Cosmetic Delivery Systems
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Many of the features that appear in SPC discuss the active ingredients however their benefits are lost if the material is not delivered to the required site at a beneficial level by an appropriate delivery system. This feature is going to look at some of the delivery systems currently on offer from suppliers from around the world.

The functionality of an active ingredient depends on its intrinsic biological activity and the concentration needed to achieve that biological effect when delivered from a formulation to its biological target. Thus the formulation should contain a sufficient starting concentration, it should be released from the formulation after deposition on the target surface, and it should penetrate through a variety of biological barriers. Arlasolve DMI [INCI: Dimethyl isosorbide] from **Croda** is claimed to help at each of these stages.

Arlasolve DMI-PC is a non-volatile medium polarity solvent that is miscible with water and organic media. Once deposited on the skin surface, it can increase the polarity of the surface skin layers and help carry the biologically active material through layers of variable polarity. This delivery enhancement effect is more apparent for hydrophilic active ingredients than for lipophilic, especially in emulsions. Arlasolve DMI-PC is miscible with a wide range of ingredients, including most organic solvents, non-ionic surfactants and water and can be formulated into a variety of delivery systems, including clear gels, foams, creams, lotions, sprays and ointments.

Ethylhexyl glycerin available as Kopcerin from **WSB i**s a clear, colourless liquid with characteristic odour that is a multi-functional additive for cosmetic preparations. It acts as an effective emollient leading to an improved skin feeling with no stickiness after application and can replace glycerin in formulations where enhanced penetration is an advantage. It has deodorising

properties and improves preservative efficacy and is soluble in alcohols, glycols and glycol ethers.

Another material claimed to enhance the bioavailability of actives is Hydrolite 5 [INCI: Pentylene glycol] from **Symrise**. It is soluble in water and cosmetic esters and experiment shows that 5% added to a formulation significantly improves skin permeation of cosmetic actives such as caffeine and carnosine. It also has skin moisturising properties, enhances preservative efficacy and improves water-resistance of sunscreen formulations.

It is possible to make the active itself be part of an enhanced delivery system. Glycacid Eco [INCI: Glycerin, hydrolyzed glycosaminoglycans] from **CR&D** is a biotechnological product composed of precursors of mucopolysaccharides with a high concentration of the fundamental monomer of hyaluronic acid, hyalobiuronic acid. Its small molecular size enhances intradermal penetration and is especially useful for water retention in the connective tissue and deep moisturisation. It also increases the permeability of connective tissue, which makes it an important penetration factor for hydrophilic active ingredients such as plant extracts.

Glycacid Eco from **CR&D** is a precursor to hyaluronic acid, which is then produced within the skin by natural metabolism. CUBE3 from **Principium** is a full-spectrum biotechnological fraction of sodium hyaluronate that targets short-term anti-ageing effects. Described as a unique 3-in-1 ingredient that improves the health of the epidermis by a strengthening of the barrier function of the skin. CUBE3 enhances skin penetration of other lipophilic and hydrophilic active ingredients to optimise their activity and shows an immediate lifting effect when evaluated by elasticity, smoothness and number and depth of wrinkles. Another material from Principium is Difference; a fraction of sodium hyaluronate that targets long-term anti-ageing effects.

Avocado oil may also be considered as its own delivery system. It is made up principally of the glycerides of oleic, palmitic, linoleic, linolenic and palmitoleic acids and its unsaponifiable fraction contains vitamins A and E plus squalene, carotenoids, phytosterols and terpenic alcohols and these actives protect the skin against harmful agents such as UV radiation and free radicals. They are also said to activate the metabolism of fibroblasts, promote the synthesis of collagen and inhibit the enzymes responsible for its degradation.

Avogelia from **Variati** is 70% of avocado oil plus caprylic/capric triglyceride, aqua, glycerin, potassium cocoyl hydrolyzed rice protein, sodium cocoyl rice amino acids and tocopheryl acetate. Avogelia can be used to produce stable emulsions by incorporating lipids at concentrations of up to 30% and by the careful use of viscosity modifiers emulsion viscosity can be adjusted to form products for spray applications as well as lotions and creams.

Olive glycerides available as Olifeel from **Amedeo Brasca** is claimed to enhance skin penetration because of its biocompatible triglyceride content. Tests demonstrate its superior penetration properties compared to caprylic/capric triglycerides and sweet almond oil. Also claimed is enhanced resistance to oxidation and increased emulsion stability due to its content of polar diglycerides.

Emulsions are a favoured means of delivering skin care actives and those that promote the formation of liquid crystal structures are known to improve penetration into the stratum corneum. There are a number of such emulsifiers available including Olivem 1000 from **B&T**, which is a mild, PEG-free, primary oil-in-water emulsifier derived from olive chemistry. Olivem 1000 [INCI: Cetearyl olivate, sorbitan olivate] promotes liquid crystal formation which leads to a biomimetic structure that can improve long-term skin

hydration, improve delivery of active ingredients and provide a pleasant skin feel.

AAK produces two emulsifiers based on citric acid esters; Akoline GC [INCI: Hydrogenated vegetable glycerides citrate] and Akoline LC [INCI: Glyceryl stearate citrate]. Both are capable of forming liquid crystals if combined with non-ionic emulsifiers such as mono/diglycerides, polyglycerol esters or ethoxylated fatty alcohols, making them good emulsion stabilisers and consistency improvers. They can also be combined with a high-HLB anionic emulsifier such as Akoline SL [INCI: Sodium stearoyl lactylate] to further stabilise the liquid crystals formed.

A different approach to emulsification is offered by the o/w emulsifier Inutec SL1 [INCI: Glycerin, inulin lauryl carbamate] from **GOVA**. In a mixture of oil and water, Inutec SL1 migrates quickly to the oil/water interface. The lauryl chains are firmly anchored into the oil, while the long inulin polymers tightly encapsulate the oil droplet. In this way an unbreakable film of strongly hydrated inulin stabilises the oil droplets. Inutec SL1 has very high salt tolerance, and can emulsify over 50% oil as the dispersed phase. The micro oil droplets formed by Inutec SL1 cover the skin surface so that the actives present in the emulsion are trapped on the skin under the liquid patch formed by these small droplets, which increases their availability for the skin.

A novel delivery system is the use of self-foaming AE Cosmofluor 61 and AE Cosmofluor 76 from **AE Chemie**. Both materials comprise methyl perfluorobutyl ether and methyl perfluoroisobutyl ether and are offered as non-VOC replacements for alcohol and other volatile solvents. Rapid evaporation of Cosmofluor allows faster “blooming” of fragrances and their self-foaming nature makes them of interest for delivering unique properties to products such as waterless shampoo and self-foaming hair and face masks.

Delivering oxygen to the skin is the claimed function of Gransil SiW-7100, [INCI: Methyl perfluorobutyl ether, isododecane, aqua, polysilicone-11, butylene glycol, decyl glucoside] from **Grant Industries**. Skin cells require oxygen in order to produce ATP cellular energy but it loses its oxygen capacity with age. Lack of oxygen is said to encourage the proliferation of anaerobic bacteria such as *p. acnes* and to slow wound healing. The Gransil SiW-7100 gel entraps oxygen-carrying methyl perfluorobutyl ether into an elastomer matrix with an external water phase to manage evaporation in manufacturing and on application.

Fiflows from the **Innovation Company** are very volatile perfluoro compounds that are not soluble in oil or water but create a third phase in emulsions. Fiflows normally contain air, but they can be enriched with other gases such as oxygen. Currently there are five variants within the range, three are designed to deliver oxygen over different time periods; one is to add volume to skin and one to provide instant bubbling effects for skin care applications where visual foaming is desired. Products with Fiflows need to be packaged in airless packaging.

Encapsulated actives are a well-stablished means of delivering actives into the stratum corneum and are often associated with sustained release mechanisms.

Nusil Silicone Technology has created a variant on encapsulation under its trade name CareSil whereby silicones are encapsulated within coacervate membranes of amodimethicone. The internal phase can be a silicone compound such as trifluoropropyl dimethicone or dimethicone/vinyl dimethicone crosspolymer and materials that are soluble in it such as perfume. It is possible to make clear gels incorporating CareSil encapsulates which are then broken on application to release fragrance and silicone textures.

Ultra Filling Spheres from **BASF Beauty Creations** are composed of two biopolymers: hyaluronic acid of low molecular weight and konjac, a

polysaccharide of high molecular weight. Filling Spheres technology is based on the ability of dehydrated and cross-linked spheres to penetrate the upper layers of the epidermis and to absorb the water that evaporates from the deep dermis. Because of their hygroscopic properties, the volume of the spheres increases rapidly and once inflated, they tighten the skin, smoothing out wrinkles and leaving an elastic skin surface with long lasting hydration.

Beauty Creations also markets PatcH2O; a molecular network of natural biopolymers with a high concentration of a moisturising complex comprising glycerin, serine, trehalose and urea. PatcH2O is said to offer optimal hydration by acting on two levels. On the surface of the skin, the novel and unique combination of hyaluronic acid, alginate and pullulan form a molecular mesh of moisturising actives and this is gradually released into the stratum corneum. Clinical evidence suggests that hydration starts after about 30 minutes and may last for up to 48 hours.

Encapsulating active ingredients within lamellar clay structures is the process patented by **Prolabin and Telfarm**. Currently the range includes azelaic acid, oleic acid, glycyrrhetinic acid and resveratrol and in each case the active is protected from its environment by the clay structure. This protection is also afforded to the user, who gains the benefit of the active material delivered over a period of time, so minimising any potential irritating reaction to the material. For example glycyrrhetinic acid is a proven anti-inflammatory and skin soothing compound but it is virtually insoluble in water. By enclosing it within the clay matrix it can be delivered to the skin where it is slowly released. The clay matrix also protects the glycyrrhetinic acid from light, oxygen, humidity and heat and it permits an easy dispersion of product to produce a homogeneous dispersion of the active in pastes, gels and emulsions.

Biogenics is a company that specialises in microemulsion technology to enable the delivery of otherwise unstable active ingredients to the skin. For example epigallocatechin gallate is a powerful antioxidant found in green tea however it is insoluble and inherently unstable. By encapsulating it within the amphiphilic polymers, poloxamer 338 and poloxamer 235, it becomes water-soluble and is stabilised. It is marketed as BioGenic EGCG-200. BioGenic Salic-200 is salicylic acid rendered water-soluble by encapsulation with polydextrose and dextrin and Biogenics also provide colour changing encapsulated iron oxides under the trade name BioGenic Magicolor.

Salvona markets several different encapsulation systems: SalSphere technology enables the encapsulation and controlled delivery of a wide variety of actives in sub-micron spheres; MultiSal is a double-layered encapsulation of actives in microspheres, which are loaded with SalSpheres and HydroSal is an aqueous suspension of sub-micron spheres suitable for large surface area applications such as fragrance, antimicrobial, and insect repellent products. All three systems provide time-release capabilities with release of actives from SalSpheres and HydroSals being triggered by heat and skin enzymes and from Multisal by moisture and pressure on application. Also from **Salvona** are Microbeads ColorFX; visual beads approximately 300 microns in diameter that provide a colour-change effect upon rubbing. They can be incorporated into various skin and hair care products to convey an immediate change such as whitening, tanning or blemish reduction.

Softspheres from **Kobo** are a delivery system consisting of soft beads that can contain active ingredients. The beads provide a visual impact in formulations and can be crushed on the skin to release active ingredients. Softspheres are made from a combination of agar and a copolymer. The mixed agar/copolymer matrix traps active molecules by means of ionic bonds and hydrophobic

interactions with the copolymer. Softspheres are available containing hyaluronic acid, oil-soluble vitamins, natural oils and ceramides. Their size ranges from 1 to 2.8 mm and are recommended for use in transparent gels, shower gels and shampoos, emulsions, soap and tooth paste.

Kobo also produces Glycospheres, which are supramolecular configurations organised around a solid inner core of modified starch. This is powerfully hydrophilic and endows the particle with its chemical and physicochemical stability as well as its biocompatibility. A single layer of fatty acids is covalently grafted at the periphery of this central core, endowing the particle with a peripheral lipophilic nature, without modifying its internal hydrophilic nature. The Glycosphere can thus organise polar lipids and hence retain and deliver lipophilic active agents. There are numerous variations available from **Kobo**, with the emphasis on protecting the active from environmental degradation until it is delivered to the intended site within the stratum corneum.

Liposomes in their various forms remain the principal means of delivery actives to the lower layers of the stratum corneum, Liposomes are hollow spheres that are enclosed by one or more bilayer membranes that consist of phospholipids and particularly of phosphatidylcholine, which is obtained either from eggs or soya beans. The amphiphilic nature of phosphatidylcholine allows the liposomes to self-aggregate in aqueous solution to form spherical structures and they may be used to deliver either water-soluble or oil-soluble actives. Because of their cell-like composition, liposomes are efficient biomimetic vectors highly adapted for cosmetic products to improve ingredient percutaneous absorption and efficacy, acting as a non-skin-irritating penetration enhancer.

According to literature available from **Lucas Meyer** each phospholipid-based structure has different physico-chemical properties through the skin and can be considered as a vectorization system able to encapsulate active molecules.

Formed with natural components of cell membranes, they have a high affinity to the stratum corneum and can therefore enhance the bioavailability of entrapped molecules to the epidermis. These vectorization systems also benefit from phospholipids biological properties offering moisturising, restructuring and protective effects.

It is possible for a manufacturer to create its own liposomes and **Lucas Meyer** has simplified this process with its Pro-Lipo Neo technology. Pro-Lipo Neo is a ready-to-use mixture of selected phospholipids already organised in lamellar bilayers in an appropriate medium. This pro-liposome structure requires only the addition of a water phase to spontaneously form, at room temperature, an alcohol free suspension of multilamellar liposomes of a mean size of 250 nm. This is small enough to present high cutaneous absorption and release the entrapped ingredients. Pro-Lipo Neo technology allows the selection of the type and concentration of the ingredients to entrap with hydrosoluble active ingredients residing in the internal cavity and liposoluble active ingredients in the lipid bilayer of the membrane.

Brookosome liposomes from **Lonza** are available in two forms, dispersed and emulsified. Dispersed Brookosome liposomes are produced with solutions of water-soluble agents which are captured in the interior of the vesicle as well as being present in the continuous phase of the dispersion. Dispersed Brookosome liposomes are generally 200 nm or less in diameter and are translucent in appearance. Emulsified Brookosome liposomes capture lipids within the bilayer of the vesicles and are up to 300 nm in size and opaque in appearance. Various ones are available including Brookosome ACE, which contains retinyl palmitate with tocopheryl acetate and Brookosome ACEBD, described as a complimentary combination of three vitamins to help protect lipid membranes from free radical attack.

A variation on liposomes is Lipodisq from **Malvern Cosmeceuticals**. Lipodisq is a biodegradable particle system developed specifically to deliver oily or lipophilic active agents including fat soluble vitamins and botanical extracts into the stratum corneum. The structure of Lipodisq is based upon natural high density lipoproteins responsible for transporting fats around the body. Like their natural counterparts, Liposdiq are biodegradable being formed from membrane phospholipids, surfactants and co-surfactants derived from vegetable sources that are readily broken down by skin enzymes.

Typically the size of Lipodisq are 10-40 nm depending on the chosen actives so they are able to penetrate the aqueous pores that surround the fatty lamellar layers of the stratum corneum. Lipodisq then become trapped in the stratum corneum where they degrade slowly to release their contents into the deeper layers of the skin The outer layer of the skin therefore acts as a reservoir for the active substance ensuring a more even release profile. Currently Lipodisq are available containing ascorbyl palmitate, retinol and a mix of niacinamide with sodium ascorbyl phosphate but other actives can be carried by Lipodisq including botanicals, fragrances, oils, esters, and pharmaceutical actives.

Protecting the active ingredients from oxidation until they are delivered to the skin is as an important part of delivery systems as is improving cutaneous penetration. Many of the systems already described make this claim and the Cap't System developed by **Lucas Meyer** specifically addresses this problem.

Capt-System B9 is a suspension of liposomes of folic acid that protects it from photodegradation. According to an *in-vitro* test, the photo-induced degradation of the folic acid is less marked in the liposomal form of Capt-System B9 compared to free folic acid. Capt-System E is a pro-liposome containing a hydrophilic medium and d-tocopherol. In the presence of water and at room temperature, Capt-System E spontaneously forms liposomes of vitamin E. The

liposomal form protects and stabilises tocopherol and increases its skin diffusion and bioavailability. Capt-System E-Q10 is a mini-emulsion combining CoQ10 with d-tocopherol, which fights against free radicals in a synergistic way, thus offering a high antioxidant protection to the skin. Concentrated in very small oily droplets, the antioxidant efficacy of both molecules is improved.

Niosomes from **Naturalis** are claimed to be the most elastic and flexible of all the delivery systems. They are fully deformable therefore able to squeeze through the pores in the stratum corneum, penetrate the skin and fully reform to deliver the active. There are a number of noisome products available from Naturalis including Nio-Age that protects skin from free radicals; Nio-Aactive that revitalises, restores and reinforces skin's metabolism and Nio-Complex that consists of quercetin, morinda citrifolia seed extract and pure magnolol/honokiol extracted from Magnolia bark, which has anti-wrinkle and anti-ageing properties.

For more information about liposomes and other related structures these were covered in detail in SPC, May 2013.

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