absorption into the skin. It protects skin from damaging free radicals, pollution, stress and ageing. It firms, rejuvenates and repairs skin. It hydrates and protects skin from damaging factors, from the environment and ageing. It tightens loose pores while firming the facial contours⁵⁴.



Fig. 7: Charmzone DeAGE CRD Red-Addition

MICROEMULSIONS

Microemulsions are stable, transparent (or translucent), dispersions of oil and water stabilized by an interfacial film of surfactant molecules and having diameter <100 nm. Microemulsion formation usually involves a combination of three to four components – water, oil, surfactant/s and co-surfactant/s⁵⁵.

A micro-emulsion formula is a complex and clinically proven time lapse system that penetrates skin quickly and thoroughly. The best wrinkle treatments utilize technologically advanced ingredients that deliver an array of powerful, anti-ageing and skin-repairing agents to the cells of the skin. Even hours after you have applied them, the best wrinkle creams are still working hard at keeping your skin hydrated, wrinkle-free and void of scaly patches and other signs of ageing. And unlike the costly and only mildly effective wrinkle treatments of the past, the best wrinkle creams of today work wonders on your skin, typically showing signs of noticeable improvement in just the first few weeks of daily usage⁵⁶.

Skinlastin™ is a micro-emulsion formula with a time lapse system so it penetrates skin quickly and thoroughly. Its technologically advanced ingredients deliver a host of powerful anti-ageing repairing agents to the cells of the skin to help you look more youthful and radiant⁵⁷.



Fig. 8

NANOEMULSIONS

Nanoemulsions consist of very fine oil-in-water dispersions, having droplet diameter smaller than 100 nm. Compared with microemulsions, they are in a metastable state and are very fragile systems by nature⁵⁸. Nanoemulsions are another process in skin creams. Emulsion just means mixing two unblendable liquids (like oil and vinegar in a salad dressing) where one of the liquids is suspended in the other. In nanoemulsion, as opposed to just plain emulsion, one liquid disperses in nano-scale droplets throughout the other. Nanoemulsions, unlike normal emulsions are so fine that they can be sprayed on. Companies that sell them claim that nano emulsions can transport beneficial compounds deep into the skin and in high concentrations. Nano gold is also being used in one moisturiser available in the UK, allegedly bringing healing and anti-oxidant properties⁵⁹.

Procter and Gamble's Olay™ brand was designed with nanoemulsion technology in 2005⁶⁰. Marie Louise Vital Nanoemulsion α-VC & Crème α-VC-use nanotechnology to deliver a powerful proprietary blend of anti-ageing & skin brightening ingredients to address your anti-ageing concerns⁶¹.



Fig. 9

LIQUID CRYSTALS

Liquid crystalline phase is thermodynamically stable and represents a state of incomplete melting. Liquid crystals form multilayers around the emulsion droplets, decreasing the vander Waal's energy and increasing the viscosity which increases the emulsion stability. Lipophilic materials such as vitamins, incorporated into liquid crystalline matrix, are protected from both thermal and photo-degradation. Emulsions containing liquid crystals have been observed to have a rate of active release much slower than those without this stabilizing component due to multilayer structure of liquid crystalline material around droplet⁶².

One such liquid crystal containing anti-ageing formulation is Cosmedix opti crystal Age-defying liquid crystal eye serum with liquid crystals to replenish damaged, thinning skin around the eyes, and growth factors and alpha lipoic acid to dramatically diminish the appearance of eye lines and wrinkles. Opti-Crystal is the ultimate tool in anti-ageing eye care⁶³.



Fig. 10

MULTIPLE EMULSIONS

Multiple emulsions are a type of polydisperse systems allowing controlled release of active entrapped compounds. They are of two types: w/o/w type and o/w/o type⁶⁴. Ascorbic acid and vitamin A have been successfully formulated showing improved stability and release profile⁶⁵.

PARTICULATE SYSTEMS

Microparticulate Systems

Microparticles are solid polymeric particles falling in the range of 0.1–1000 micron and include microsphere and microspheres. In general, microparticles are used in cosmetics to avoid incompatibility of substance, reduce odour of actives and for protection of substances prone to oxidation or action by atmospheric moisture⁶⁶.

Example of antiageing formulation containing microparticles is Pond's Gold Radiance Night Cream. Pond's Gold Radiance with real gold microparticles is a powerfully concentrated formula that blends into the skin to instantly restore a youthful radiance and fade visible signs of ageing⁶⁷.



Fig. 11: Pond's Gold Radiance Night Cream Anti-Ageing Wrinkles

Microspheres

Microspheres, typically defined as spherical microparticles between 1 micron and 1000 microns (1 mm) in diameter, have been widely used in personal care and the cosmetics industry over the past decade. In skin care lotions and creams, microspheres can help deliver a soft and smooth feel, excellent lubricity and soft focus effects that reduce the appearance of fine lines and wrinkles. Microspheres have numerous advantages in the personal care and cosmetics industry. Due to their unique geometry and the smallest surface area to volume ratio of any shape, microspheres offer beneficial properties such as ball bearing effect for superior texture, light scattering or "optical blurring" for minimising lines and wrinkles, gentle but effective exfoliation, as well as the ability to house colorants and active ingredients. The use of microspheres in the personal care and cosmetics industry is growing as microspheres are getting incorporated into an increasing number of anti ageing creams⁶⁸.

CR1 Moisturiser is an example of microsphere containing anti-ageing formulation. It is a deeply hydrating cream with anti-ageing collagen tripeptide microspheres which adheres to the skin upon application stimulating collagen synthesis thus reducing signs of wrinkles⁶⁹.



Fig. 12: CR1 Moisturiser Containing Microspheres

Microsponges

Microsponges are polymeric delivery systems consisting of porous microspheres, each microsphere consisting of a myriad of interconnecting voids within a non-collapsible structure with a large porous surface. The porous sphere polymers vary in diameter from

5 to 300 micron^{70, 71}. The microsponge technology is essential small air tight spheres that are filled with the active ingredient enabling them to easily find their way to wrinkles and other damaged areas. Due to gradual product release, microsponge helps to increase the effectiveness and tolerability⁷².

Microsponge technology is a proprietary system of microparticles that entrap pharmaceutical and cosmetic active ingredients to enhance their performance in topically applied dermatological products. Widely regarded as a leading technology for addressing skin conditions such as acne, hyper pigmentation, actinic keratosis, ageing and photo damage, HBS patented Microsponge delivery system provides sustained release technology for reducing irritation of a wide range of APIs and other skin care actives thereby increasing patient/client compliance, enhanced formulation stability ensuring long term product efficacy, extended shelf life and superior skin feel and exceptional product aesthetics.

Their characteristic feature is the capacity to adsorb or "load" a high degree of active materials into the particle and on to its surface. Its large capacity for entrapment of actives, up to three times its weight, differentiates Microsponge products from other types of dermatological delivery systems⁷³.

Pure Dose Pearls with Microsponge Technology is very effective against wrinkles. Perlabella Retinol Facial Serum is encapsulated in a patented Microsponge system, which provides time-released delivery of Retinol into the skin⁷².



Fig. 13

NANOPARTICULATE SYSTEMS

Nanoparticulate systems include nanospheres and nanocapsules and can be defined as submicron colloidal systems having a mean particle diameter of 0.003–1 micron. Nanocapsules differ from nanospheres in that the former is a reservoir type of system, whereas the latter is a matrix system. Polymer composition for both is identical and includes biodegradable synthetic polymers like polyamides, cross-linked polysiloxanes or modified natural products such as, gelatin and albumin⁷⁴.

Active ingredients such as vitamin A, retinol and beta-carotene must get to the deeper layers of the skin if their anti-ageing and other beneficial properties are to be most effective. L'Oreal developed a tiny polymeric shell capable of guiding the active ingredients to the right place in the skin. By reducing the active ingredients to a very small size and coating them with a biodegradable polymer, the company found that the nanocapsules were small enough to pierce through the first layers of the skin. The skin's natural enzymes eat at the surface of the nanocapsule and release the active ingredients below, in the lower layers of the skin. Products containing these nanocapsules hit the market in higher-end brands such as Lancôme six years ago⁷⁵.

Soleil Soft-Touch Anti-Wrinkle Sun Cream SPF 15 by Lancôme is an example of nanocapsule containing anti-ageing formulation.

An anti-wrinkle sun cream SPF15 helps to preserve skin's youth effectively. SPF15 offers optimal protection against the sun. It contains exclusive ingredients to guarantee a long-lasting effect. It

promotes a gradual, even & beautiful tan instantly. It is suitable for all skin types containing Vitamin Nanocapsules⁷⁶.



Fig. 14: Soleil Soft-Touch Anti-Wrinkle Sun Cream SPF 15

Nanospheres

Nanospheres are microscopic fragments used to deliver active ingredients into the deep layers of the skin. This advanced technology plays a very beneficial role in protecting against actinic ageing, which is 90% of the ageing of our skin. Nanosphere technology is incorporated into some of Arbonne's anti-ageing skin care (RE9 NutriMinC) and hair care products⁷⁷.

NutriMinC RE tackles the effects of ageing and sun damage. It incorporates nanospheres which fights free radicals with antioxidants⁷⁸.



Fig. 15

SOLID LIPID NANOPARTICLES AND NANOSTRUCTURED LIPID CARRIERS

Solid lipid nanoparticles (SLNs) are novel colloidal delivery systems with many cosmetic and dermatological features, such as enhanced skin hydration, protection against degradation, active penetration enhancement, and controlled-release properties⁷⁹. Nanostructured lipid carriers (NLC) are mixtures of solid and fluid lipids, in which the fluid lipid phase is embedded into the solid lipid matrix⁸⁰.

Alpha-lipoic acid encapsulated SLN and NLC formulations demonstrated antioxidant activity at similar level of 0.01-10 μm to pure alpha lipoic acid with low cell cytotoxicity and good physical stability⁸¹.

Commercially available products, NanoRepair Q10® cream and NanoRepair Q10® serum (Germany), which were introduced to the cosmetic market in October 2005 epitomises the success of NLCs⁸². Through the first application of NLC technology for the encapsulation of lipophilic active ingredients, SLNs (Nanopearls®) containing Q10 is prepared. It is able to fully unleash its energy-supplying and antioxidant effect, to counteract premature skin ageing and ensure that collagen-and elastic-degrading enzymes are inhibited⁸³.



Fig. 16

NANOTOPES AND NANOCRYSTALS

Nanocrystals are aggregates comprising several hundred to thousands of atoms that combine into a cluster, used for the delivery of poorly soluble actives. Typical sizes of these aggregates are between 10-400 nm and they exhibit physical and chemical properties somewhere between that of bulk solids and molecules⁷⁷.

The first cosmetic products appeared on the market recently; Juvena in 2007 (rutin) and La Prairie in 2008 (hesperidin). Rutin and hesperidin are two, poorly soluble, plant glycoside antioxidants that could not previously be used dermally. Once formulated as nanocrystals, they became dermally available as measured by antioxidant effect. This dermal use of nanocrystals is protected by patents⁸⁴.

Juvena Juvedical Age-Decoder fluid & Cream is an example of nanocrystal containing anti-ageing formulation. Skin Nova Technology for optimal skin renewal is combined for the first time with an innovative NanoCrystal Technology to work effectively and entirely against the ageing process. Juvena Age-Decoder Face Fluid provides an optimal environment for cell renewal and also works in the inner part of the cells, making the consumer look year's younger⁸⁵.



Fig. 17

NANOTOPES

Recent advancement in liposomes includes monolayered Nanotopes™ particles, which comprises of membrane having well defined ratio of a phospholipid (i.e., lecithin) and a co-surfactant⁸⁶. Nanotopes™ are ultra small carriers with a unilamellar membrane of a diameter between 20–40 nm. They can encapsulate cosmetic actives, as well as, oils. Nanotopes™ transport the actives to the target skin layers thus initiating an anti-ageing and anti-wrinkle activity.

Tinoderm™ Nanotopes is a registered trademark of Ciba Specialty Chemicals Inc. Its product range for anti ageing activity is –

Ciba Tinoderm™ A- Nanotopes™ with encapsulated Vitamin A palmitate

TINODERM™ A - used in skin care products with anti-wrinkle properties and prevents skin from premature ageing.

Ciba Tinoderm™ E-Nanotopes™ with encapsulated Vitamin E acetate.

Nanotopes™ transport the precursor of Vitamin E to the target skin layers where it protects the cell membranes from damage of free oxygen radicals, and at the same time, acts as a skin moisturiser.

Ciba Tinoderm™ P- Nanotopes™ with D-Panthenol

It is used in products for sensitive, irritated and stressed skin⁸⁷.

Ristra Anti Wrinkle Night Cream is one such anti-ageing formulation containing nanotopes. Nanotope loaded anti wrinkle cream works effectively breaking through into the skin to overcome the ageing effects caused by free radicalism. It also contains olive oil to maintain the moisture of the skin to keep it smooth and soft⁸⁸.



Fig. 18: Ristra Anti Wrinkle Night Cream is one such anti-ageing formulation containing nanotopes.

FULLERENES

Fullerenes (singular: Fullerene) are ball-shaped molecules build from carbon atoms. The so-called Buckminster fullerenes C₆₀, or buckyballs, are the currently most adequately investigated molecules of that type. Fullerenes are currently applied in cosmetics. Since C₆₀ molecules have a high electron affinity (radical scavengers) due to which they are supposed to absorb many free radicals (reactive molecular species) that are responsible for ageing of the skin, they are used, in anti-ageing creams⁸⁹.

UNT Elixirin C60 Precious Eye Complex - Brightening Eye Cream is an example of anti-ageing formulation containing fullerenes. The anti-ageing and brightening benefits of Radical Sponge® Fullerene in ELIXIRIN C60 SERUM is proven by its high acclaims since its first launch. It is an infusion of wrinkle-fighting, elastin-strengthening and skin-brightening elements to protect, treat, and illuminate the delicate eye area⁹⁰.



Fig. 19

CYCLODEXTRINS

Cyclodextrins (CDs) are cyclic oligosaccharides containing a minimum of six d-(+)-glucopyranose units attached by a (1, 4) glucosidic bonds. The three natural CDs are alpha, beta and gamma which differ in their ring size and solubility. Most of the molecules fit into the internal CD cavity forming a complex and the resulting structure is called CD clathrates or inclusion complexes. Complexation with CDs can bring about stabilization of the active ingredient against oxidative, photolytic and thermal degradation⁹¹. Cyclodextrin-retinol complexes patented by Wacker are now found

in a wide variety of antiwrinkle creams manufactured under the name CAVASOL®⁹².

Regenerative Anti-Ageing Face Cream, Silk Effect is an example of cyclodextrin containing anti-ageing formulation. It is an antiageing treatment favouring cellular regeneration and fighting against the skin ageing process. Beta Cyclodextrins/Retinol, contributes to renewal of epithelial tissues⁹³. It reduces wrinkles and supports the restoration of UV-damaged tissue⁹⁴.



Fig. 20: Regenerative Anti-Ageing Face Cream, Silk Effect

FUTURE TRENDS IN ANTIAGEING FORMULATIONS

Anti-ageing remains a key area of new product development and has been growing in importance rapidly as consumers become more and more aware of how they are perceived in and outside the workplace.

According to Mintel, anti-ageing is the fourth most prevalent claim in skin care. Europe was the largest anti-ageing skin care market in 2010. Consumers want to look good for their age as long as possible which can be seen by the upcoming trend in use of anti ageing products and demands. A handful of technologies which have been a success are liposomes, nano emulsions and metal oxide nanoparticles. Now, due to increased demands and awareness amongst consumers, newer technologies have emerged. Future and novel trends include the use of fullerenes, nanotopes, nanocrystals, microsponges in the cosmetic products.

Fullerenes were launched several years ago but due to consumer concerns with nanotechnology fell from favour⁹⁵. Global Anti-Ageing Products Market to reach \$291.9 Billion by 2015, according to New Report by Global Industry Analysts¹.

Table below summarizes the nanomaterials used in the antiageing formulations⁹⁶.

Active ingredients/delivery system	Trade name	Manufacturer	Use
Ascorbyl palmitate, Tocopherol , retinol/ liposomes	Rovisome ACE Plus	Rovi Cosmetics International GmbH	Anti-ageing, wrinkle reduction.
Vitamin E/Nanotopes	Tinoderm E	Ciba Specialty Chemicals	Anti-inflammatory, anti-ageing.
Coenzyme Q10,Niacinamide/Liposomes	Ageless Facelift cream	I-Wen Naturals	Anti-ageing, anti-oxidative, wrinkle reduction.
Micro-encapsulated VitaminC (5%)	Ultimate Anti-Ageing Cream	Provin Cosmeceuticals	Anti-ageing, wrinkle reduction.
CoenzymeQ10,Vitamin E acetate/Nanoemulsion	Nano-Lipobelle H-EQ10 cream	Mibelle Biochemistry,Switzerland	Anti-ageing, anti – inflammatory.
Pro-Retinol A/Nanoparticles	Revitalift	L'Oreal	Anti-wrinkle, anti-ageing.
CoenzymeQ10/Nanostructured lipid carriers	Cutanova Nano Repair Q10 Cream	Dr.Rimpler GmbH	Revitalising , anti-ageing
Black current seed oil/Nanostructured lipid carriers	Nanolipid Restore CLR	CLR Chemisches Laboratorium Dr.Kurt Richter GmbH	Revitalising,anti-ageing
Vitamins A,E,C/Nanoemulsion	Nano-Lipobelle H-AECL	Mibelle Biochemistry, Switzerland.	Anti-wrinkle, antiageing.
VitaminE,Panthenol/Nanocapsules	Lancôme Soleil Soft-Touch Anti-Wrinkle Sun Cream SPF 15	L'Oreal	Revitalising, anti-ageing.
Grape seed extract, Vitamin E,Green tea extract/ Fullerenes	Circuit Addict Firming Antioxidant Serum	Circuit Skin Cosmeceuticals Inc.	Revitalising, anti-ageing.

CONCLUSION

Our society highly values health and beauty. Thus antiageing formulations are becoming increasingly popular. Number of companies utilizing nanomaterials sell antiageing products in the market which due to their unique property of beneficial delivery to the skin renders extended efficacy. New technologies and techniques are creeping in the field of nanotechnology to improve the cosmetic market even more, although a lot of research and human studies in this field is required to obtain a real life data.

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