| O1-1 | **26 years of encapsulation for cosmetic applications and we still expect a lot!** |  |
|---|---|---|

**Perrier E.**
LVMH Recherche, 185 Av de Verdun, F-45800 St Jean de Braye, France,
eperrier@research.lvmh-pc.com

## INTRODUCTION

Cosmetic is at the interface of several science domains, from cell biology and chemistry, to genetic, image analysis, statistic, going through human sciences such as philosophy, psychology and behaviour. These interactions are even more complex than expected because of quick moving not harmonized legislations and fashions.
In this network of connexion and fast moving tracks, encapsulation is one of the weapons that could be used by cosmetic formulators to innovate, or more frequently, to solve incompatibility problems occurring during their work.

## WHAT ABOUT HISTORY?

### *Roots*

Liposomes are a good example of such science of interfaces: they were first introduced by Parfums Christian Dior in 1984 in a body product to enhance the penetration of some active compounds in the deep part of the skin and to target adipocytes. Such liposomes were co-developed with Orleans University and Pasteur Institute and were already quite elaborated. Sugars with strong affinity of cell membranes were grafted on the surface of such liposome to contribute to the expected cell selectivity. The same year, L'Oreal was launching Niosomes which were synthetic liposome formed by using amphiphilic molecules.

In 1986, first microspheres were introduced in a cosmetic product proposed by Gatineau in France. They were made of collagen reticulated by interfacial polymerisation and were encapsulating some active compounds to protect them. Such spheres were around 400 microns and were coloured, in order to provide an aesthetic cosmetic product for consumers.

### *Meaning*

That means that in 1986, the cosmetic industry has already identified many crucial **properties** of encapsulation that are of main importance for customers:

- to enhance penetration for a better efficacy,
- to target some specific cells in order to deliver better
- to protect unstable ingredients
- to use visible encapsulation systems as a marketing tool.

Since that time, encapsulation, vectorization, entrapment have been proposed through many different **tools**: liposomes or vectors with non-polymeric membranes, cyclodextrins, micro- and nano- spheres or capsules or particles, etc…but the main question we have to answer is linked with the historical findings: are their some new properties which have been introduced in cosmetics with those new tools? It is scientifically, technically, interesting to have new tools, new encapsulation systems but are we providing some perceivable innovations to the consumers of cosmetic products and if yes, what are they? Encapsulation is an expensive tool and real proof of efficiency as well as perceivable advantages by consumers are keys to promote their use!

## "PROPERTIES", BETTER THAN "TOOLS"

### *Penetration and bioavailability*

Encapsulation is able to modify the penetration of active compounds:
* by increasing the ability of molecule to penetrate (mostly by using liposomes, or penetration enhancing system..): efficacy of the molecule should be increased,
* by storing the molecule in the upper part of the skin (mostly by using micro or nano spheres): bioavailability is increased.

Innovation is crucial in this area: how to increase the efficacy of active compounds without increasing their concentrations? How to increase the tolerance without decreasing their concentrations? How results are able to be compared in ex vivo or in vivo experiments with already existing encapsulation tools?

Moreover, what material is used to make the membrane and how ingredients are released, practically, on the skin, at ambient temperature, while production of cosmetic formulations includes most of the time, some high temperature steps? How to control exactly where and when active compounds are released?

### *Cell and tissue targeting*

Different encapsulation tools are able to target the delivery of active compounds around some specific cells of the skin (using affinity molecules), to target them in tissues (hair, greasy skin, upper or deeper part of the skin, etc) or to target them inside cells (poly-anionic molecules).
But being more precise is again a key in this area. For instance, less than 1% of the epidermal cells are melanocytes, but only those cells are responsible about melanin formation which provides protection and colour to the skin. Being able to target on a highly specific way those cells would be of major interest, for their inhibition (whitening cosmetic products) as well as for their stimu-

lation (pigmentation and protection, moon-tanning cosmetic products…).
Targeting also means that encapsulation tools used are small and deformable enough to penetrate between the cells in the epidermis: how to develop particle with such properties, to demonstrate such penetration ex vivo and in vivo? What is the "dilution factor" after encapsulation, of active compounds using such vectors? What is the position of such vectors vs the cosmetic regulation on nanos?

***Active Compound protection***
This property is most probably the more difficult to obtain. The incorporation of encapsulation systems in cosmetic formulation represent a great challenge, because of the composition of cosmetic formulations and because of the severity of stability tests performed. As a matter of fact, cosmetic formulations are usually based on a high concentration of water (O/W emulsion and water-based gels), contains surfactants, and are subject to intensive stability studies before they are introduced on the market, both for quality and regulation reasons. For instance, using 45-50°C during 3-6 months stability studies is a classic method to evaluate the stability and compatibility of active compounds in a cosmetic formulation. Loss of more than 10% of active compounds in these conditions induces regulatory rejection of the formulation.
Moreover, the portfolio of active compounds usable for cosmetic applications is quite stable due to regulatory or toxicological constraints. For this reason, the use of already very well known, efficient but unstable active compounds will increase in the future, in case we are able to stabilise them in formulations.
Stabilising means to protect them from other ingredients of formulations or from oxygen because they react oxidize while loosing their properties. Having microspheres membranes impermeable to oxygen would allow, together with the use of the right antioxidant, to protect such sensitive molecules.

Some capsules may have this impermeable property, but produced from wax, they trap permanently active compounds without releasing them, which do not allow a good bioavailability and efficacy, and reject their ability to be used in an "efficient" cosmetic formulation.

***Other expected properties***
The success of visible microspheres, simple or double encapsulation, are linked with (cosmetic) fashion. Coloured inert particles of cellulose are now used in mass market cosmetic formulations, to play the same role. They are not microspheres but they look like, and have a very low price.

More important than encapsulation and encapsulation yield themselves, we believe that the way active compounds are RELEASED is the most important question to answer. In this area, very poor studies have been performed, while this is the key for a reasonable cosmetic use of such encapsulation systems. What are the ingredients that are used to make the membrane of such spheres? Are those ingredients (polymers, cross linking agents…) acceptable or usable in the skin metabolism, are they safe and regulated for cosmetic use? Are they able to be stimulated to induce the opening of the particles and the release of active compounds? To which stimulations could we expect to have active compound release in a cosmetic environment? Are we able to demonstrate now or in the future, some releases linked with UV, with pH, with the microflora composition of the skin, with the proteolytic activities of the different part of the skin? How the new tools could compare with other already existing tools, because we need to increase really the efficiency, not to have something new only….

We are far away from being able to answer to those meanwhile crucial questions. And we only stay, at this stage to the first level of the subject: answering the technical, the scientific needs of encapsulation applied in the cosmetic field. Things are becoming even more difficult when we try to reach the second step, which is "what is perceivable by consumers"? Comparison using positive and negative standards would be appropriate in this scope in the future.

## CONCLUSIONS

Toxicological profiles of active compounds as well as a permanent consumer expectation of stronger and quicker efficacy, will both induce a even more intensive quest of efficient and safe formulations in the future. Those formulations will need to be formulated with the right concentration of active compounds, able to target, to reach and to deliver the right concentrations at the right place, and at the right moment.
The needs are huge, and the market is able to transform laboratory trials into success if the complex environment of cosmetic is understood with humility (regulatory, safety, efficiency…) and if "real", and even better "perceivable" advantages could be obtained and compared with existing systems. We believe that intensive collaborations could allow new tools to be promoted, but we always need to remember that we are looking for new or enhanced "properties", not for new "tools" (encapsulation systems).

## REFERENCES


- Perrier E. et al. (1998) *Cross linked plant protein particles, in particular microparticles or nanoparticles, preparation method and cosmetic, pharmaceutical or food compositions containing same*. European Patent EP0966268
- Perrier E., Hart J. (2005) *Smart vectorizations: enzymatically activated encapsulation technology*. in *Delivery System Handbook for Personal Care and Cosmetic Products*, Meyer R. Rosen (USA), pp798-816.