Opportunities for (bio)encapsulation in cosmetics

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INTRODUCTION

As always, it is difficult to separate perception and reality in cosmetics, even for what benefits (bio)encapsulation can offer in this ever-changing, trend-sensitive field. But the benefits are real, albeit sometimes somewhat overstated. This overview presentation will focus on the skin delivery benefits of encapsulation techniques, in particular on new opportunities offered by drug targeting via hard encapsulation techniques.

Although the perception of the general public is that everything can just be claimed in cosmetics, the reality is quite different. The cosmetic industry is in fact heavily regulated. The legal definition of a cosmetic in Europe is "Substances or preparations intended to be placed in contact with the various external parts of the human body or with the teeth and the mucous membranes or the oral cavity, with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odours and/or protecting them or keeping them in good condition. They must not cause damage to human health when applied under normal or reasonably foreseeable conditions of use" (6th Amendment [93/95/EEC] to the European Cosmetic Directive [78/68/EEC]). The law also requires that "sufficient and appropriate" evidence is provided for the claims that are being made. Therefore, efficacious products are required that clean, perfume, change the appearance, correct the body odour, protect the body or keeps it in good condition. These effects are caused by the incorporation of active ingredients in cosmetic products.

Most cosmetic scientists think that the only thing one needs to do to ensure that an efficacious product is obtained, is to include the right concentration of the active in the formulation, but new formulation approaches like Formulating for Efficacy (Wiechers J.W., 2004) have shown that this is not correct. A 1% formulation optimized for delivery may deliver more than a 2% formulation that is not optimized for skin delivery. The formulation has an enormous influence on the performance of the active ingredient.

There are three main routes for skin penetration into the skin. The most prominent route it that of the bulk of the stratum corneum, the so-called intercellular pathway. This model has often been compared to the 'brick-and-mortar' model where the bricks are the corneocytes and the mortar the intercellular lipids. These lipids (ceramides, free fatty acids and cholesterol and some cholesterol sulphate) constitute the main barrier towards skin penetration, especially when they appear in the orthorhombic packing. Alternative routes for skin penetration are the two shunt pathways, the transfollicular route (along the infundibulum surrounding the hair) and the appendageal route (via the sweat glands). Which route is taken depends on the polarity of the penetrating molecule, its molecular weight and the lack or presence of charged groups.

Skin penetration can be divided into a couple of sequential and different steps. First a chemical diffuses within the formulation towards the skin surface, the stratum corneum. Thereafter, it partitions into the stratum corneum and then diffuses within the stratum corneum towards its lower layer, the stratum corneum/viable epidermis interface. From there, it partitions into the viable epidermis. Then it diffuses through the viable epidermis, partitions into the dermis, diffuses through

the dermis, penetrates into the fat layers or into the blood vessels. In between, it can bind to proteins, receptors, enzymes where it can be bound, metabolised, etc.

There are a couple of different approaches that the cosmetic formulator can take to enhance the delivery of active ingredients into the skin. First of all, the partition coefficient of the formulation needs to be matched with the partition coefficient of the active and the skin by selecting the right polarity of the formulation. In short, this means that the active must prefer to be in the stratum corneum, the most outer layer of the skin, over being in the formulation. This creates a driving force for the active to leave the formulation and enter the skin. Second, skin penetration enhancers can be used that temporarily reduce the barrier function of the stratum corneum, thereby allowing more chemical to enter the skin. This is much more frequently used in pharmaceutical formulations than in cosmetic product forms as this approach normally results in transdermal delivery rather than dermal delivery. Finally, one can reduce the path length of diffusion as is done, for instance, when using microneedles (Wiechers J.W., 2008).

So, where do (bio)encapsulated materials fit in? They represent some of the cosmetic delivery systems that are available to the cosmetic formulator. Skin delivery is the process of getting the right chemical to the right site at the right concentration for the correct period of time (Wiechers J.W., 2008). Delivery systems are systems that help to achieve that and should therefore, by definition, affect one of these four aspects of delivery. Encapsulation systems are most frequently used to affect the first aspect, namely, to protect a chemically labile active ingredient from degrading prior to reaching its target site in the skin. Liposomes and cyclodextrins are a prime example of that. Figure 1 shows the enhanced stability of linoleic acid encapsulated in cyclodextrins (Regiert M., 2008). When using a 4 to 1 ratio of cyclodextrin to linoleic acid, the shelf-life of the chemically labile linoleic acid is greatly prolonged. Liposomes often serve a similar protective function, although they are also claimed to enhance the skin penetration of active ingredients as shown in Figure 2. Blume claims this to be regulated via the water gradient (Blume G., 2008). How this is working on the molecular level is still a topic of debate. An interaction of liposome (components) with the skin lipid organization in the skin that constitutes the main barrier in the skin is one of the proposed theories. One thing is clear by now; liposomes do not penetrate intact as research with the flexible liposomes has indicated (Blume G., 2008 ; Loan-Honeywell P., 2008).

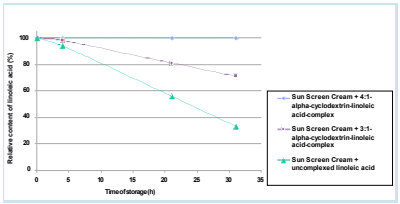

Figure 1 : *The stability of linoleic acid is increased by forming a 4:1 complex with α-cyclodextrin. Reproduced with permission from Regiert M. (2008).*

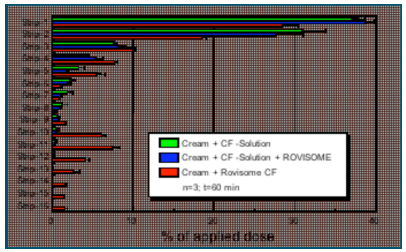

Figure 2 : *Skin penetration of carboxyfluorescein (CF) incorporated in a cream, the same cream with added empty liposomes, or CF incorporated within these liposomes. The skin penetration profile is fundamentally different when CF is incorporated within the liposomes. Figure kindly provided by Dr. Gabriele Blume (2002).*

NEXT PRODUCT APPLICATIONS FOR ENCAPSULATION IN COSMETICS

The recent work on transfollicular delivery has demonstrated that this route of skin penetration is much more prominent that hitherto anticipated. It can be as much as 60% of total skin penetration that penetrates via the transfollicular route (Frum Y., 2007). Interestingly, it was found that micro- and nano-particles accumulate in the infundibulum (the opening where the hair follicle resides) and can stay there for a considerable period of time, for as long as 10 days (see Figure 3)!

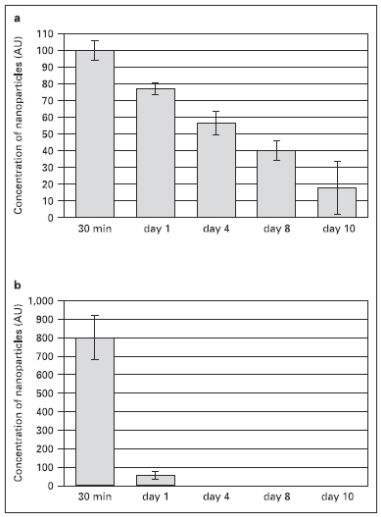

Figure 3: *Kinetics of the storage of nanoparticles a) in hair follicles and b) in the stratum corneum. Note that the concentration of nanoparticles is lower in the orifices surrounding the hair follicles but that they reside there much longer than in the stratum corneum, where the decline is much faster. Reproduced from Lademann, J. et al. (2006).*

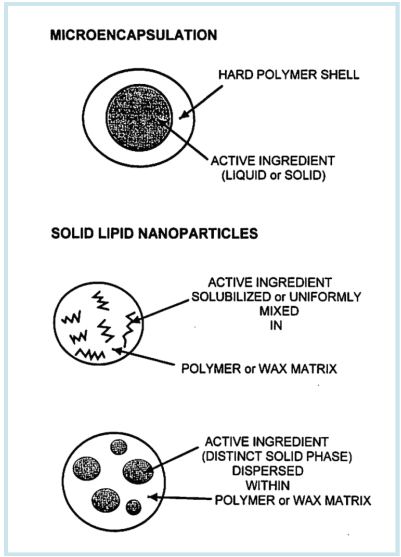

Figure 4 : *Schematic comparing microcapsules with SLN's.*

That is why new cosmetic delivery systems are suggested in which solid lipid nanoparticles (SLN's) and nano-structured lipid carriers (NLC's) (Souto E.B., 2008) are suggested to combine the benefits of each. When applied on the skin, SLN's and NLC's will accumulate in the infundibulum where it will stay behind, while the rest of the formulation is being removed. The active ingredients in the SLN's and NLC's can subsequently be released from these systems by either gradual dissolution of the carrier into the surrounding sebum, or by release from the system into the sebum. This offers new product possibilities for especially those chemicals that work in or near the infundibulum, such as anti-acne preparations, hair-growth and deodorant products (Wiechers J.W., 2009).

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