Delivery Systems 2018
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The cosmetic industry is very dynamic with new active ingredients constantly added to the material inventory that formulators have at their disposal, however, they will not achieve the desired effect unless delivered from suitable products and this feature focuses on how they can be optimised to target the relevant skin cells.

The first question to ask is what does the formulator wish to achieve? In cosmetics, the main concern is to reach cutaneous cells while limiting the passage into the blood circulation. The objectives of topical therapy can therefore be classified into two major areas: to modulate or assist the barrier function of skin and to administer an active ingredient to one or more skin layers while minimising systemic involvement [Ref 1].

The stratum corneum (SC) is an effective barrier of stratified skin cells that has evolved to stop penetration of undesirable material into the subcutaneous layers of skin. It suffers from dehydration, excessive exfoliation or conversely, failure to exfoliate; inflammation caused by pollutants or sun exposure and irritation reactions to some cosmetic ingredients. Not all delivery systems are designed to penetrate the SC; UV absorbers applied from sun care products need to cover the outer layer in a homogenous film. To formulate sun protection compositions to provide maximum protection it is important that they spread readily and provide an even, water-resistant film on the skin. Sun care delivery systems were covered in SPC [Ref 2], and the same systems could be adapted for adding protective films against pollutants on the skin surface.

Anti-Pollution formulations rely on forming a physical barrier to prevent particles and other harmful substances from reaching the skin and on the delivery of actives to neutralise free radicals and deactivate toxins. Both these attributes can be achieved with high internal phase emulsions (HIPE) that have a water phase typically greater than 90%. The polygonal packing of water droplets in the structure creates stable viscous systems without the use of added thickeners. HIPEgel Aqua [Isopropyl palmitate, polyglyceryl-3 oleate, coco-caprylate/caprate, sorbitan sesquioleate] from **Alchemy Ingredients** may be used to form HIPE formulations. Both water soluble and oil soluble actives are present in the structure and water-soluble actives are encapsulated by a thin film of oil. The fine layer of oil forms a physical barrier on the skin to prevent entry of particulates leading to extra protection and it maintains a controlled release of actives.

Various materials are known to assist penetration of the SC, commonly termed penetration enhancers they include surfactants, particularly those with a decyl or dodecyl alkyl chain, organic solvents, unsaturated fatty acids, liquid crystal emulsifier systems, urea, dimethyl isosorbide, dimethylsulphoxide, dimethylformamide, urea, 2–pyrrolidone, N-methyl-2–pyrrolidone, decylmethylsulphoxide, propylene glycol and pentylene glycol and ethylhexyl glycerin. These are generally available as commodity items but for detailed information on pentylene glycol refer to a brochure published by **Symrise** on Hydrolite S and for ethylhexyl glycol **Gattefosse** has published a brochure on Transcutol CG.

There are many systems designed to assist penetration of the SC, often characterised by the suffix "~somes", e.g. liposomes, niosomes, ultrasomes, marinosomes, phytosomes, oleosomes, photosomes, transferosomes and vectorsomes. Transferosomes consist of phospholipids and cholesterol surfactant molecules such as sodium cholate. They are ultra-deformable and able to penetrate intact into skin. Vectorsomes from the **Innovation Company** are new hexagonal structures with very high volume internal space for actives. They vectorise by surface charge differential between the pH of skin (5.1/5.5), and that of the blood at live cells level, pH 7.38. Encapsulation in microspheres, microsponges and porous polymeric systems is favoured for controlled release

systems and the mechanism of ~somes and microspheres were described in SPC 2013 [Ref 3] and SPC 2014 [Ref 4]. Slightly different to these is a liquid polymer system supplied by **Inolex**. It is a trimethylpentanediol/adipic acid copolymer trade named Lexorez-TL8. Described as a polymeric liquid reservoir of low molecular weight, it facilitates uniform distribution of actives throughout the stratum corneum for an extended period and the active will slowly penetrate the viable epidermis and dermis.

Encapsulation of actives protects them from their environment and assists in targeted delivery. Coderaser from **Infinitec** comprises trehalose, palmitoyl proline, dipalmitoyl hydroxyproline and acetyl cysteine in alginate capsules. The active ingredients are targeted at increasing the collagen levels in lips to decrease vertical lines caused by ageing, sun exposure and smoking. The alginate capsules are said to favour the encapsulation of hydrophilic actives, exhibit viscoelastic properties and to Improve active bioavailability.

Retinol is a precursor for the synthesis of endogenous retinaldehyde and retinoic acid and is considered essential for the formation and maintenance of skin. However, retinol is subject to legal limits, can cause irritation and poses stability challenges. **Infinitec** launched vitAlease at In-Cosmetics, Amsterdam, 2018. vitAlease is 7% retinol encapsulated in a carnauba wax-based capsule [Aqua, Copernicia cerifera (Carnauba) cera, retinol, glycerin, propanediol, sodium cocoamphoacetate, tocopheryl acetate, BHT, BHA, xanthan gum]. It is said to be a natural, biodegradable lipid carrier, with low toxicity and good physical stability and it is suitable for water-soluble delivery systems. After application the capsules release free retinol over a three-hour period and this sustained release decreases potential irritation effects caused by short-term high-level exposure.

Berg + Schmidt GmbH encapsulates retinol in BergaCare SmartLipids. These are lipid particles of submicron size made of a complex mixture of solid waxes and liquid oils carefully selected to obtain an imperfect crystal structure, so lipophilic actives can be encapsulated and protected within them. These structures physically protect retinol against chemical degradation and, due to their submicron size, they attach themselves to skin, which ensures a prolonged release of retinol. In addition, the particles form a protective layer on the skin surface, which helps restore the natural skin barrier and normalise cell functions of stressed skin. The particle concentration of the BergaCare SmartLipids concentrate is 17% with a retinol content of 2.3%. At In-Cosmetics, Amsterdam 2018, Berg + Schmidt introduced BergaCare SmartCrystals Rutin. Rutin is a powerful antioxidant, but its poor solubility in both water and oil makes it difficult to formulate. BergaCare SmartCrystals Rutin gives a higher dissolution rate and increased saturation solubility, creating a high flow of molecules penetrating the skin so rutin becomes significantly more bioavailable and bioactive than conventional rutin powder.

Coenzyme CQ10 is a powerful antioxidant in powder form and delivering particulate matter into the skin is a problem that **Mibelle Biochemistry/Safic Alcan** resolved by incorporating it into nanoemulsion format. This renders CoQ10 water-dispersible with improved bio-availability and three strengths are available containing 1%, 5% and 7% CoQ10. Mibelle also produces Nano-Lipobelle DN CoQ10, which is a mixture of CoQ10 and tocopherol encapsulated in different droplets in a nanoemulsion. Having both CoQ10 and tocopherol in a transparent nanoemulsion provides a high bioavailability of both actives and topical application in skin care formulations is said to rejuvenate skin.

An alternative method to deliver actives that are prone to degradation by exposure to air and water is to incorporate them in anhydrous formulations. The permeability of silicones makes them suitable

for controlled release applications and they are used widely in transdermal delivery systems. 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 matrix. **Dow** created an anhydrous formulation based on a silicone elastomer, a silicone emulsifier and glycerin incorporating 5% and 10% vitamin C and tests show that it remained stable for an extended period and that when topically applied the vitamin C was released slowly into the SC and epidermis.

Not quite a nano-emulsion as droplet size is 100-1000nm but from **Vantage** is an innovative low viscosity liquid made using ultrasonic cavitation. This high shear process combines a carefully selected plant-based phospholipid with jojoba oil to produce Desert Whale Jojoba Milk [Aqua, Simmondsia chinensis (jojoba) seed oil, propanediol, phospholipids, glycerin, sodium hyaluronate, xanthan gum]. Thanks to this process and choice of lipids, a unique, stable oil-in-water emulsion structure is created with oil droplets significantly smaller than those found in standard emulsions. The micro-droplets have a very high surface area, which improves their absorption into skin and hair and jojoba oil and phospholipids are quickly delivered to where they are needed, providing hydration, lipid replenishment, non-greasy emolliency, conditioning, softening and smoothing benefits. The special phospholipid used in Desert Whale Jojoba Milk has also been shown to activate certain genes responsible for cell regeneration; keratinocyte differentiation, proliferation and growth; as well as pathways related to skin tissue hydration and anti-inflammation. **Vantage** uses the same technology to prepare Active Performance Bio-Shield containing bio-mimetic lipids and hyaluronic acid and Active Performance Argan Milk that simplifies the addition of argan oil to surfactant systems.

Whenever discussing delivery systems, it is impossible to avoid liposomes, which are artificial phospholipid membranes that can facilitate the passage of active principles across the stratum corneum. These sub-microscopic vesicles comprise amphiphilic molecules with an aqueous cavity encapsulated by one or more bimolecular phospholipid sheets, separated from each other by aqueous layers. The polar head group forms the interface at both the external and internal surfaces of liposomal bilayers. The phosphatidyl moiety consists of two fatty acids, which are ester bridged to glycerol phosphate.

Lucas Meyer Cosmetics has always been at the forefront of liposome development and provides Pro-Lipo Neo [Propanediol, lecithin] developed to enable formulators to create customisable natural liposomes, allowing complete control over the type and concentration of the ingredients to entrap for optimal efficacy. It is a ready-to-use mixture of selected phospholipids already organised in lamellar bilayers by their solubilisation in an appropriate medium and requiring only the addition of a water phase to spontaneously form, at room temperature, a suspension of multilamellar liposomes of a mean size of 250 nm. This type of liposome is small enough to present high cutaneous absorption and release the entrapped ingredients while membranes merge with skin.

New liposomes from **Mibelle** are Lipobelle Soyaglycone and Lipobelle Glacier. Lipobelle Soyaglycone is a liposomal preparation of genistein, which is the biologically active form of the most abundant isoflavone in soy. Genistein not only stimulates the production of collagen but it also prevents its degradation by matrix metalloproteinases. Lipobelle Glacier is a liposomal preparation of Swiss glacier water. The glacier water is encapsulated by lecithin molecules, which ensure that the moisture is carried into the deeper layers of the epidermis.

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Not all delivery systems are marketed to deliver actives into the skin; Emulmetik 320 [Hydrogenated lecithin, polyglyceryl-10 laurate] from **IFF/Lucas Meyer** offers fragrance encapsulation. The fragrance is released and intensified when the capsule breaks, caused either by rubbing the skin, by hair motion or with the natural reaction from skin contact. A similar effect is claimed for SalScent [Propylene glycol, nonoxynol-9, hydroxypropylcellulose, polyvinylpyrrolidone, beta-cyclodextrin, polyvinyl alcohol, sodium carboxymethylcellulose, phenoxyethanol, ethylhexylglycerin] from **Salvona**. When used to encapsulate fragrance it increases fragrance value by boosting longevity, releasing on demand and easing formulation. It can be employed in clear water or hydro-alcoholic bases without the need for any specialised equipment and provides moisture-triggered bursts of fragrance.

Ref 1 Patravale, V. B. and Mandawgade, S. D. (2008), Novel cosmetic delivery systems: an application update. International Journal of Cosmetic Science, 30: 19-33. doi:10.1111/j.1468-2494.2008.00416.x

Ref 2 SPC – Sun care 2018

Ref 3 SPC Delivery systems 2013

Ref 4 SPC Delivery systems 2014.

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