

## Delivery Systems

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Previous features focused on skin care and natural actives and on enhancing SPF values in sun care, all of which benefit from delivery systems formulated to target specific sites on application and that is the focus of this feature.

**Infinitec Activos** is a company that specialises in delivery systems and has worked to transfer medical and pharmaceutical technologies to the cosmetic field. Infinitec maintains that delivery systems should provide a better response over time by improving the bioavailability of the active. Based on a system used to target and kill cancerous cells it has developed Cosmetic Drones, also called ligand-mediated targeting, as actively-targeted delivery systems. Infinitec describes it as utilising affinity ligands on the surface of carrier particles for specific retention and uptake by receptors on targeted cells. Cosmetic Drones ligands are peptides and can be actively-targeted to keratinocytes, fibroblasts, melanocytes, skin neurons and adipocytes and can release various active ingredients for multiple cosmetic applications. To help describe the Cosmetic Drones system **Infinitec** has produced a YouTube presentation that can be viewed at <https://youtu.be/5YeRLPk6Szw>.

One of the many delivery system from **Infinitec** is **Activys** based on polyunsaturated fatty acids from marine algae. **Activys** has a flexible structure consisting of saturated and unsaturated fatty acids, which allows greater penetration into deep layers of the skin for release of its active content. The delivery system itself is then metabolised and has anti-inflammatory properties. Currently two variants are available; **Activys Anti-pollution** and **Activys Anti-glycation**.

Encapsulated delivery systems are well known: using micro-sponge technology based on cellulose **Amcol** has developed **Microsponge Natural**. Active ingredients are isolated deep within the core of the **Microsponge Matrix**. Through a combination of friction and diffusion, the actives are steadily released from the matrix providing sustained release of the active as well as reducing irritation. **Microsponge Natural** is an off-white free-flowing powder that can be readily dispersed in gels, emulsions and powders and is available loaded with a variety of actives. An example is **Microsponge N Retinol**, which showed a 30% reduction in wrinkles versus the baseline for panellists in a clinical trial and there was also a significant reduction in irritation. Other **Microsponge** ingredients include salicylic and glycolic acids and tea tree and other plant oils.

**Glycospheres** from **Kobo Products** are a delivery system that provides protection and enhanced stability of both hydrophilic and lipophilic active ingredients. They comprise supramolecular configurations that are organised around a solid inner core made of hydrophilic, modified starch coated with a lipophilic layer of fatty acids. The core contains cationic groups making **Glycospheres** an ideal system for anionic, hydrophilic actives such as enzymes that can be entrapped within the inner core. **Glycospheres** can also entrap and deliver lipophilic ingredients through cohesion between the lipid layer and polar lipids around the periphery of the sphere. Many variants are available from **Kobo** including **Gs-AHP** loaded with acetyl hexapeptide-8, **Gs-BC** with beta-carotene and **Gs-PPY** containing papain.

**SUNPMMA-P** from **Sunjin Beauty Products** is a porous polymer microsphere [INCI: Methyl methacrylate crosspolymer] with an average particle size of 8 microns and able to absorb 1.7-2.1cc/g oil. It can be pre-loaded with other ingredients such as adenosine, collagen and glycerin to make them easier to incorporate into formulations and released on the skin over time. It can also be

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supplied ready for loading by manufacturers of cosmetic products and a YouTube presentation shows how this is done in the laboratory <https://www.youtube.com/watch?v=Sf8zhoBBSLY>.

**Mibelle Biochemistry** utilises solid lipid nanoparticles for improving peptide delivery into skin. They enable the use of physiologically acceptable lipids and the avoidance of organic solvents in the preparation process, ensuring protection of sensitive molecules from the environment and imparting controlled release characteristics. The actives are produced by hot high-pressure homogenisation of hydrogenated lecithin with shea butter as a molten lipid carrier for the hydrophilic peptide. In this way the physicochemical properties of the resultant product, such as particle size, entrapment efficiency and in vitro release are optimised. The method was used to prepare Perfection Peptide P7 with proven anti-aging properties [Ref 1]. The latest offering from Mibelle based on this technology is SensAmon P5, described as a TRPV1 inhibitor peptide from sea anemone that reduces sensitive skin reactivity to protect it from overreacting to environmental stimuli.

Nano-lipid carriers is description given to its eCapsules system of delivering actives from a matrix of marine polymers by **Naturethic**. They comprise biodegradable and organic solid lipids in a matrix of marine polymers. Depending on the lipophilic nature of the material they may have an active enriched lipid core, an active-enriched lipid shell or a combination of both. eCapsules are available already loaded or Naturethic offer a bespoke service to customers.

Skin is a patchwork of dry, normal and oily zones, depending on the part of the body, the density of the sebaceous glands, the exposure to external aggressions and an individual's genetic make-up, suggests **BASF**. Affinisphere from **BASF** is a delivery system with improved affinity for different skin zones that releases an active ingredient where needed. Affinisphere contains the sebum regulating molecule, zinc gluconate, and is coated with fatty acid chains on the surface to provide increased affinity for the lipid-rich areas of the stratum corneum [INCI: Aqua, butylene glycol, xanthan gum, sodium stearate, atelocollagen, zinc gluconate, sodium hyaluronate, sodium chloride]. The microspheres are biodegradable and undergo enzymatic digestion by the skin's microbiome to release the active.

**BioGenics** encapsulates a series of actives to make them more stable. For example, epigallocatechin gallate (EGCG) is the most effective catechin in green tea and acts as a powerful antioxidant. However, EGCG has poor solubility in water and can discolour easily due to oxidation and decomposition. BioGenic EGCG-200 uses micro-emulsion technology to solubilise EGCG and the EGCG is stabilised using lipophilic and hydrophilic stabilisers. Another example is caffeine, which is used in cosmetics to enhance microcirculation and help to reduce cellulite, however, it has poor solubility in water. BioGenic Caffeine-210 uses oligomer complex technology to solubilise caffeine and the molecular scale complex enables the caffeine to be rapidly absorbed through the skin.

Sveltine from **BASF** are plant liposomes composed of soy lecithin surrounded by a matrix of marine collagen and glycosaminoglycans. The surrounding layer has a stabilising function and reinforces the liposome bilayers, preventing their deterioration until needed. The slimming complex is concentrated in the core of the liposome and comprises caffeine for activating lipolysis, escin for improving cell drainage, carnitine for activating fat degradation and Centella asiatica extract for restructuring the dermis.

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Liposomes are one of the most popular methods of improving skin penetration. Lipodisq Technology from **Malvern Pharmaceuticals** offers a number of benefits over the more traditional phospholipid liposomes. They are usually more stable and robust in formulations and offer the advantage of being transparent when formulated into clear aqueous systems, even if the active contained in the Lipodisq is a hydrophobic ingredient. The structure of Lipodisq is based upon natural high-density lipoproteins responsible for transporting fats around the body. Like their natural counterparts, they are biodegradable, being formed from membrane phospholipids from vegetable sources that enzymatically break down in the skin. A wide range of actives including ascorbyl palmitate, retinol and niacinamide can be incorporated into Lipodisq for enhanced delivery. They are also available loaded with dihydroxyacetone for improved self-tanning products and a bespoke service is available.

**E.G. Actives** has a range of phospholipid stabilised products, which act as selective and controlled transport systems for actives to the skin. They are shown to increase the absorption and penetration of the active ingredient as well as increasing their stability. Olive Active Maslinico LPD helps to rejuvenate the skin cells and enhance the denseness of the skin and its firmness, and the Olive Active Hidroxitirosol LPD helps boost SPF, as well as soothing and repairing the skin. It is an effective electron scavenger with a pronounced anti-oxidant effect that offers several advantages over Q10 and vitamins C and E including better stability and skin whitening.

Make your own liposomes! This is made possible using Pro-Lipo Neo from **IFF-Lucas-Meyer**, which is a ready-to-use mixture of selected phospholipids already organised in lamellar bilayers by their solubilisation 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 mainly bilamellar liposomes with 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. Able to entrap hydro-soluble and lipo-soluble active ingredients, Pro-Lipo Neo technology enables the user to customise liposomes by selecting the type and concentration of the ingredients to entrap.

Cytovector Ferulic from **BASF** is an intracellular delivery system for targeted action that delivers ferulic acid directly to the interior of skin cells. It contains nanometric liposomes comprising 5% soy lecithin and 2% quaternised soy proteins embedded in a 1% hydroxyethyl cellulose gel. These highly positively charged proteins form strong ionic bonds that provide elevated affinity for skin cells, even in low concentration and in a broad pH range. Tests comparing percutaneous absorption of Cytovector liposomes with standard ones showed that although both penetrated to a depth reached by six tape strippings the standard liposome was readily rinsed away whereas Cytovector was very wash resistant. It is recommended for reducing pigment spots and evening the complexion.

**Bicosome** is a start-up Italian company that develops and commercialises high-performance cosmetic and dermo-pharmaceutical ingredients based on its Bicosome technology. Bicosomes resemble the skin's natural biological structures and naturally recognise the different skin environments and respond accordingly. When applied to the skin, the structures penetrate through the intercellular spaces until they reach their target layer. Once there the bicosomes reassemble into bigger aggregates, releasing the active ingredients. Various examples are available including Bicotene Antiox for sun repair and protection and Bicowhite Complex that whitens and brightens skin and specifically reduces melanin levels in hyper-pigmented areas. The bicosomes remain

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anchored in the skin, for long-lasting effects and become integrated into the skin's lipid matrix, strengthening the tissue until re-moved by the skin's natural desquamation process.

Niosomes from **Naturalis** are a vesicle delivery system developed with a bilayer formed from polyglyceryl esters. These single chain surfactants form a vesicle that is extremely elastic and deformable and is therefore able to provide maximal skin penetration. Niosomes are highly hydrophilic and thus penetrate the skin by following the osmotic gradient. This encapsulation system increases active delivery, provides sustained and controlled release of actives and reduces skin irritation.

Phytosomes from **Indena** are a delivery system determined by the interaction in a solvent of a botanical derivative with natural phospholipids. They differ from liposomes where the active compounds are dissolved in the cavity of the micelle and the ratio between the active compounds and the carrier is about 1:10. In Phytosomes the active compounds are part of a molecular dispersion with H-bonds, van der Waals and dipolar intermolecular forces and the ratio between the active compounds and the carrier is about 1:2-3. They have a high affinity for skin and provide a reservoir effect by slowly releasing their active content. Many variants are available from Indena including Phytosomes containing *Boswellia serrata*, *Centella asiatica* and *Gingko biloba*.

While the majority of delivery systems are targeted at improving skin penetration the opposite effect is required for delivering sun protection molecules where an unbroken film on the skin surface is required. The CosmoSurf range from **Surfatech** are a novel series of multi-domain polymers, a term used to describe any polymer that incorporates at least two groups that vary in solubility or physical state. CosmoSurf polymers vary in solubility between different solvents and when the solvents evaporate the CosmoSurf Polymer will "flip" phases and form an even film on the skin. The added advantage of CosmoSurf polymers is that the film also offers a degree of water resistance and can be used to deliver other hair and skin care actives. **Surfatech** also produces Spider Esters that are multi-legged molecules rooted to a central body. The extremities of the legs and the body are oil soluble but contain polyoxyalkylene groups in the middle of the leg chains. This arrangement allows actives that are soluble in polar solvents to be incorporated into the oil phase of a formulation.

Improving the delivery of water-resistant films containing UV absorbers is also the claim made for Avalure Flex-6 Polymer from **Lubrizol**. It is a non-ionic hydrophobically modified polyurethane [INCI: Polyurethane-62, trideceth-6] with a hydrophilic backbone and hydrophobic chain ends that is water-dispersible and thickens by associative technology. It is pH tolerant between pH 3-7 and salt tolerant up to 4%. It is particularly recommended for sun protection products containing metal oxides that should be applied as an even film on the skin surface. A detailed presentation describing the technology of Avalure Flex-6, Avalure AC-120 and Avalure UR-450 polymers and their use in delivering film-forming properties in various applications is available from Lubrizol and its distributors.

Another group of materials claiming to deliver water-resistance to sunscreen products is Viamerines from **Aldivia**. They are natural polyglycerides synthesised from vegetable oils using green chemistry principals and three variants are available. They can be used with metal oxide sunscreens in anhydrous products and with organic sunscreens in emulsions. Tests show that adding 2.5% Viamarine WH36 [INCI: Hydroxystearic/linolenic/oleic polyglycerides] to an emulsion allows it to pass the standard water-resistance test and the addition of 5% increases SPF value by 47%. As with most materials featured in this article, a descriptive presentation is available from the supplier.

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Encapsulating organic UV absorbers is a way of delivering them in a form that may protect skin from irritation and the absorbers from losing efficacy through photodegradation. An example is SunCat MTA from **Bio-Nest**, which is a double encapsulate containing a pre-solubilised mixture of sunscreens to give a micronised core enwrapped in a double-layered sphere, 1 micron in diameter. The spheres have a negatively charged outer surface and they form a continuous even layer when applied from an emulsion on the skin. SunCat MTS [INCI: Aqua, ethylhexyl methoxycinnamate, butyl methoxydibenzoylmethane, octocrylene, phospholipids, 1,3-butylene glycol] aids formulation as it is a specific ratio of sunscreens premixed and optimised to achieve desired SPF and is added in the final stages of product manufacture. It provides a longer and safer skin residence time; high levels of oil are not required as the absorbers do not need additional solubilising and they allow the skin to breathe freely. Neither is skin penetration required for colour cosmetics and the same technology that improves application of sunscreens to the skin may also be used for even applications of pigments.

ATL Coasphers from **Advanced Technology Laboratory** are a wet type of sphere encompassing oil or fragrance droplets in a capsule of fish gelatine that comes in five standard sizes and a wide range of colours. Coasphers can be added to water-based products to give a visual effect and a burst of fragrance or a soothing application of oil to the skin. ATL Magicspheres are a wet type sphere prepared from hydrogenated lecithin and wax that impart an oily, silky feeling to the skin. They are amphiphilic, containing hydrophilic materials absorbed in their core and hydrophobic ingredients in the outer shell. Different combinations of active materials are available and the combination of water and oil provides intensely hydrated skin.

Providing prolonged delivery of actives from a surface film that also inhibits water loss is the claim made for Micropatch Serine from **BASF**. Micropatch technology is based on the association of different bio-polymers to form a three-dimensional micro-network at molecular scale in which actives can be entrapped. This structure is maintained when incorporated in a water-based cosmetic formula and on application it protects skin from drying by limiting trans-epidermal water loss and it provides a smooth and even film on the surface. Micropatch Caffeine delivers caffeine to stimulate lipolysis by increasing cellular levels of cyclic AMP. Cyclic AMP activates protein kinase A and subsequently activates a series of cascading effects that finally lead to increased lipolysis and a reduction in fatty tissue. It is recommended for contouring face care products, anti-cellulite treatments and under eye bag correctors. Other Micropatch ingredients from BASF include Micropatch Serine that delivers the amino acid serine directly to the skin surface to further improve skin hydration; Smartvector UV-CE for releasing anti-oxidant vitamins and Cylasphere Retinol agar micro-capsules for controlled retinol release. For treating dry scalp and hair BASF produces Micropatch H2O that contains hyaluronic acid, pullulan and an alginate from brown seaweed plus trehalose, glycerin, serine and urea to hydrate the scalp and provide a silky-smooth feel.

Other ways of improving delivery of actives include incorporating penetration enhancers and by careful selection of the oil phase and emulsifying agent. Transcutol CG from **Gattefosse** is ethoxydiglycol and studies show that 2% added to a spray tan formula significantly improves the quality of the final tan. Hydrolyte 5 from **Symrise** is pentylene glycol and tests show it to improve the bioavailability of actives such as caffeine and carnosine. Sabosol RF from **Sabo** [INCI: Coco-glucoside, squalene, sodium surfactin] is a natural biomimetic skin lipid product designed to protect and restore skin barrier. Silisoft Spread MAX from **Momentive** is a non-ionic organo-modified siloxane copolymer that can reduce the surface tension of personal care formulations improving the spreading of actives and inorganic pigments on skin and hair.

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Xtend and MC<sup>2</sup> are new products from **Sinerga** that are different blends of extracts with tetrahydropiperine (THP) extracted from black pepper. The THP helps increase the skin permeation to increase the effectiveness of the actives in the formulation. In Xtend [INCI: Glycerin, Pueraria lobata root extract, alcohol denat., tetrahydropiperine, Uncaria tomentosa extract] the effect of the THP permeating the skin enhances the anti-inflammatory and collagen renewing properties of the extracts. Sinerga describes MC<sup>2</sup> as a skin bio revitaliser that counterbalances daily energy drops by waking up and empowering cellular metabolism. It is based on ginseng saponins and açai polyphenols [INCI: Glycerin, alcohol denat., tetrahydropiperine, Panax ginseng root extract, aqua, Euterpe oleracea fruit extract].

Inutec SL1 [INCI: Glycerin, inulin lauryl carbamate] from **Gova** is a highly efficient o/w emulsifier that forms very small oil droplets. A study clearly shows that delivery of the active ingredient, Centella asiatica, was 50% greater when formulated into an Inutec SL1 emulsion compared to a traditional emulsifier system. Emulsiphos [INCI: Potassium cetyl phosphate, hydrogenated palm glycerides] from **Symrise** promotes the formation of liquid crystalline structures similar to skin lipids. By their nature, the liquid crystalline structures of such emulsions do not disrupt the skin lipid structure and help the skin to maintain its natural moisture content. Amphisol K from **DSM** is potassium cetyl phosphate that forms liquid crystals. It has proved very efficient in the dispersal of metal oxide sun filters on the skin.

For something quite different SalSphere SalOxy from **Salvona** is a micro-sphere delivery system encapsulating a blend of perfluorocarbon molecules loaded with oxygen. On application oxygen is released to form a rich, foaming lather that is claimed to encourage the growth of new cells and production of collagen. It is also said to enhance overall hydration and to help uneven skin tone look brighter and more luminous. SalSphere SalOxy is a combination of decafluoropentane, water, polyhydroxystearic acid, isononyl isononanoate, cocamidopropyl PG-dimonium chloride phosphate, Butyrospermum parkii (shea butter), glyceryl stearate, stearic acid, cetearyl alcohol, sodium lauroyl glutamate and cocamidopropyl betaine dimethylamine. Although supplied as a ready to use product it can also be used as base for additional actives and aesthetics.

Ref 1 F. Suter, D. Schmid, F. Wandrey, F. Züllli, Heptapeptide-loaded Solid Lipid Nanoparticles for Cosmetic Anti-Aging Applications, European Journal of Pharmaceutics and Biopharmaceutics (2016)

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