Cosmetic Delivery Systems
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Cosmetic delivery systems take many forms: it could be said that any cosmetic product that provides a benefit to the user is a delivery system. A shampoo delivers cleansing aids; a hair conditioner delivers detangling properties, a lipstick delivers colour. There are also trans-dermal delivery systems that transport therapeutic drugs through the skin but these are beyond the scope of cosmetics. Somewhere in between these two extremes are ingredients that enhance penetration into the stratum corneum or that provide sustained or targeted release of cosmetic actives and also systems that protect actives from degradation before delivery and these are the subject of this feature.

In the opening chapter of his book [Ref 1] on skin delivery systems the late Johann Wiechers wrote that the efficacy of any product containing a functional ingredient is determined by two factors: the intrinsic activity of the active molecule and the delivery of this molecule to its site of action. It is also necessary to deliver an active molecule at sufficient concentration to its intended site for enough time for it to be effective. Wiechers summed this up as the 4R's of delivery: the Right concentration of the Right chemical to the Right site for the Right period of time. To the 4R's could be added a 5th, at the Right cost.

Not all delivery systems are designed to penetrate skin or hair; hair styling products coat the hair shaft with polymer and sun creams must coat the skin with a protective layer of UV absorber. Nor do all moisturisers need to penetrate into the stratum corneum (SC); petrolatum remains one of the most effective skin moisturising agents because it forms an occlusive layer on the surface, thus retarding transepidermal water loss (TEWL).

Traditionally, enhancing skin penetration was achieved by the use of skin softening materials like urea or by using solvents like ethanol, propylene glycol, dimethyl sulfoxide and various low molecular weight esters. More recently the benefits of using unsaturated fatty acids like oleic and linoleic acid; liquid crystal emulsifier systems; microencapsulation; liposomes, nanosomes and niosomes have been realised. Also triggered or sustained release of the active after application is a recognised method of improving the efficacy of the active. Nanoparticles are seen as another effective way of delivering active agents into the SC but development of this technology is inhibited by fear of the new within Europe.

Certainly not new but still very effective are liposomes, which traditionally are spherical vesicles consisting of a central aqueous core surrounded by multilamellar bilayers of lipids and liposoluble actives, separated from each other by a layer of water. They are formed by the activity of phospholipids, which are found in lecithin. **Lucas Meyer** has always been at the forefront of promoting this technology and its latest suggestion are Pro-Lipo liposomes.

Unlike traditional liposomes Pro-Lipo liposomes are a single layer of water-soluble ingredients encapsulated within a phospholipid bi-layer incorporating lipids, which protect the active ingredient while enhancing skin penetration. Pro-Lipo liposomes are prepared *in-situ* by the user by first mixing the Pro-Lipo in an aqueous solution of the water soluble ingredients followed by the addition of the oil and oil-soluble

ingredients. Different grades are available and Lucas Meyer publishes information on which to use for a given application and how to prepare them.

Multi-layer liposomes are also available from **Lucas Meyer** under its Capt-System trade name. This encompasses a number of different systems with active ingredients vectorised at specific targets. According to the product information brochure each phospholipid-based structure has different physical and chemical properties and can be considered as a vector 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. Actives include tocopherol, folic acid, co-enzyme Q10 and phytosphingosine.

Liposystem Complexes from **I.R.A.** are lamellar concentrates that instantaneously form liposomal vesicles when added to water. They are based on lecithin and glycerin and include a wide range of actives like caffeine, co-enzyme Q10, retinol and retinyl palmitate. Variants are also available that include salicylic acid and glycolic acid for chemical exfoliation, DHA for self-tanning and arbutin for skin lightening. Lysofix from **Kemin Industries inc.** is a natural emulsifier extracted from soybeans to provide a lysophospholipid that is also an effective delivery system for cosmetic actives.

Whereas the majority of moisturising agents are topically applied and are expected to work by carrying water into the stratum corneum Ultra Filling Spheres from **BASF Beauty Creations** work by penetrating the upper layers of the epidermis to absorb the water that evaporates from the dermis. Ultra Filling Spheres are composed of two biopolymers: hyaluronic acid of low molecular weight and a polysaccharide called konjac glucomannans of high molecular weight. Cross-linking of both components creates small but highly hygroscopic spheres..

Ultra Filling Spheres are supplied in a base of ethylhexyl palmitate and trihydroxy stearin and are dispersed in the oil phase of emulsions. The spheres penetrate the SC and then rapidly increase in volume as they absorb water from the skin. They are claimed to absorb 24x their weight of water and to expand 17x in volume. The effect is a plumping of the skin from inside out, which smoothes wrinkles and fine lines at the surface of the skin and water loss is inhibited as it is retained within the spheres.

Glycospheres from **Kobo Products** are biomimetic vesicles that allow entrapment, protection and transport of cosmetic active ingredients in the upper layers of the stratum corneum. Glycospheres are made up of three parts: a hydrophilic solid cationic core of the cross-linked polysaccharide palmitoyl hydroxypropyltrimonium amylopectin/glycerin crosspolymer, a middle lipophilic layer of fatty acids and an external layer of polar lipids. Glycospheres entrap hydrophilic active ingredients which are retained by high energy ionic bonds until released in the skin under increased ionic charge. Alternatively lipophilic active ingredients can be loaded into the middle layer and in both cases the active ingredients are protected and their stability and activity greatly enhanced.

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Induchem AG supplies Unispheres, which are a mixture of mannitol, lactose or xylitol and microcrystalline cellulose. Unispheres soften with water but retain their shape until rubbed onto skin or hair, when they break easily, releasing the active contents. Standard Unispheres are available with a wide variety of contents including vitamins A & E and co-enzyme Q10 and each standard bead is available in a variety of colours to visibly enhance the products in which they are incorporated. Induchem has produced an informative brochure detailing optimum formulating conditions and handling procedures for Unispheres during manufacture.

Microencapsulation is a much-used method for improving delivery systems: natural ingredients, essential oils and vitamins are encapsulated to protect them from the deteriorating effects of the environment or for optimal release and performance in the final product. Emollients used in skincare and hair care products can be encapsulated for added product features and to improve handling properties. Encapsulation can help mask odours or to retard evaporation of volatile ingredients such as fragrance oils, which can dramatically increase the useful life of fragrance-based products such as room freshener sprays.

There are many techniques for encapsulation including complex coacervation, whereby encapsulation takes advantage of the reaction of aqueous solutions of cationic and anionic polymers such as gelatine and gum acacia. Interfacial polymerisation is characterised by wall formation via the rapid polymerisation of monomers at the surface of droplets or particles of dispersed core material. Another method is to form an o/w emulsion where the aqueous portion of the emulsion is rich in a water-soluble polymer that gels when cooled. The emulsion is forced through small holes in a rotating cup in an oil bath and resulting droplets are cooled to form gelled polymer-matrix beads containing dispersed droplets of oil that are dried and collected. **Microtek Laboratories** of Ohio, USA, specialises in these and other encapsulation techniques and services a wide range of industrial applications including microencapsulation of key ingredients for the personal care industry.

I.R.A. offers encapsulated active ingredients based on cyclodextrin and trade named Cyclosystem Complexes. Cyclodextrins are cyclic oligosaccharides obtained from enzymatic digestion of starch that form inclusion complexes around the active ingredient. This is held in equilibrium until topical application when molecules of the active undergo slow but sustained release. I.R.A. claims that Cyclosystem Complexes increase the bio-availability of an incorporated active, show improved activity based on time-release effect and increased stability of actives as they are protected from chemical and physical attacks in the complex environment.

Caffeine is a popular additive for products designed to treat cellulite and improve the microcirculation system but it is not very water-soluble. The **Biogenics Company** of Korea has rendered caffeine water-soluble at up to 10% by encapsulation technology. Caffeine is encapsulated within an oligomer complex comprising maltodextrin, urea, xanthan gum and hydroxyethylcellulose. At 5% concentration it remains transparent in water and aqueous gels and experiment shows that it is readily absorbed through the epidermis.

The **Biogenics Company** has used the same encapsulation technology to deliver epigallocatechin gallate in a stable and water-soluble form. Epigallocatechin gallate is the principal antioxidant active from green tea but it is not very water-soluble or stable, however by encapsulating it in an oligomers complex Biogenics has overcome these dual problems. The technology has also been used to render salicylic acid water-soluble at up to 4% without loss of efficacy in its antimicrobial and exfoliant properties. Trade named Salic-210 it contains salicylic acid, polydextrose, dextrin, amyl pectin and niacinamide.

Tagra uses different kinds of acrylic and cellulose polymers saturated with functional carboxy- and hydroxy- groups, which form microcapsules when added to cosmetic formulations. They are said to convert liquid active components into a dry solid system, to protect and stabilise reactive substances from degradation and to facilitate handling. Numerous versions are available from Tagra including ones containing, retinol and retinol palmitate, ascorbic acid, tocopheryl and essential fatty acids. There are also variants that encapsulate essential oils and cosmetic pigments.

Through an exclusive multi-capillary injection technology, **Provital, S.A.** has obtained a three dimensional matrix that retains actives and controls their sequential release on the skin. The matrix is obtained from the seeds of Caesalpinia spinosa that are rich in galactomannans. This matrix forms part of Hydromanil and due to its structure the oligosaccharides are retained inside the matrix. When Hydromanil HGL is topically applied the oligosaccharides enter in direct contact with the skin and are slowly released from the matrix exercising their moisturising action over time.

Oleosomes are structures found naturally in oil bearing plant seeds and serve as natural storehouses of energy used by the seed until germination. They are found in virtually all crops, including safflower, almond and sunflower. Oleosomes are spheres 1-5 microns in diameter, which consist of a centre core of emollient plant oils and vitamin E, surrounded by a phospholipid membrane and stabilised by a protein coat. **Botaneco** has developed and patented a large scale, process to extract oleosome structures intact and they are supplied under the trade name Hydresia.

Hydresia SF2 are oleosomes extracted from safflower oil that can act as the primary emulsifier at use levels of 3-5%, contributing to enhanced product stability and supporting natural claims. Although products containing oleosomes absorb quickly into the skin and can replenish skin lipids, clinical studies show that oleosomes are significantly milder on the skin when compared to ethoxylated non-ionic emulsifiers.

To oleosomes, niosomes and liposomes we can now add Florasomes from **Floratech**, which are soft spheres of jojoba esters which deliver active ingredients such as vitamins, fragrances, pigments, and enzymes directly to the skin. They are approximately 1mm in diameter and it is recommended that they are suspended in a gel network using a crosspolymer thickener such as carbomer that creates polymeric links throughout the continuous phase. It is claimed that Florasomes enable micro-sized droplets of oil to be delivered from an aqueous gel without using solubilisers or sacrificing clarity. They are broken up on application to release their contents and at the same time deliver emolliancy from the jojoba esters.

There are even more members of the *~somes* family and a presentation by **Naturalis Life Technologies** shows the structure and properties of phytosomes, pharmacosomes, ethosomes, sphingosomes and proniosomes, all of which have the same basic vesicle structure. **Naturalis** supplies proniosomes, which are based on PEG-free non-ionic emulsifiers with a maltodextrin or similar coating and either cholesterol or lecithin. They are supplied as a semi-solid liquid crystal gel or as a dry granular powder, which on hydration form niosomes. The presentation goes into the composition, structure and applications in detail and also shows the results of skin permeation studies.

The final *~somes* to appear in this feature are Rovisomes from the **Rovi Company.** Rovisomes consist of an external, lipophilic membrane, which surrounds the internal, hydrophilic nucleus. Rovi claims that Rovisomes consist of a phospholipid comprising 80 % phosphatidylcholine. The fatty acid of these phospholipids is mainly unsaturated linoleic acid, which provides the liposome with a flexible membrane that enables deeper penetration of the stratum corneum and epidermis.

Still based on phospholipids but entrapping oil and oil-soluble actives within their central core Lipodisq from **Malvern Cosmeceutics** is a biodegradable particle system developed specifically to deliver oily or lipophilic active agents. The outside of the Lipodisq consist of an intensely hydrophilic shell to ensure water solubility surrounding a hydrophobic core. They are smaller than traditional liposomes, ensuring better skin penetration to deliver fat soluble vitamins and botanical extracts into the stratum corneum. The outer layer of the skin therefore acts as a reservoir for the active substance ensuring a more even release profile as the Lipodisq degrades slowly, releasing its contents into the deeper layers of the skin.

NuNu gel from **Koda** uses new technology to provide effective moisturisation from clathrates of galactoarabinan acrylate and glycerol. The galactoarabinan acrylate polymers encase water molecules in a cage-like matrix from which water cannot escape until the structure is destroyed. When applied to the skin the equilibrium of the clathrate matrix is disrupted by the salts and acid pH of the skin, breaking the structure and releasing the water and water-soluble active materials. Koda claims that because of NuNu gel's unique random distribution of galactoarabinan acrylate and pure galactoarabinan in the matrix structure it effectively works towards reducing the appearance of fine lines and wrinkles. The acrylate polymer forms the gel clathrate while the pure galactoarabinan provides bioactivity upon release to the skin.

Delivery skin benefit agents via wash-off products is a challenge that **Amerchol** claim to have overcome by the use of its SoftCat SK Polymers. SoftCAT SK Polymers have greater emollient deposition efficiency than traditional cationic polymers, potentially resulting in improved skin hydration and the alleviation of skin dryness. The Amerchol brochure on SoftCat SK Polymers describes the deposition of sunflower oil and ethylhexyl methoxycinnamate from shower gels. They can also deliver surfactant-soluble ingredients such as fragrances to skin and have the ability to form crystal-clear formulations. There are four variants of Softcat SK Polymers and although all four have the INCI designation Polyquaternium-67 they have undergone different levels of hydrophobic substitution to modify their individual properties.

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Delivering colour was mentioned in the opening paragraph: a little different from the usual are the so-called Magicolours from the **Biogenics** company of Korea. They consist of iron oxide colours encapsulated in such a way that they appear colourless until rubbed onto the skin when the capsule wall is disrupted and the colour revealed. They are recommended for dispersal in water-in-oil and water-in-silicone emulsions to produce novel make-up effects.

A patent filed by Avon [Ref 2] describes iron oxide pigments encapsulated in a layer of silicon oxide such that they have a refractive index of about 1.4 - 1.6. This closely matches the refractive index of skin and the pigments appear more transparent and natural looking. **Ch. Hansen** of Denmark encapsulates food colours to protect them against adverse pH conditions during food processing. Based on natural colours they have improved stability to light and oxidation and are available in water and oil dispersible forms.

Many of the materials described are certified by Ecocert and in every case the supplier has provided extensive information about the material and the results of *in-vitro* and/or *in-vivo* testing to show that the material can comply with Weicher's 4Rs maxim for effective skin delivery systems.

Ref. 1 Wiechers, J.W., Skin Delivery Systems, 2008 ISBN 978-932633-37-5

Ref 2 USP 8,277,785, Cosmetic compositions with encapsulated pigments and a method for using

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