

This article was published in Journal of Microencapsulation, 33(1), 1-17, 2016  
<http://dx.doi.org/10.3109/02652048.2015.1115900>

*Review*

## Encapsulation of cosmetic active ingredients for topical application – A Review

Francisca Casanova\*, Lúcia Santos\*†

\* LEPABE, Departamento de Engenharia Química, Faculdade de Engenharia da Universidade do Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal

† E-mail: [lsantos@fe.up.pt](mailto:lsantos@fe.up.pt); tel.: +351225081682; fax: +351225081449

Keywords: encapsulation; cosmetics; topical application; controlled release; critical aspects

**Abstract:** Microencapsulation is finding increasing applications in cosmetics and personal care markets. This paper provides an overall discussion on encapsulation of cosmetically active ingredients and encapsulation techniques for cosmetic and personal care products for topical applications. Some of the challenges are identified and critical aspects and future perspectives are addressed. Many cosmetics and personal care products contain biologically active substances that require encapsulation for increased stability of the active materials. The topical and transdermal delivery of active cosmetic ingredients requires effective, controlled and safe means of reaching the target site within the skin. Preservation of the active ingredients is also essential during formulation, storage and application of the final cosmetic product. Microencapsulation offers an ideal and unique carrier system for cosmetic active ingredients, as it has the potential to respond to all these requirements. The encapsulated agent can be released by several mechanisms, such as mechanical action, heat, diffusion, pH, biodegradation and dissolution. The selection of the encapsulation technique and shell material depends on the final application of the product, considering physical and chemical stability, concentration, required particle size, release mechanism and manufacturing costs.

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## 1. Introduction

Microencapsulation has been widely explored by the pharmaceutical, food, cosmetic, textile, personal care, agricultural, chemical, biotechnology, biomedical and sensor industries. There are numerous possibilities to use microencapsulation as a technique to obtain products with high added value and therefore widespread interest has developed in microencapsulation technology (Hammad et al., 2011; Dubey et al., 2009; Wesselingh et al., 2007; Ghosh, 2006; Benita, 2005).

The cosmetics and personal care products sector is a multi-billion dollar international market and has shown great expansion. To be successful in such a competitive and demanding sector, the products must differentiate, which can be achieved by means of using emergent technologies, such as microencapsulation (Martins et al., 2014; Euromonitor, 2011; Michael et al., 2009). Cosmetic and personal care products often contain biologically active substances that are unstable and sensitive to temperature, pH, light and oxidation. Thus these substances may undergo undesired reactions that lead to the reduction or loss of their effectiveness or even lead to the degradation of the cosmetic product. Thus, microencapsulation technologies have been proposed to increase stability, to protect against degradation, and also to direct and control the release of active ingredients used in cosmetic products. In addition, the topical and transdermal delivery of cosmetic active ingredients requires safe and non-toxic means to reach the target destination sites within the skin. Thus, microencapsulation has been used in the development of cosmetic formulations that are more stable, more effective and with improved sensory properties, having found an increasing number of applications in this market (Pardeike et al., 2009; Soest, 2007; Sinko, 2006; Lumsdon et al., 2005; Rosen, 2005; Gallarate et al., 1999). Published patents in the area of microencapsulation suggest that both industrial and academic sectors are urging to explore this area, namely in the fields of cosmetics and personal care products for topical application (Coreana Cosmetics Co. Ltd, 2001; R.P. Scherer Corporation, 1996; Shaklee Corporation, 2000; L'Oreal, 1998; Sunsmart, Inc. and Sibmicro

Encapsulation Technologies, Inc., 1998; Maybelline Intermediate Company, 1999; Conopco Inc. and D/B/A Unilever, 2010; Durand, 1995; Capsutech Ltd., 2008).

This paper reviews current research on encapsulation approaches for cosmetic and personal care applications, focusing on microencapsulation applied to cosmetics for topical use. Examples of reviewed cosmetic ingredients include antioxidants, sun filters, fragrances, moisturizers and anti-aging, tanning and whitening agents. Recent and future developments in this field are addressed, some of the challenges are identified and the importance of various factors involved in the formulation and stabilization of topical preparations are discussed.

## **2. Microcapsules and Encapsulation techniques**

Micro-encapsulation is a process of encapsulating a material containing an active ingredient (core material), in a shell of a second material (shell/wall material), permanently or temporarily. This results in small capsules with many useful properties, termed microcapsules (Figure 1a). Such capsules have diameters between one micron and a few millimeters. Microcapsules whose diameter is in the nanometer range are referred to as nanocapsules (Kaur et al., 2013; Jyothi et al., 2010, Benita, 2005). The small size of these capsules provides a large surface area that is available for sites of adsorption and desorption, chemical reactions, light scattering, etc. This is one positive and important feature of microcapsules (Gutcho, 1976; Arshady, 1999).

Core materials in microcapsules may exist in the form of a solid, liquid or gas phase. Depending on the application, a wide variety of core materials can be encapsulated. The size of the core material plays an important role for diffusion, permeability and controlled release. The shell material can be permeable, semi-permeable or impermeable. Compatibility of the core material with the shell is an important criterion for enhancing the efficiency of the microencapsulation (Estevinho et al., 2013; Hammad et al., 2011; Ghosh, 2006).

The morphology of the internal structure of a microcapsule depends largely on the selected shell materials and the microencapsulation methods that are employed. Microcapsules can be classified as mononuclear, polynuclear or matrix type (Figure 1b) (Chhotalal et al., 2013; Dubey et al., 2009; Ghosh, 2006).

Microcapsules are usually characterized mainly by particle size and shape and encapsulation efficiency. Microcapsules zeta potential, drug loading, solvation, bulk density, tap density, compressibility index, Hausner's ratio (an index of flow ability of microcapsules) and the angle of repose can also be determined (Estevinho et al., 2013; Hammad et al., 2011). The size and shape of the prepared microcapsules can be determined by light and scanning electron microscope. Encapsulation efficiency (content of core material effectively encapsulated) depends on several variables, such as the chemical nature of the core (molecular weight, chemical functionality, polarity and volatility) shell material properties and the chosen microencapsulation technique (Selvaraj et al., 2012; Martins et al., 2010; Jyothi et al., 2010; Gander et al., 1995).

Although a variety of techniques have been reported for microencapsulation, no single process is adaptable to all core materials or product applications. The choice of the most suitable method depends on the application of the microsystem, particle size required, physical and chemical properties of the core and the shell, release mechanism intended, production scale and costs. Thus, appropriate combination of starting materials and synthesis methods can be chosen to produce encapsulated products with a wide variety of compositional and morphological characteristics, and the microencapsulation process must be custom-tailored in order to provide a satisfactory outcome, considering the intended application. Microencapsulation techniques can be broadly divided into two main categories, namely chemical and physical, with the latter being further subdivided into physico-chemical and physico-mechanical techniques (Silva et al., 2007; Wilson et al., 2007). Table 1 outlines common methods used to encapsulate

ingredients and the size of produced particles. Such methods have been described by Dubey et al. (2009), Ghosh (2006), Silva et al. (2007), Wilson et al. (2007) and Fairhurst et al. (2008).

Solvent evaporation/extraction is one of the most commonly used encapsulation techniques at laboratory scale, as it is a simple technique suitable for the preparation of microcapsules loaded with different kinds of cores, both hydrophobic and hydrophilic, however this method is not easily applicable on a large scale, and thus is not widely used for industrial applications. A schematic representation of the solvent evaporation process is presented in Figure 2. In this method a water insoluble polymer is dissolved in a water immiscible volatile organic solvent, like dichloromethane or chloroform, into which the core material is also dissolved or dispersed. The resulting solution is added dropwise to a stirring aqueous solution having a suitable stabilizer to form small polymer droplets containing the encapsulated material. The core material can also be dispersed or dissolved in this aqueous solution instead. With time, the droplets are hardened to produce the corresponding polymer microcapsules. This hardening process is accomplished by the removal of the solvent from the polymer droplets either by solvent evaporation (by heat or reduced pressure), or by solvent extraction (with a third liquid which is a precipitant for the polymer and miscible with both water and solvent) (Li et al., 2008, Hung, 2010; Sri et al., 2012; Dubey et al., 2009; Giri et al., 2012; Freitas et al., 2005).

Spray drying is one of the most common methods used for microencapsulation (Estevinho et al., 2013). This process has some advantages over other methods, such as large equipment availability, possibility of employing a wide variety of encapsulating agents, potentially large-scale production, simple equipment, good efficiency, reduced storage and transport costs and low process cost. Moreover, the process is adaptable to a wide range of feedstock and product specifications, as it can be used with solutions, suspensions, slurries, melts and pastes. Microencapsulation by spray drying is thus a simple and low cost commercial process that has been used to encapsulate mainly flavors (Estevinho et al., 2013), enzymes (Estevinho et al.,

2014a, 2014b, 2012), oils, and pigments, but also thermo-sensitive products, such as microorganisms and essential oils, since the required high temperature is only applied for a very short period of time. A schematic representation of the spray drying process is presented in Figure 3. The ingredient to be encapsulated is added to the carrier (the ratio of core to carrier can be optimized for each individual ingredient) and the mixture is homogenized. An emulsifier may also be added at this stage. This mixture is then fed into the spray dryer with circulating hot air and atomized, which can be made by different types of atomizers: pneumatic atomizer, pressure nozzle, spinning disk, fluid nozzle and sonic nozzle. The solvent (water) is evaporated by the hot air and the shell material encapsulates the core. Small particles are deposited in the collection vessel where they are collected (Chávarri, 2012; Wilson et al., 2007; Bodmeier et al., 1998; Yin et al., 2009).

### **3. Microencapsulation in Cosmetics**

Delivery systems and microcapsules play an important role in the cosmetics and personal care industries nowadays. They offer an ideal and unique carrier system for active ingredients, allowing the controlled and targeted release, isolation and protection of the active compounds, improved stability and efficacy, safe administration, to mask undesirable properties of the active components, such as their odor, and also the improvement of the tactile and visual appearance of a variety of cosmetic and personal care products. Controlled release technologies are used to deliver compounds at prescribed rates, together with improved efficacy, safety and convenience. In these industries there is a constant look for new and novel delivery systems to safely incorporate many of the new and sensitive active ingredients of the cosmetic products. Development of new delivery systems can allow an easier and simpler use and development of critical emulsion systems. Often in these systems sensitive active ingredients must be added in a special and difficult way under very controlled conditions (e.g. temperature and water/oil

content). Microencapsulation has the potential of delivering active ingredients in some difficult systems, e.g. containing glycolic acid, alpha hydroxy acids, salicylic acid, high alcohol content or critical water-in-oil or silicone emulsions. They can be used to deliver active ingredients into the skin, in a safe, targeted, effective and not painful manner, to protect fragrances or volatile compounds from evaporation, to protect compounds such as antioxidants from oxidation, to protect from degradation caused by heat, light and moisture, or to control the release rate. (Pardeike et al., 2009; Rosen, 2005; Soest, 2007; Martins et al., 2010)

Microencapsulation can be used in cosmetic applications such as production of shower and bath gels, lotions and creams, hair products, sunscreens and tanning creams, makeup, perfumes, soaps, exfoliants, tooth pastes and more. Microencapsulation may help in the improvement of the cosmetic and personal care industries, as it brings innovation and allows the production of high added value products, in response to human needs and desires (Suraweera et al., 2014; Barel et al, 2001).

### 3.1. Delivery systems for topical application

A delivery system is a method of holding, carrying and transporting an active ingredient. It is any type of vehicle that takes an active ingredient to a target site. A delivery system can control the release rate of an active ingredient from a formulation at an optimal rate. A number of pathways are possible for the transportation of molecules through the skin. The intercellular route occurs at the interface between cells through the lipid bilayers, following a tortuous permeation pathway. In contrast, transcellular pathways can occur directly through the cells. Transportation via the hair follicles or sweat ducts is also possible (Wiechers, 2008; Flynn, 2002; Moghimi, 1999).

Topical application of cosmetic formulations often requires the successful delivery of active ingredients through the skin's barriers to reach the target skin layer. The main resistance to



transdermal transport lies in a layer of cells joining the epidermis to the stratum corneum, which itself limits the transport. The stratum corneum has a highly impermeable nature and permeability through this layer has remained one of the major challenges in effective transdermal delivery. While the lipophilic stratum corneum contains about 13% water, the inner skin epidermis layers become significantly more hydrophilic, containing 50% water, while the dermis contains 70%. It should also be noted that there are wide variations in permeability at different body sites (e.g. face vs. legs vs. palms) which together with factors such as age and external environment can influence the skin's barrier function. (Lam et al., 2014; Harding, 2004; Forster, 2009; Wiechers, 2008; Elias, 2004; Rein, 1924).

It is generally reported that the transport of molecules through the epidermis is restricted to molecules of low molecular mass (<500 Da) and moderate lipophilicity (partition coefficients log Kow values between 1 and 3), having enough solubility in the lipid domain of the stratum corneum, while still having sufficient hydrophilic nature to allow partitioning into the skin inner layers. As some active cosmetic substances are too hydrophilic to pass through the stratum corneum or too lipophilic to partition into the epidermis, encapsulation techniques with the appropriate shell materials can overcome this problem by delivering the level of lipophilicity needed for the desired application. Mathematical models can be used to predict skin permeability, which are generally based on quantitative structure-permeability relationships (QSPR), diffusion mechanisms or combinations of both. At the same time the compound should still have the lipophilic or hydrophilic characteristics that allow its solubilization in the cosmetic itself and ensure its stability during formulation, storage and application of the product. (Jain et al., 2006; Ammala, 2013; Forster 2009; Wiechers 2005; Barry, 2002; Muller et al., 2002; Muller et al., 2000)

Critical aspects should be considered when delivering a cosmetic active ingredient through the skin, such as the right site of action of the cosmetic ingredient, the right concentration of the

components, and the correct application time of the product on the skin. It should be considered the influence of the formulation type, formulation polarity, stratum corneum polarity, skin lipid organization and the influence of droplet size on skin delivery. The cosmetic delivery should also avoid undesirable transdermal delivery and keep the functional molecule in a specific skin layer. (Wiechers, 2008; Fu, 2005) Common functional ingredients used in topical application cosmetics are UV filters, antioxidants, moisturizers, skin lightening ingredients, and molecules with anti-aging properties, acting either on the surface of the skin or in specific layers within the skin.

Several skin delivery systems used in cosmetic products have already been reported (Wiechers, 2008; Rosen 2005; Barry, 2002). These include skin delivery from emulsions, vesicles, liposomes, solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), phytosomes, transferosomes, nanocrystals and cubosomes. However micro and nanoencapsulation of actives for cosmetic and pharmaceutical applications have shown a wider range of applications, since the advantages of different encapsulation technologies were made evident, as discussed in this review.

(Kristl et al., 2010; Pardeike et al., 2009; Chanchal et al., 2008; El Maghraby et al., 2008; Fairhurst et al., 2008; Puglia et al., 2008; Wiechers, 2008; Kaur et al., 2007; Rosen, 2005; Barry, 2002; Flynn, 2002)

### 3.2. Encapsulating Materials for cosmetic applications

The correct choice of the shell material is essential according to the intended application, as it influences the encapsulation efficiency and stability of the microcapsules. Factors to be considered while selecting a wall material for topical applications include toxicity, biocompatibility, stability, viscosity and mechanical properties, compatibility between the

active ingredient and the wall material, release of the active ingredient from the vehicle into the skin, enhancement of active penetration into the stratum corneum, intended particle size and microscopic properties of the surface of the microparticles and processing and economic factors. Since most encapsulating materials do not have all the required properties, a common practice involves a combination of wall materials (Silva et al., 2014b; Abla et al., 2013; Estevinho et al., 2013a).

Encapsulating materials can be selected from a wide variety of natural and synthetic polymers. The protection of cosmetic active agents in micro-sized carriers with the purpose of controlled release over a certain period of time has been a question of considerable research. The most commonly used shell materials in cosmetics include polysaccharides (gums, starches, celluloses, cyclodextrines, chitosan), proteins (gelatin, casein, soy proteins), lipids (waxes, paraffin, oils) and synthetic polymers (acrylic polymers, polyvinyl alcohol, poly(vinylpyrrolidone)). Inorganic materials, such as silicates, clays and polyphosphates, can also be used as second polymers. (Pawar et al., 2010; Cattaneo et al., 2010; Pedro et al., 2009; Matsuda et al., 1999; Tarimci et al., 2011; Lee et al., 2012; Wille, 2006)

Biopolymers (natural polymers) and biodegradable polymers, such as chitosan and aliphatic polyesters like poly(lactic acid) (PLA) and copolymers of lactic and glycolic acids (e.g. PLGA - poly(lactic co-glycolic acid)), are the encapsulating materials with greater interest for applications in the field of skin delivery systems. These materials are natural, non-toxic, non-reactive when in contact with the human tissues and can be broken down or metabolized and removed from the body via normal metabolic pathways, while other compounds can potentially accumulate in body tissues and cause irritation. Their properties (such as degradation rate and mechanical properties) are strongly defined by structural characteristics, like the composition of the co-polymer, molecular weight and nature of the chain end groups, and these polymers can be chemically functionalized for improved properties (Haddadi et al., 2008; Mishra et al.,

2008; Stevanovic et al., 2007; Ammala, 2012). Chitosan, for example, is insoluble in water and organic solvents, only being soluble in acidic solutions, which frequently limits its application (Silva, 2014). It is possible, however, to modify chitosan structure in order to produce water soluble chitosan, which is easily soluble in neutral aqueous solutions, increasing the range of applicability of this compound (Estevinho et al., 2014a, 2013a, 2013b).

The core material encapsulated is the active ingredient to be used, and depends on the final cosmetic product where the capsules will be incorporated and the desired function. Commonly used core materials in cosmetic products for topical application are reviewed in section 3.4.

### 3.3. Controlled release

Encapsulation should allow the core to be isolated from the external environment until release is desired. Therefore, the release at the appropriate time and place is an extremely important property in the encapsulation process, improving the effectiveness, reducing the required dose of additives and expanding the applications of compounds of interest. The main factors affecting the release rates are related to interactions between the shell material and the core. Additionally, other factors influence the release, including the volatility of the core, the ratio between the core and the wall material, particle size and viscosity of the wall material. The main mechanisms involved in the core release are diffusion, degradation, use of solvents, pH, temperature and pressure. In practice, a combination of more than one mechanism is used. Diffusion occurs especially when the microcapsule shell is intact, and the release rate is governed by the chemical properties of the core and the shell material and some physical properties of the shell. Ganza-González et al. (1999) formed chitosan microcapsules that liberated metoclopramide by diffusional mechanisms. Degradation release occurs when enzymes, such as proteases, carbohydrases and lipases, degrade proteins, polysaccharides or

lipids comprising the shell. Itoh et al. (2006) prepared biodegradable chitosan capsules encapsulating proteins and explored the enzymatic degradation of the capsules in the presence of chitosanase by scanning electron microscopy (SEM). In contact with a solvent, the shell material can dissolve completely, quickly releasing the core or start to expand, favoring release. The pH release can occur when pH changes result in alterations in the shell material solubility, enabling the release of the core. Changes in temperature can promote core release, either by temperature-sensitive release, where materials expand or collapse when a critical temperature is reached, or by fusion-activated release, which involves melting of the shell material due to temperature increase. Hofmeister et al., (2014) presented a facile synthesis method for polymer nanocapsules with high diffusion barrier and stimuli-responsive release properties: temperature and pH change can be used as trigger to open the capsules, and the release kinetics can be tailored depending on the polymer shell composition. Pressure release occurs when pressure is applied to the capsule wall, e.g. the release of some cosmetic active ingredients during friction against the skin upon application of the cosmetic product. Less common release mechanisms include ablation (slow erosion of the shell) and biodegradation. The different release mechanisms of encapsulated materials provide controlled, sustained or targeted release of the core material and the release mechanism depends on the nature of application, (Dubey et al., 2009; Nack, 1970).

#### 3.4. Cosmetic active ingredients encapsulated for topical application

Studies on the use of encapsulation techniques for the delivery and controlled release of cosmetic active ingredients for topical application cosmetics are presented in Table 2 and are discussed.

Retinol or vitamin A (VA), in cosmetics for topical application (creams, skin serums, anti-aging products), acts as an antioxidant and enhances the appearance of dry or damaged skin by

reducing flaking and restoring suppleness. Jennings *et al.* (2001) encapsulated VA in glyceryl behenate SLN through a melt solidification method, to evaluate the potential use of SLN in dermatology and cosmetics. These were tested with respect to their influence on ingredient penetration into the skin and the release profiles were studied using Franz diffusion cells. SLN dispersions were further processed to convenient topical dosage forms, such as hydrogels and oil/water creams, to mimic professional use in cosmetic carriers, and SLN proved to be stably incorporated in these forms. Myung-Han *et al.* (2001) entrapped retinol within inorganic microspheres obtained from sol-gel reaction of TEOS (Tetraethyl orthosilicate) in o/w/o multiple emulsions as microreactors, where the retinol was emulsified as an internal oil phase in an aqueous solution prior to emulsification into an external oil phase. Microspheres obtained with the addition of NH<sub>4</sub>OH as a catalyst when the concentration of TEOS was at the  $R_w$  value of 4 showed the slower release of retinol into the external ethanol phase and higher loading and encapsulation efficiencies. Dong-Gon *et al.* (2006) encapsulated retinol into chitosan nanoparticles for cosmetic and pharmaceutical applications and reconstituted it into aqueous solutions. Solubility of retinol was shown to be able to increase by encapsulation into chitosan nanoparticles more than 1600-fold. Retinol was stably and efficiently encapsulated into the chitosan nanoparticles.

Ascorbic acid (vitamin C) has a variety of biological, pharmaceutical and dermatological functions as described following; it promotes collagen biosynthesis, provides photo protection, causes melanin reduction, scavenges free radicals and enhances the immunity. These functions are closely related to the well-known antioxidant properties of this compound. Vitamin C, however, is very unstable to air, moisture, light, heat, metal ions, oxygen, and alkalinity, and it easily decomposes into biologically inactive compounds. Therefore, the applications of vitamin C in the fields of cosmetics, dermatologicals, and pharmaceuticals are limited despite of its useful functions. Thus to overcome chemical instability of vitamin C, extensive studies have

been tried on encapsulation and immobilization of vitamin C (Bor-Yann et al., 2006; Yang et al., 2003; Yamamoto et al., 2002). Yang et al. (2003) demonstrate a method of encapsulating and stabilizing the vitamin C in an inorganic layered material like hydrated layered metal oxide with high biocompatibility and skin affinity, so that it can be applicable as the cosmetic ingredient. The authors describe a ternary encapsulation system in detail and discuss its physico-chemical properties along with its chemical stability, controlled release behavior, biological activity and transdermal delivery efficiency. The system exhibited an enhanced storage stability and a sustained releasing of vitamin C, and was very helpful in delivering vitamin C molecules into the skin through the stratum corneum, facilitating transdermal penetration of vitamin C in topical application.

$\alpha$ -Tocopherol or vitamin E (VE) is widely used as a strong antioxidant in many medical and cosmetic applications, but is rapidly degraded due to its light, heat and oxygen sensitivity (Poljsak et al., 2014; Oresajo et al., 2012). Thus  $\alpha$ -tocopherol formulations have to avoid contact with light, heat or air. Drug loaded carriers are an attractive opportunity, particularly if they are made of biocompatible macromolecules. Duclairoir et al. (2002) investigated and characterized lipophilic drug loading capacities of gliadin nanoparticles loaded with vitamin E and generated by a desolvation method. The optimum encapsulation efficiency was close to 80%.

Catechins are major antioxidants in green tea (*Camellia sinensis* or *Camellia assamica*), but as they do not permeate well into the skin, the application of green tea in cosmetic products has so far been limited (Peres et al., 2012). Wisuitiprot et al. (2011) evaluated the cutaneous absorption of catechins from an extract of green tea and from green tea extract-loaded chitosan microcapsules. The results suggested that chitosan microcapsules significantly improve the ability of catechins to permeate skin and effectively prevented enzymatic changes of the catechins.

Caffeine is being increasingly used in cosmetics due to its high biological activity. It is used as an active compound in anti-cellulite products, it has potential antioxidant properties, protecting cells against the UV radiation and slowing down the process of photo-aging of the skin, it increases the microcirculation of blood in the skin and it also stimulates the growth of hair (Herman, 2013). Canguero et al. (2011) prepared alginate microspheres by an emulsification/internal gelation technique for the improvement of absorption of caffeine through an *in vitro* skin permeation study performed by Franz diffusion cells. The results revealed that microencapsulation of caffeine by emulsification/internal gelation method can be an alternative for the transdermal delivery of this drug.

Recently, it has been reported that the topical application of quercetin inhibits oxidative skin damage and the inflammatory processes induced by the solar UV radiation. However, essential requirement to ensure the effectiveness of quercetin as photoprotective agent is its stability in topical formulations, namely its photostability (Scalia et al., 2013; Nichols et al., 2010; Yusuf et al., 2007). Scalia et al. (2009) studied lipid microcapsules as a biocompatible system for reducing the instability of quercetin during exposure to sunlight. The obtained lipoparticles were characterized, release studies were performed and microencapsulated quercetin was introduced in a model cream formulation (oil-in-water emulsion) and irradiated with a solar simulator. The light-induced decomposition of quercetin in the cream vehicle was markedly decreased by incorporation into the lipid and this photostabilization effect was maintained over time. Moreover, the chemical instability of quercetin, during 3-month storage of the formulations at room temperature and in the dark, was almost completely suppressed by the lipid microparticle system.

Rosmarinic acid (RA) has a number of interesting biological activities, e.g. antioxidant, anti-carcinogenic, antimicrobial and anti-inflammatory. Despite its strong antioxidant activity, it has limited use in cosmetics due to low water solubility, discoloration and chemical instability



(Budhiraja et al., 2014). Kim et al. (2010) prepared RA-loaded polycaprolactone (PCL) microspheres using emulsion solvent evaporation method and characterize them with different surfactants used in the formation process. Long-term stability of RA was also evaluated in cosmetic formulations. Emulsions containing RA-loaded PCL microspheres showed a better long-term stability of the RA compared with those containing only RA. These results suggest that RA may be stably and efficiently encapsulated into polycaprolactone microspheres.

Yerba mate (*Ilex paraguariensis*) is a plant which presents a high content of caffeoyl derivatives and other phenolics. Some of the pharmacological properties attributed to yerba mate, such as anti-inflammatory and anti-aging, have been related to this high content of polyphenols. Harris et al. (2011) prepared chitosan nanoparticles and microspheres for the encapsulation of natural antioxidants extracted from yerba mate. Nanoparticles were prepared by ionic gelation of chitosan hydrochloride and sodium tripolyphosphate and microspheres were prepared by the spray-drying method. The effect of the encapsulating systems on the active compound stability and its release properties was investigated. The encapsulation efficiency was near 100% and 45 to 90% of polyphenols was delivered from ILE (*Ilex paraguariensis* extract) microspheres after 4 h, depending on the conditions studied (namely the pH). The products obtained in the mentioned and in other studies allowed to control the release of natural antioxidants and therefore these encapsulating methods are a promising technique for cosmetic applications (Barroso et al., 2014).

Resveratrol, a naturally occurring polyphenol, has attracted considerable interest for different application onto the skin, as it is an antioxidant that protects cells against oxidative damage, a compound that reduces inflammation, and it appears to offer anti-aging skin benefits. However, resveratrol has low bioavailability, and this has been associated with its poor water solubility, its low stability against environmental stress and its inability to reach a target site to exert the desired health effect. Encapsulation offers a potential approach for enhancing the solubility of

resveratrol, stabilizing it and improving its bioavailability (Soto et al., 2015; Ndiaye et al., 2011; Baxter, 2008). Scognamiglio et al. (2003) investigated the potential of nanocarriers to deliver resveratrol into the skin. Transfersomes with different surfactants and ethanol-containing vesicles with different lipid composition encapsulating resveratrol were prepared and characterized. The nanocarriers had a size between 83 and 116 nm with a high resveratrol encapsulation efficiency ( $\geq 70\%$ ). However, permeation studies carried out on Franz diffusion cells, showed that only ethanol-containing vesicles based on sulfur polymer cement were able to promote permeation through the skin.

Rutin (Vitamin P, RU) is a bioflavonoid that is extracted from various plants and used in cosmetics as an antioxidant and emollient, however its use in cosmetic and pharmaceutical products is limited by its poor physico-chemical stability. Banjare et al. (2012) developed sustained release nanoparticles of rutin delivered by topical route. Rutin-loaded nanoparticles were prepared by nanoprecipitation technique using ethylcellulose (EC) as polymer. The nanoparticles were characterized in terms of particle size, morphology, yield, encapsulation efficiency and *in vitro* release. It was observed that different RU: EC: Tween 80 ratios varied particle sizes along with yield and encapsulation efficiency. The release profile of rutin was fit into various kinetic models to study the mechanism of drug release. Among these the highest correlation coefficient was shown for the Higuchi plot. These nanoparticles can be used as the convenient model system for increasing the retention of rutin in the skin. Berlier et al. (2013) prepared, characterized and tested rutin inclusion complexes with MCM-41 mesoporous silica and the effect of surface functionalization with aminopropyl groups (NH<sub>2</sub>-MCM-41) on the molecules properties was studied. The study showed a greater accumulation in the skin for the rutin complexed with NH<sub>2</sub>-MCM-41 particles. Not only antioxidant properties of rutin were maintained after immobilization but the immobilization of rutin in aminopropyl silica resulted

in better performance in terms of activity and photostability, suggesting the importance of functionalization in stabilizing organic molecules within silica pores.

Linoleic acid (LA) or vitamin F is an unsaturated fatty acid used as an emollient and thickening agent in cosmetics. There is some research showing it to be effective in cell regulation and skin-barrier repair, as well as an antioxidant and an anti-inflammatory. Linoleic acid is also known to have a whitening effect on hyper-pigmented skin. This component is often encapsulated in liposomes for topical application due to its low solubility in aqueous solution. Yasutami et al. (2004) evaluated the effect of liposomalization on the whitening activity of linoleic acid towards UV-stimulated hyper-pigmented skin. Liposomal LA (0.1%) showed a whitening effect similar to 10.0% non-liposomal LA, indicating that liposomal formulations are favorable for the transdermal application of linoleic acid since this compound showed to be more effective when encapsulated and thus lower concentrations are needed for the same whitening effect.

Lycopene, a lipophilic carotenoid, has been known as an effective antioxidant in supporting the cutaneous defense system. Lycopene is also a pigment and can be used for delivering a desirable skin color. However, it is unstable when exposed to light and water. Luxsuwong et al. (2014) isolated lycopene from tomatoes and developed a vesicular delivery system to entrap and stabilize the lycopene in the aqueous system. The vesicular delivery system was prepared from a combination of ascorbic acid-6-palmitate (AP), cholesterol and dicetyl phosphate using a thin film hydration method. The results showed that lycopene could be stabilized in the vesicles and its scavenging activity against DPPH (2,2-diphenyl-1-picrylhydrazyl) free radicals was superior to the free lycopene solution.

UV filters protect cosmetics and personal care products from deterioration by absorbing, reflecting, or scattering UV rays. When used as sunscreen ingredients, these compounds can also protect the skin from UV rays, which may cause erythema, accelerated skin ageing (photo-ageing) and the induction of skin cancer (Vela-Soria et al., 2014). However many UV filters

penetrate into the skin causing photo-allergic and photo-toxic reactions, as well as skin irritations, establishing an urgent need for the development of safer sunscreen formulations (Jain et al., 2010). Amongst various approaches utilized to improve the performance of sun-screening agents, the use of multiparticulate delivery systems is gaining increasing attention amongst researchers. Marcato et al. (2008), prepared and characterized solid lipid nanoparticles (SLN) of cetyl palmitate and polymeric nanoparticles of poly( $\epsilon$ -caprolactone) as carriers of benzophenone-3, a UV filter, with the main goals to reduce the penetration of this sunscreen into the skin and its effective concentration. The particles were characterized in terms of morphology, encapsulation efficiency and *in vivo* toxicity. Lacerda et al. (2010) have prepared aqueous dispersions of NLCs (nanostructured lipid carriers) by a hot high pressure homogenization technique using carnauba wax and isodecyl oleate. Particle size of the prepared lipid carriers was 0.3–8  $\mu\text{m}$  and encapsulation efficiency between 12 and 90%, depending on the active substance/lipid ratio. Scalia et al. (2010) evaluated lipid microcapsules loaded with the UVB filter ethylhexyl methoxycinnamate (EHMC) and the UVA filter butyl methoxydibenzoylmethane (BMDBM, Avobenzone) for their effect on the sunscreen agents percutaneous penetration. Encapsulated BMDBM and EHMC were introduced into oil-in-water emulsions and applied to human volunteers. Skin penetration was investigated *in vivo* by the tape-stripping technique. A reduction in the *in vivo* skin penetration of EHMC and BMDBM was achieved by the cream containing microencapsulated UV filters, as opposed to nanoencapsulated, and the inhibiting effect on permeation attained by the lipid microcapsules was more marked in the deeper stratum corneum layer, showing that the lipid microcapsules should preserve the UV filter efficacy and limit potential toxicological risks. Studies have been performed for other sunscreens, such as octyl methoxycinnamate (OMC), octyl salicylate, Butyl Methoxydibenzoylmethane (BMDBM) and titanium dioxide (Jiménez et al., 2004; Vettor et al., 2010; Alvarez-Román et al., 2001; Gogna et al., 2007; Bennat et al., 2001; Scalia et al., 2009).

Essential oils are volatile and liquid aromatic compounds existing in natural sources, usually plants. They are mainly used in cosmetic applications as fragrances, but some essential oils can also be used for relaxation and healing skin applications. These compounds can be encapsulated for protection from evaporation or oxidation caused by heat, light and moisture. Anchisi et al. (2006) evaluated the stability and release of chitosan beads loaded with volatile molecules of *Mentha piperita* essential oil in a cosmetic formulation. Properties such as morphology, size, swelling ability, encapsulation efficiency and stability in time of *Mentha piperita* essential oil were assessed during the use phase of the cosmetic formulation. Other fragrances can also be encapsulated for cosmetic application. Aurapan et al. (2010) encapsulated six fragrances: camphor, citronellal, eucalyptol, limonene, menthol and 4-*tert*-butylcyclohexyl acetate, which represent different chemical functionalities, with a polymer-blend of ethylcellulose, hydroxypropyl methylcellulose and poly(vinyl alcohol) using solvent displacement. The process gave  $\geq 40\%$  fragrance loading capacity with  $\geq 80\%$  encapsulation efficiency at the fragrance:polymer weight ratio of 1:1 and at initial polymer concentrations of 2000–16,000 ppm, and the obtained fragrance-encapsulated spheres showed hydrodynamic diameters of less than 450 nm.

Urea is a natural component of the stratum corneum and might be regarded as a penetrating moisturizer, possessing a high osmotic effect and being commonly used in skin care and dermatological formulations. However a serious drawback of using urea in cosmetic emulsions is its lack of stability in water containing products, and such decomposition not only makes the urea biologically unavailable, but it can also cause discoloration and emulsion instability. Also, the evaporation of vehicle causes the urea to crystallize on the skin surface. Urea products must be kept in acidic pH to avoid decomposition of urea to ammonia, but acidic urea products can lead to burning or stinging sensations. Haddadi et al. (2008) described the formulation and characterization of O/W and W/O creams containing urea-loaded microcapsules prepared with

PLGA in order to encapsulate and stabilize urea. The release pattern of urea was examined, which varied among different formulations. The results showed that the release from O/W creams followed Higuchi kinetics while the release from W/O creams showed the zero order kinetics, and the creams containing microparticulated urea had slower release than free urea creams.

Glycolic acid is used in many cosmetic products as a moisturizer. Unfortunately, to achieve greater glycolic acid cosmetic benefits the greater is the potential for skin irritation and burning. Therefore, topical controlled delivery systems loading glycolic acid may optimize the acid cosmetic properties lowering its side effects. Perugini et al. (2000) evaluated different types of microparticulate systems for glycolic acid encapsulation, such as liposomes, liposomes modified by chitosan addition and chitosan microspheres. In vitro tests were also performed to evaluate the feasibility of microparticulate systems in modulating glycolic acid release. The results obtained show that liposomes are always suitable to modulate glycolic acid release and that the best condition to achieve this control is obtained by the liposomal systems in which glycolic acid/lipid molar ratio is 5:1. Further significant release control is obtained by addition of chitosan into the liposomes, while chitosan microspheres are not able to control glycolic acid release even after crosslinking.

Salicylic acid has been widely used in the treatment of dry skin conditions and also helps reduce acne symptoms. However, it has the disadvantages of being a mild to strong irritant. Hence, its control can be achieved through encapsulation in liposomes. Bhalerao et al. (2003) prepared liposomes entrapping salicylic acid by the thin film hydration technique. The results showed the formation of bilayered liposomes in the particle size range of 0.2–0.8276  $\mu\text{m}$  with a maximum entrapment efficiency of 42.6%.

Benzoyl peroxide (BPO) is commonly used in topical formulations for the treatment of acne and as an anti-bacterial agent (Dreno, 2004). However, skin irritation is a common side effect,

and it has been shown that controlled release of BPO to the skin could reduce this problem. Nokhodchi et al. (2005) and Jelvehgari et al. (2006) examined whether the type of topical formulation (cream, gel and lotion) can affect the release behavior of BPO from microsponges with the aim to prepare suitable controlled release formulations for BPO. Microcapsules were prepared using an emulsion solvent diffusion method and it was shown that the drug:polymer ratio, stirring rate and volume of the dispersed phase influenced the particle size and drug release behavior of the formed microsponges, and that the presence of an emulsifier was essential for microsphere formation. The release data showed that the highest release rate was obtained from lotions containing BPO microcapsules and the lowest was obtained from cream formulations, which are therefore preferred for lower irritation effects due to the gradual release. The studies reported in this section revealed the potential of microencapsulation for cosmetic purposes, showing that cosmetic active ingredients may be stably and efficiently encapsulated and suggesting the need to explore new delivery systems to be applied topically to overcome the limitations of topical delivery and effectiveness of some compounds. Different kinds of studies are crucial to determine whether encapsulating formulations are favorable for the transdermal application of cosmetic active ingredients. Studies on the characterization of microcapsules and microencapsulation efficiency and loading capacity using appropriate encapsulation methods are central and the starting point to evaluate the efficacy of the microencapsulation approach for the desired cosmetic ingredient. Release studies and skin permeation studies are also essential to determine the efficacy of the microsystem for the intended application. Studies of the microcapsules incorporated in cosmetic formulations to evaluate core stability and activity are crucial as well, since only then will be possible to evaluate the real efficacy of microencapsulation for cosmetic application.

### *3.5. Critical Aspects*

Critical aspects should be considered when delivering a cosmetic active ingredient through the skin using a microencapsulation system. Technical, quality, ethical and economic issues should be considered when the mass production of cosmetics using microencapsulation technology is implemented. One of the bigger challenges involves the scale-up of the microencapsulation process to achieve the high reproducibility of the microencapsulated cosmetic formulations (Lam et al., 2014).

Although there are instances where capsules produced are used directly in a product, in most cases the capsules must be fastened to a substrate or suspended in a medium for proper functioning in the end use. Here two problems are encountered: the need for a proper method of applying capsules to the substrate and the need to avoid adverse effects of substrate on capsule stability. Adverse effects of cosmetic formulation on the stability of the capsule should be avoided, namely the use of solvents or other substances that tend to leach core material through the capsule or intrude through the shell before and during the application period, or that might interfere with subsequent capsule release. Cosmetic formulations must be designed so that the capsule contents and shell remain intact during the time the product is formulated, transported and stored prior to consumption (Nack, 1970).

Microcapsules employed in cosmetics may need to be easily crushed on the skin during application for core release, but they also need to have sufficient rigidity so that their structure is not modified during manufacture, storage or transport of the cosmetic formulation, since sufficient active core material must remain encapsulated at the desired time release. (Handjani et al., 1993).

The capsules and products containing capsules are stored at widely varying conditions. Factors of concern include temperature, humidity, pressure, light, or other forms of radiation and air pollutants. Capsules containing volatile materials or certain reactive chemicals must be protected from excess temperature to avoid premature evaporation or decomposition of the core



contents. If the core is hygroscopic capsules may absorb water from a high humidity atmosphere to the point of wall rupture in some cases. Conversely, capsules containing some water in the core may lose water by evaporation in a low humidity environment, thereby reducing the reactivity of the capsular system. Excessive pressure on capsules in storage, such as certain slow release fertilizers, may cause blocking or welding together of the capsules so that the product is no longer free-flowing. Stacking of capsule-containing products may cause premature rupture of capsules in the bottom layers of the stack. Both fungal and bacterial degradation can be a problem in cosmetic formulations using biodegradable materials. Sometimes it is therefore necessary to add preservatives to extend the shelf life, but their undesired influences should be considered and controlled. Natural preservatives, such as tea tree oil and grapefruit seeds oil, have proven to be effective. Low levels of benzalkonium chloride may also be added, serving a dual purpose of anti-microbial agent and emulsifier (Ammala, 2012; Nack, 1970).

Cosmetic ingredients and delivery systems are quickly introduced and removed from the market. Therefore they need to carry strong innovations, visible to consumers if possible and perceived by them as a real innovative material. New encapsulation technologies have emerged, which need to be quickly adaptable to any new active compounds in a very simple and dynamic way. The technical and economic aspects should be taken into consideration while selecting the appropriate type of delivery system to enhance the safety, stability, extended efficacy and to enhance the aesthetic appeal of the final product. Perhaps the most important criterion for judging the over-all performance of a capsular product relates to economics. It is important to understand if the consumer is willing to pay for the extra cost of microencapsulation. It should be taken into consideration the production costs of the product, as well as marketing, consumer education, distribution patterns, and price consciousness costs. After all, a product is effective and successful only if it appeals to a consumer who is willing to use it and pay for it.

Unfortunately, there are no direct answers to this problem, and it is evident that such a situation calls for careful product development and market studies. (Perrier, 2012; Patravale, 2008)

Safety is also essential to assure product's sustainability in the market and repeated purchase. The cosmetic products need to be perfectly known in terms of composition and traces of undesirable components, such as heavy metals and traces of compounds that could be perceived as dangerous by consumers, they have to be demonstrated to be toxicologically safe, they should not use animal tests that are banned for the cosmetic industry and they should be proposed in a way that will not be the subject of media and/or non-governmental organization attacks. These products have to fulfill cosmetic regulations for all the countries where such materials are introduced through cosmetic formulations. Legal and safety responsibilities of cosmetics and skin delivery systems as well as the marketing and dermatological perspectives of these responsibilities should be taken into account. Special attention should be made to European Cosmetic Regulation 1223/2009, which introduces new rules for the use of nanomaterials in cosmetic products. Nanomaterials must be explicitly authorized and must be labelled in the list of ingredients with the word "nano" in brackets following the name of the substance. Products containing nanomaterials not otherwise restricted by the Cosmetics Regulation will be the object of a full safety assessment at EU level if the Commission has concerns (European Commission, 2013; Perrier 2012; Wiechers, 2008).

### *3.6. Commercial products*

Several companies have developed innovative technologies for the production of microcapsules, which allow the encapsulation of different active agents for cosmetic purposes. Microcapsules Technologies, Inc developed the Microsil® microcapsules, specifically designed for the cosmetic industry. These capsules, made of silicone copolymers, may encapsulate UV filters, retinol, dihydroxyacetone (DHA), natural oils, etc., and show excellent

skin acceptance and flawless toxicology, being considered hypoallergenic (Microcapsules Technologies, 2015). Tagra Biotechnologies has developed the RND™ Microencapsulation Technology, a patented method of providing stability, efficiency and controlled/immediate release for non-water soluble ingredients. This technology enables the production of encapsulated ingredients conforming to worldwide cosmetic regulations and suitable for a wide range of formulations. (Tagra Biotechnologies, 2015). Lipo Technologies designs microencapsulation applications for bath gels, lotions, tanning, makeup, aromatherapy, etc. From controlled release to the isolation of actives, their comprehensive line of technically innovative delivery methods offers virtually unlimited formulation possibilities. BotanoCap's technology consists of proprietary microencapsulation that enables the slow release of volatile compounds, such as essential oils. The companies' technology has full control over the particle size and the release profile of the encapsulated compound and it facilitates the use of these active compounds for a wide range of applications (Botano Cap, 2015). Materium Inc. has developed an innovative technology for the production of hollow silica microspheres - Matspheres 424 series. Their technology allows the encapsulation of different active agents inside silica microcapsules for extended release in specific applications, including cosmetics and perfumes (Materium Innovations, 2015). Microtek Laboratories, Inc. designs and produces delivery systems specifically tailored to consumer needs, always keeping the final product and application in mind. The company has special expertise in the microencapsulation of various materials, including caffeine, vitamins and fragrances (Microtek Laboratories, Inc., 2015). Pellets Company developed several products involving microencapsulation techniques, including Colorlets and Pearlets (colored shimmering visual microspheres customer designed as delivery system for ingredients such as fragrances, glitters, pigments, vitamins, herbextracts etc.), Oralets (microcapsules to delivery actives in tooth pastes for oral health), softlets (aqueous gel microcapsules which incorporate with polymers, pearl powder, and hydrophobic

actives) and amazing color (high concentrated pigments microcapsules) (Pellets, 2015). Natural odours and polymers, PVT, LTD developed Sphera™ Microcapsules, which allow the delivery of vitamins, essential oils and fragrances etc. in form of a fine powder for personal care cosmetics.

### *3.7. Perspectives*

Despite the fact that the use of the presented delivery systems for cosmetics of topical administration is a promising application area, a lot remains to be elucidated about the encapsulation methods discussed. At this stage only the first level of technical and scientific needs of encapsulation applied in the cosmetic field have been addressed. Further research needs to be carried out for a better understanding of the reasons for materials modifications, effects and transitions at every stage, since the product production to its final topical application. Moreover a better understanding is needed of how such systems modify the diffusion of actives into the skin, how the particles interact with the lipids of the stratum corneum and how they affect penetration (Perrier, 2012; Patravale, 2008). Further studies need to be performed moving forward to have a “real life” data since, although transdermal delivery is relatively well understood, the main factors affecting dermal delivery are still unknown, due to the measuring difficulties in this domain and the many parameters to be taken into account in the formulation processes. Many principles of the microencapsulation methods are yet unavailable for use on an industrial scale, being only published as patents. (Wiechers, 2008)

Nevertheless, comparative clinical trials where cosmetic products use encapsulation systems provide attractive results showing the interest of the delivery systems on the intensity of the cosmetic effect of the formulations or on the speed to reach the maximum efficacy, showing that encapsulation has a tremendous potential in cosmetics products. Considering the more aggressive regulations, it is important to use the same ingredients but encapsulated, in order to

create new properties. Nowadays, cosmetics are more than beauty, they are personal care products, as they repair, stimulate and balance skin functions and hydrate, vitalize and regenerate the skin, and are also good complements in many skin disorder treatments. In addition, the gap between cosmetics and pharmaceuticals is closing with the increasing use and availability of the called “cosmeceuticals”. These products contain many natural substances, such as vitamins, oils and therapeutic extracts, which would greatly benefit from the use of the encapsulation technology. Encapsulation will be used as one important tool for formulators in the future: to target some specific cells for a better delivery (e.g. targeting melanocytes to reduce pigmentation mechanisms or adipocytes in order to reduce fat storage is crucial for a stronger activity of cosmetic formulations); to protect unstable ingredients (e.g. some components are incompatible and if separated in the formula through encapsulation this instability disappears); to reduce the side effects of molecules by increasing their efficacy, since the dosage can be reduced (e.g. encapsulated retinol reduces side effects of retinol) or to use visible spheres as a marketing tool. Some trends that the consumers are likely to see in the future include improved systems that release their actives via pH and temperature modulation. (Estanqueiro et al., 2014; Perrier, 2012) A tremendous hope is in the future of delivery systems in the cosmetic area.

#### **4. Conclusions**

Nowadays, there is a growing trend towards more complex and sophisticated products with consumers expecting improved product performance and formulators aiming for a greater competitive advantage in cosmetic and personal care markets. Microencapsulation has been applied in a wide variety of products from different areas, and studies have shown an enormous potential to provide the core with advantageous features, resulting in superior quality products, including in the cosmetic industry. Through the efforts of the cosmetic industry, nano and microparticle formulations for the skin have definitively been an economic success.

Encapsulation of cosmetic and personal care products ingredients has become very popular, attractive and technologically feasible, consequences of the added value associated with the generated products, but also because compound's functionality can be effectively preserved or even enhanced. The efforts made to obtain a better understanding concerning the mechanisms of the novel formulations at the molecular and supramolecular level have led to new formulation processes and could open new prospects in the area of active delivery by means of encapsulated systems. Microparticle formulations have proved to be innovative and effective cosmetic delivery systems and successful in improving the efficacy of active compounds with cosmetic interest. These formulations have a great future in the cosmetic science and it is predicted that this technology will continue to expand. Nevertheless consumers are more demanding and microencapsulation remains a challenging technology where it is important to increase the operative window in terms of processes and encapsulation materials. Much effort through research and development is still needed to identify and develop new materials and to improve and optimize the existing methods of encapsulation for the better use of microencapsulation and expand its potential applications.

### **Declaration of interest**

The authors declare no conflict of interest.

### **Acknowledgments**

This work was funded by FEDER funds through the Operational Programme for Competitiveness Factors – COMPETE, ON.2 - O Novo Norte - North Portugal Regional Operational Programme and National Funds through FCT - Foundation for Science and Technology under the projects: PEst-C/EQB/UI0511, NORTE-07-0124-FEDER-000025 - RL2\_ Environment & Health.

## References

Alvarez-Román R, Barré G, Guy RH, Fessi H. (2001) Biodegradable polymer nanocapsules containing a sunscreen agent: preparation and photoprotection. *European Journal of Pharmaceutics and Biopharmaceutics*, 52(2): 191–195.

Ammala A. (2013) Biodegradable polymers as encapsulation materials for cosmetics and personal care markets. *International Journal of Cosmetic Science*, 35: 113–124.

Anchisi C, Meloni MC, Maccioni AM. (2006) Chitosan beads loaded with essential oils in cosmetic formulations. *Journal of Cosmetic Science*, 57(3): 205-214.

Anwar H, Weissbrodt J, Kunz B. (2010) Microencapsulation of fish oil by spray granulation and fluid bed film coating, *Journal of Food Science*, 75(6): 359-351.

Arshady, R. (1999) Microspheres, Microcapsules and liposomes: general concepts and criteria. In: *Microspheres, Microcapsules and Liposomes - Preparation and Chemical Applications*. 1: 11-45. Citus Book Inc, UK.

Aurapan S, Supason W, Natchanun L, Teerakiat K, Sunatda A. (2010) High loading fragrance encapsulation based on a polymer-blend: Preparation and release behavior *International Journal of Pharmaceutics*, 391(1–2): 267–273.

Banjare L, Ghilare N. (2012) Development of biocompatible nanoparticles for sustained topical delivery of Rutin. *International Journal of Pharmaceutical & Biological Archives*, 3(2): 326-32.

Barel A, Paye M, Maibach H. (2001) *Handbook of Cosmetic Science and Technology*, New York: Marcel Dekker.

Barroso MR, Barros L, Dueñas M, Carvalho AM, Santos-Buelga C, Fernandes IP, Barreiro MF, Ferreira ICFR. (2014) Exploring the antioxidant potential of *Helichrysum stoechas* (L.) Moench phenolic compounds for cosmetic applications: chemical characterization, microencapsulation and incorporation into a moisturizer. *Industrial Crops and Products*, 53: 330–336.

Barry BW. (2002) Transdermal drug delivery. In: Aulton ME (ed.), *Pharmaceutics: The Science of Dosage Form Design*, Chapter 33, London: Churchill Livingstone.

Baxter R. (2008) Anti-aging properties of resveratrol: Review and report of a potent new antioxidant skin care formulation. *Journal of Cosmetic Dermatology*, 7(1): 2-7.

Benita S. (2005) *Microencapsulation: Methods and Industrial Applications*, Second Edition Drugs and the Pharmaceutical Sciences, CRC Press.

Bennat C, Müller-Goymann CC. (2000) Skin penetration and stabilization of formulations containing microfine titanium dioxide as physical UV filter. *International Journal of Cosmetic Science*, 22(4): 271-83.

Berlier G, Gastaldi L, Sapino S, Miletto I, Bottinelli E, Chirio D, Ugazio E. (2013) MCM-41 as a useful vector for rutin topical formulations: Synthesis, characterization and testing. *International Journal of Pharmaceutics*, 457(1): 177–186.

Bhalerao S, Harshal A. (2003) Preparation, Optimization, Characterization, and Stability Studies of Salicylic Acid Liposomes. *Drug Development and Industrial Pharmacy*, 29(4): 451–467.



Bodmeier R, Chen HG. (1988) Preparation of biodegradable poly(dl-lactide) microparticles using a spray-drying technique. *Journal of Pharmacy and Pharmacology*, 40:754–757.

Bor-Yann C, Yuan-Haun L, Wu-Ching L, Feng-Huei L, King-Fu L. (2006) Understanding the characteristics of L-Ascorbic Acid-Montmorillonite Nanocomposite: Chemical Structure and Biototoxicity. *Biomedical Engineering Applications, Basis & Communications*, 8(1): 30-36.

Botano Cap, 2015. Available at: <http://www.botanocap.com>

Budhiraja A, Dhingra G. (2014) Development and characterization of a novel antiacne niosomal gel of rosmarinic acid. *Drug Delivery*, Early Online: 1-8.

Cangueiro M, Carvalho P, Rosado C, Reis CP. (2011) In vitro transdermal delivery of drug loaded alginate microspheres. I National Symposium on Nanoscience and Biomedical Nanotechnology, Lusophone University of Humanities and Technology, Lisbon, Portugal.

Capsutech Ltd. (2009) Cyclodextrin-containing polymers and uses thereof. Patent WO 2007072481 A2.

Cattaneo MV. Topical delivery systems based on polysaccharide microspheres. In: Rosen, M.R. (ed.) *Delivery System Handbook for Personal Care and Cosmetic Products*, 273–282, Norwich, New York: William Andrew, Inc.

Chanchal D, Swarnlata S. (2008) Novel approaches in herbal cosmetics. *Journal of Cosmetic Dermatology*, 7(2): 89–95

Chávarri M, Marañón I, Villarán M. (2012) Encapsulation Technology to Protect Probiotic Bacteria, Chapter 23 in *Probiotics*. Edited by Everlon Cid Rigobelo.

Chen AZ, Li Y, Chau FT, Lau TY, Hu JY, Zhao Z, Mok DKW. (2009) Microencapsulation of puerarin nanoparticles by poly(L-lactide) in a supercritical CO<sub>2</sub> process. *Acta Biomaterialia*, 5(8) 2913–2919.

Chen-Guang L, Kashappa G, Xi-Guang C, Andhyun-Jin P. (2005) Linolenic Acid-Modified Chitosan for Formation of Self-Assembled Nanoparticles. *Journal of Agricultural and Food Chemistry*, 53: 437–441.

Chhotalal AK, Chavda JR, Soniwala MM. (2013) To Study Effect of Polymer, Core Ratio on Yield & Size Distribution of Microcapsules. *International Journal of Pharmamedix India*, 1(2): 281-290.

Ciriminna R, Pagliaro M. (2013) Sol–gel microencapsulation of odorants and flavors: opening the route to sustainable fragrances and aromas. *Chemical Society Reviews*, 42(24); 9243–9250.

Cocero M, Martin A, Mattea F, Varona S. (2009) Encapsulation and co-precipitation processes with supercritical fluids: Fundamentals and Applications. *Journal of Supercritical Fluids*, 47: 456-555.

Conopco, Inc., D/B/A Unilever. (2010) Topical composition comprising coloring antioxidants. Patent US 20090162306 A1.

Coreana Cosmetics Co., Ltd. (2001) Cosmetic material containing triple- encapsulated retinol. Patent US 6908625.

Di Marco M, Shamsuddin S, Razak KA, Aziz AA, Devaux C, Borghi E, Levy L, Sadun C. (2010) Overview of the main methods used to combine proteins with nanosystems: absorption, bioconjugation, and encapsulation. *International Journal of Nanomedicine*, 5: 37–49.

Dong-Gon K, Young-II J, Changyong C, Sung-Hee R, Seong-Koo K, Mi-Kyeong J, Jae-Woon N. (2006) Retinol-encapsulated low molecular water-soluble chitosan nanoparticles. *International Journal of Pharmaceutics*, 319(1–2): 130–138.

Dreno B. (2004) Topical antibacterial therapy for acne vulgaris. *Drugs*, 64(21): 2389-97.

Dubey R, Shami TC, Bhasker Rao K. (2009) Microencapsulation Technology and Applications. *Defence Science Journal*, 59(1): 82-95.

Duclairoir C, Orecchioni A, Depraetere P, Nakache E. (2002)  $\alpha$ -Tocopherol encapsulation and in vitro release from wheat gliadin nanoparticles. *Journal of Microencapsulation*, 19(1): 53-60.

Durand M. (1995) Method for the protection of dihydroxyacetone, a dihydroxyacetone protected by this method, and a cosmetic product containing such a protected dihydroxyacetone. Patent US 5458872 A

El Maghraby GM, Barryc BW, Williams AC. (2008) Liposomes and skin: From drug delivery to model membranes. *European Journal of Pharmaceutical Sciences*, 34(4-5): 203–222.

Elias PM. (2004) The epidermal permeability barrier: from the early days at harvard to emerging concepts. *Journal of Investigative Dermatology*, 122(2): 36-39.

Estanqueiro M, Conceição J, Amaral H, Lobo J. (2014) Solid Lipid Nanoparticles and Nanostructured Lipid Carriers in moisturizing cosmetics. *Nanotechnonoly and Delivery*, 9(5): 43-47.

Estevinho, B.N., Damas, A.M., Martins, P., Rocha, F. (2012) Study of the Inhibition Effect on the Microencapsulated Enzyme  $\beta$ -galactosidase. *Environmental Engineering and Management Journal*, 11, 1923–1930.

- Estevinho, B.N., Damas, A.M., Martins, P., Rocha, F. (2014a) The Influence of Microencapsulation with a Modified Chitosan (Water Soluble) on  $\beta$ -galactosidase Activity. *Drying Technology Journal*, 32, 1575–1586.
- Estevinho, B.N., Damas, A.M., Martins, P., Rocha, F. (2014b) Microencapsulation of  $\beta$ -galactosidase with different biopolymers by a spray-drying process. *Food Research International Journal*, 64, 134–140.
- Estevinho, B.N., Rocha, F., Santos, L., Alves, A. (2013) Microencapsulation with chitosan by spray drying for industry applications – A review. *Trends in Food Science & Technology Journal*. 31, 138–155.
- Estevinho, B.N., Rocha, F., Santos, L., Alves, A. (2013) Using Water Soluble Chitosan for Flavour Microencapsulation in Food Industry. *Journal of Microencapsulation*, 30, 571–579.
- Euromonitor. (2011) Beauty and personal care 2011: corporate strategies in and beyond the BRICs, in: Euromonitor International (Ed.).
- Fairhurst D, Loxley A. (2008) Chapter 17: Micro- and Nano-encapsulation of Water- and Oil-soluble Actives for Cosmetic and Pharmaceutical Applications. Particle Sciences Inc., Bethlehem, PA, USA.
- Flynn GL. (2002) Cutaneous and transdermal delivery-processes and systems of delivery. In: Banker G.S, Rhodes C.T. (ed.), *Modern Pharmaceutics*, Chapter 8, New York: Marcel Dekker.
- Freitas S, Merkle H, Gander B. (2005) Microencapsulation by solvent extraction/evaporation: reviewing the state of the art of microsphere preparation process technology. *Journal of Controlled Release*, 102(2): 313 – 332.

Forster M, Bolzinger MA, Fessi H, Briançon S. (2009) Topical delivery of cosmetics and drugs. Molecular aspects of percutaneous absorption and delivery. *European Journal of Dermatology*, 19: 309–323.

Fu X, Ping Q, Gao Y. (2005) Effects of formulation factors on encapsulation efficiency and release behaviour in vitro of huperzine A-PLGA microspheres. *Journal of Microencapsulation*, 22(1): 57 – 66.

Gallarate M, Carlotti ME, Trotta M, Bovo S. (1999) On the stability of ascorbic acid in emulsified systems for topical and cosmetic use. *International Journal of Pharmaceutics*, 188(2): 233-241.

Gander B, Blanco-Príeto MJ, Thomasin C, Wandrey C, Hunkeler D. (2006) Coacervation and phase separation. In: Swarbrick J., Boylan J. (ed.), *Encyclopedia of Pharmaceutical Technology*, New York: Marcel Dekker.

Gander B, Merkle HP, Nguyen VP, Ho NT. (1995) A new thermodynamic model to predict protein encapsulation efficiency in poly(lactide) microspheres. *Journal of Physical Chemistry*, 99(43): 16144–16148.

Ganza-González A, Anguiano-Igea S, Otero-Espinar F J, Mendez JB. (1999) Chitosan and chondroitin microspheres for oral-administration controlled release of metoclopramide. *European Journal of Pharmaceutics and Biopharmaceutics*, 48(2): 149-155.

Ghosh SK. (2006) *Functional Coatings and Microencapsulation: A General Perspective in Functional Coatings: by Polymer Microencapsulation* (ed S. K. Ghosh), Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, FRG.

Giri TK, Choudhary C, Ajazuddin AA, Badwaik H, Tripathi DK. (2012) Prospects of pharmaceuticals and biopharmaceuticals loaded microparticles prepared by double emulsion technique for controlled delivery. *Saudi Pharmaceutical Journal*, 21(2): 125-141.

Gogna D, Jain SK, Yadav AK, Agrawal GP. (2007) Microsphere based improved sunscreen formulation of ethylhexyl methoxycinnamate. *Current Drug Delivery*, 4(2): 153-9.

Gutcho M. (1976) Microcapsules and microencapsulation techniques (Chemical technology Review). Noyes Data Corp, USA.

Haddadi A, Aboofazeli R, Erfan M, Farboud ES. (2008) Topical delivery of urea encapsulated in biodegradable PLGA microparticles: O/W and W/O creams. *Journal of Microencapsulation*, 25(6): 379–386.

Hammad U, Hemlata N, Asif M, Nainar M. (2011) Microencapsulation: Process, Techniques and Applications. *International Journal of Research in Pharmaceutical and Biomedical Sciences*, 2(2): 474-481.

Handjani RM, Kauffmann M, Huguenin F (L'Oreal). (1993) Process for the Preparation of Alginate Capsules, Apparatus for producing said Capsules and Cosmetic Compositions Containing said Capsules. US patent 5204111.

Harding CR. (2004) The stratum corneum: structure and function in health and disease. *Dermatology and Therapy*, 17: 6–15.

Harris R, Lecumberri E, Mateos-Aparicio I, Mengibar M, Heras A. (2011) Chitosan nanoparticles and microspheres for the encapsulation of natural antioxidants extracted from *Ilex paraguariensis*. *Carbohydrate Polymers*, 84(2): 803–806.

Herman A. (2013) Caffeine's mechanisms of action and its cosmetic use. *Skin Pharmacology and Physiology*, 26(1): 8-14.

Hirech K, Payan S, Carnelle G, Brujes L, Legrand J. (2003) Microencapsulation of an insecticide by interfacial polymerisation, *Powder Technology*, 130(1-3): 324–330.

Hofmeister I, Landfester K, Taden A. (2014) pH-Sensitive Nanocapsules with Barrier Properties: Fragrance Encapsulation and Controlled Release. *Macromolecules*, 47 (16): 5768–5773.

Hung LH, Teh SY, Jester J, Lee AP. (2010) PLGA micro/nanosphere synthesis by droplet microfluidic solvent evaporation and extraction approaches. *Lab Chip*, 10(14): 1820–1825.

Itoh Y, Matsusaki M, Kida T, Akashi M. (2006) Enzyme-responsive release of encapsulated proteins from biodegradable hollow capsules. *Biomacromolecules*, 7(10): 2715-8.

Jain S, Tiwari A.K, Jain NK. (2006) Topical products. In: Jain N.K (ed). *Pharmaceutical Product Development*, Chapter 7, New Delhi: CBS Publishers.

Jain S, Jain N. (2010) Multiparticulate carriers for sun-screening agents. *International Journal of Cosmetic Science*, 32(2): 89-98.

Jelvehgari M, Siahi-Shadbad MR, Azarmi S, Martin GP, Nokhodchi A. (2006) The micro sponge delivery system of benzoyl peroxide: preparation, characterization and release studies. *International Journal of Pharmaceutics*. 308(1-2): 124-32.

Jenning V, Gysler A, Schäfer-Korting M, Gohla SH. (2000) Vitamin A loaded solid lipid nanoparticles for topical use: occlusive properties and drug targeting to the upper skin. *European Journal of Pharmaceutics and Biopharmaceutics*. 49(3): 211–218.

- Jiménez M, Pelletier J, Bobin M, Martini M. (2004) Influence of encapsulation on the in vitro percutaneous absorption of octyl methoxycinnamate. *International Journal of Pharmaceutics*, 272 (1-2): 45-55.
- Jyothi N, Prasanna M, Prabha S, Ramaiah P, Srawan G, Sakarkar S. (2010) Microencapsulation Techniques, Factors Influencing Encapsulation Efficiency. *Journal of Microencapsulation*, 27(3): 187–197.
- Kas HSOL. (2000) Microencapsulation using coacervation/phase-separation: an overview of the technique and applications, In: Wise D.L., Dekker M. (ed.), *Handbook of pharmaceutical controlled release technology*, New York: CRC Press.
- Kaur I, Kapila M, Agrawal R. (2007) Role of novel delivery systems in developing topical antioxidants as therapeutics to combat photoageing. *Ageing Research Reviews*, 6(4): 271–288.
- Kaur L, Sharma S, Guleri T. (2013) Microencapsulation: A New Era in Noval Drug Delivery. *International Journal of Pharmaceutical and Bio-science*, 2(2): 456-468.
- Kim HJ, Kang KC, Pyo HB, Jeong HH. (2010) Microencapsulation of rosmarinic acid using polycaprolactone and various surfactants. *International Journal of Cosmetic Science*, 32(3): 185–191.
- Kristl J, Karmen T, Pegi AG. (2010) Current View on Nanosized Solid Lipid Carriers for Drug Delivery to the Skin. *Journal of Biomedical Nanotechnology*, 6: 1–14.
- L’Oreal. (1998) Composition comprising an aqueous dispersion of lipid vesicles encapsulating a UV screening agent with acidic functionality and uses in topical application. Patent US 5759526 A.



Lacerda SP, Cerize NNP, Re MI. (2011) Preparation and characterization of carnauba wax nanostructured lipid carriers containing benzophenone-3. *International Journal of Cosmetic Science*, 33: 312–321.

Natural odours and polymers, PVT, LTD. Available at: [www.naturalodours.com](http://www.naturalodours.com)

Lakkis J. (2007) Encapsulation and Controlled Release Technologies in Food Systems, Blackwell, Iowa, USA.

Lam PL, Gambari R. (2014) Advanced progress of microencapsulation technologies: In vivo and in vitro models for studying oral and transdermal drug deliveries. *Journal of Controlled Release*, 178: 25–45.

Lee KY, Mooney DJ. (2012) Alginate: properties and biomedical applications. *Progress in Polymer Science*, 37(1): 106–126.

Li M, Rouaud O, Poncelet D. (2008) Microencapsulation by solvent evaporation: State of the art for process engineering approaches. *International Journal of Pharmaceutics*, 363(1-2): 26-39.

Lipo Technologies, 2015. Available at: <http://www.lipotechnologies.com>

Lumsdon SO, Friedmann TE, Green JH. (2005) Encapsulation of oils by coacervation. WIPO Patent WO/2005/105290.

Luxsuwong D, Indranupakorn R, Wongtrakul P. (2014) Preparation of Vesicles Entrapped Lycopene Extract. *Journal of oleo Science*, 63(6): 645-52.

Madan PL. (1978) Microencapsulation: Phase separation or coacervation. *Drug Development and Industrial Pharmacy*, 4(1) 95–116.

Marcato P, Caverzan J, Rossi-Bergmann B, Pinto EF, Machado D, Silva RA, Justo GZ, Ferreira CV, Durán N. (2011) Nanostructured polymer and lipid carriers for sunscreen. Biological effects and skin permeation. *Journal for Nanoscience and Nanotechnology*, 11(3):1880-6.

Martins I, Barreiro M, Coelho M, Rodrigues A. (2014) Microencapsulation of essential oils with biodegradable polymeric carriers for cosmetic applications. *Chemical Engineering Journal*, 245: 191–200.

Martins I, Rodrigues S, Barreiro F, Rodrigues A. (2009) Microencapsulation of thyme oil by coacervation. *Journal of Microencapsulation*, 26(8): 667–675.

Martins I, Rodrigues S, Barreiro F, Rodrigues A. (2010) Polylactide-based thyme oil microcapsules production: evaluation of surfactants. *Industrial and Engineering Chemistry Research*, 50(2): 898–904.

Materium Innovations, 2015. Available at: <http://www.materiuminnovations.com>

Matsuda H, Arima H. (1999) Cyclodextrins in transdermal and rectal delivery. *Advanced Drug Delivery Reviews* 36(1): 81–99.

Maybelline Intermediate Co. (1999) Skin revitalizing makeup composition. Patent EP 0796077 A1.

Michael H. (2009) Chemical product engineering - The third paradigm, *Computers & Chemical Engineering*. 33(5), 947–953.

Microcapsules Technologies, 2015. Available at: <http://www.microcapsules-technologies.com>

Microtek Laboratories, 2015. Available at: <http://www.microteklabs.com>

Mishra N, Goyal AK, Khatri K. (2008) Biodegradable polymer based particulate carrier(s) for the delivery of proteins and peptides. *Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry*, 7: 240–251.

Moghimi, HR, Williams AC, Barry BW. (1999) Stratum corneum and barrier performance; a model lamellar structural approach. In: Bronaugh, R.L., Maibach, H.I (eds.), *Percutaneous Absorption*, 515–553, New York: Marcel Dekker.

Müller R, Mader K, Gohla S. (2000) Solid lipid nanoparticles (SLN) for controlled drug delivery – a review of the state of the art. *European Journal of Pharmaceutics and Biopharmaceutics*, 50 (1): 161–177

Müller R, Radtke M, Wissing S. (2002) Nanostructured Lipid Matrices for Improved Microencapsulation of Drugs. *International Journal of Pharmaceutics*, 242: 121-128.

Myung-Han L, Seong-Geun O, Sei-Ki M, Seong-Youl B. (2001) Preparation of Silica Particles Encapsulating Retinol Using O/W/O Multiple Emulsions. *Journal of Colloid and Interface Science*, 240: 83–89.

Nack H. (1970) Microencapsulation Techniques Applications and Problems. *Journal of the Society of Cosmetic Chemists*, 21: 85-98.

Ndiaye M, Philippe C, Mukhtar H, Ahmad N. (2011) The Grape Antioxidant Resveratrol for Skin Disorders: Promise, Prospects, and Challenges. *Archives of Biochemistry and Biophysics*, 508(2): 164–170.

Nguyen-Ngoc H, Tran-Minh C. (2007) Sol–gel process for vegetal cell encapsulation. *Materials Science and Engineering C – Biomimetic and Supramolecular Systems*, 27(4) 607–611.

Nichols JA, Katiyar S. (2010) Skin photoprotection by natural polyphenols: Anti-inflammatory, antioxidant and DNA repair mechanism. *Archives of Dermatological Research*, 302: 71–83.

Nokhodchi A, Jelvehari M, Siah M, Dastmalchi S. (2005) The Effect of Formulation Type on the Release of Benzoyl Peroxide from Microsponges. *Iranian Journal of Pharmaceutical Sciences*, 1(3): 131-142.

Oresajo C, Pillai S, Manco M, Yatskayer M, McDaniel D. (2012) Antioxidants and the skin: Understanding formulation and efficacy. *Dermatologic Therapy*, 25: 252-259.

Pardeike J, Hommoss A, Müller R. (2009) Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products. *International Journal of Pharmaceutics*, 366(1-2):170-84.

Patravale VB, Mandawgade SD. (2008) Novel cosmetic delivery systems: an application update. *International Journal of Cosmetic Science*, 30: 19–33.

Pawar KR, Babu RJ. (2010) Polymeric and lipid-based materials for topical nanoparticle delivery systems. *Critical Reviews in Therapeutic Drug Carrier Systems*, 27(5): 419–459

Pedro AS, Cabral-Albuquerque E, Ferreira D, Sarmiento B. (2009) Chitosan: an option for development of essential oil delivery systems for oral cavity care. *Carbohydrate Polymers*, 76(4) 501–508.

Pellets: Cosmetic and Oral care, 2015. Available at: <http://www.pellets.com.cn>

Peres I, Rocha S, Gomes J, Morais S, Pereira C, Coelho M. (2011) Preservation of Catechin Antioxidant Properties Loaded in Carbohydrate Nanoparticles. *Carbohydrate Polymers*, 86: 147-53.

Perrier E. LVMH Recherche (2012) Editorial of Bioencapsulation Innovations. Bioencapsulation Research Group.

Perugini P, Genta I, Pavanetto F, Conti B, Scalia S, Baruffini A. (2000) Study on glycolic acid delivery by liposomes and microspheres. *International Journal of Pharmaceutics*, 196(1): 51–61.

Poljsak B, Dahmane R, Godic A. (2013) Skin and antioxidants. *Journal of Cosmetic and Laser Therapy*, 15: 107-113.

Puglia C, Blasi P, Rizza L, Schoubben A, Bonina F, Rossi C, Ricci M. (2008) Lipid nanoparticles for prolonged topical delivery: an in vitro and in vivo investigation. *International Journal of Pharmaceutics*, 357(1-2): 295-304.

R.P. Scherer Corporation. (1996) Topical application emulsions. Patent US 5587149 A.

Rein H. (1924) Experimental electroendosmotic studies on living human skin. *Z. Biol Journal*, 81: 125-140.

Rosen M. (2005) *Delivery System Handbook for Personal Care and Cosmetic Products: Technology, Applications and Formulations*, Personal Care and Cosmetic Technology, William Andrew.

Santo S, Matteo M. (2009) Incorporation of quercetin in lipid microparticles: Effect on photo- and chemical-stability. *Journal of Pharmaceutical and Biomedical Analysis*, 49(1): 90–94.

Scalia S, Marchetti N, Bianchi A. (2013) Comparative Evaluation of Different Co-Antioxidants on the Photochemical- and Functional-Stability of Epigallocatechin-3- gallate in Topical Creams Exposed to Simulated Sunlight. *Molecules*, 18: 574-587.

Scalia S, Mezzena M. (2009) Co-loading of a photostabilizer with the sunscreen agent, butyl methoxydibenzoylmethane in solid lipid microparticles. *Drug Development and Industrial Pharmacy*, 35(2):192-8.

Scalia S, Mezzena M, Ramaccini D. (2011) Encapsulation of the UV filters ethylhexyl methoxycinnamate and butyl methoxydibenzoylmethane in lipid microparticles: Effect on in vivo human skin permeation. *Skin Pharmacology and Physiology*, 24(4): 182-9.

Scognamiglio I, Stefano D, Campani V, Mayol L, Carnuccio R, Fabbrocini G, Ayala F, Rotonda M, Rosa G. (2013) Nanocarriers for topical administration of resveratrol: A comparative study. *International Journal of Pharmaceutics*, 440(2): 179–187.

Selvaraj S, Karthikeyan J, Saravanakumar N. (2012) Chitosan loaded microspheres as an ocular delivery system for acyclovir. *International Journal of Pharmacy & Pharmaceutical Sciences*, 4(1): 125-132.

Shaklee Corporation. (2001) Improved stable topical ascorbic acid compositions. Patent EP 1096922 A1.

Shinde T, Sun-Waterhouse D, Brooks J. (2014) Co-extrusion Encapsulation of Probiotic *Lactobacillus acidophilus* Alone or Together with Apple Skin Polyphenols: An Aqueous and Value-Added Delivery System Using Alginate. *Food and Bioprocess Technology*, 7(6): 1581-1596.

Silva P, Fries L, Menezes C, Holkem A, Schwan C, Wigmann E, Bastos J, Silva C. (2014) Microencapsulation: concepts, mechanisms, methods and some applications in food technology. *Ciência Rural*, 44(7): 1304-1311.

Sinko PJ. (2006) Chemical Kinetics and Stability. In: *Martin's Physical Pharmacy and Pharmaceutical Sciences*, Chapter 14, Baltimore: Lippincott Williams & Wilkins.

Soest JJGV. (2007) Encapsulation of fragrances and flavours: a way to control odour and aroma in consumer products, In: Berger R.G. (ed.), *Flavours and Fragrances – Chemistry, Bioprocessing and Sustainability*, Germany: Springer.

Soto ML, Falqué E, Domínguez H. (2015) Relevance of Natural Phenolics from Grape and Derivative Products in the Formulation of Cosmetics. *Cosmetics*, 2: 259-276.

Sri J, Seethadevi A, Prabha K, Muthupsasanna P, Pavitra P. (2012) Microencapsulation: A Review. *International Journal of Pharma and Bio Sciences*, 13(1).

Stevanovic M, Savic J, Jordovic B, Uskokovic D. (2007) Fabrication, in vitro degradation and the release behaviours of poly(dllactide-co-glycolide) nanospheres containing ascorbic acid. *Colloids and Surfaces*, 59(2): 215–223.

Sunsmart, Inc., Sibmicro Encapsulation Technologies, Inc. (1998) Composite UV sunblock compositions. Patent US 5733531 A

Suraweera RK, Pasansi HGP, Herath HMDR, Wickramaratne DBM, Sudeshika SHT, Niyangoda D, Sakeena MHF. (2014) Formulation and Stability Evaluation of Ketoprofen Loaded Virgin Coconut Oil based Creamy Emulsion. *International Journal of Pharmacy and Pharmaceutical Sciences*, 6 (8): 249-254.

Tagra Biotechnologies, 2015. Available at: <http://www.tagra.com>

Tarimci N. (2011) Cyclodextrins in the cosmetic field. In: Bilensoy, E. (ed.) *Cyclodextrins in Pharmaceutics, Cosmetics, and Biomedicine: Current and Future Industrial Applications*, 131–144. Hoboken, New Jersey: John Wiley & Sons, Inc.

Vela-Soria F, Ballesteros O, Zafra-Gómez A, Ballesteros L, Navalón A. (2014) A new method for the determination of benzophenone-UV filters in human serum samples by dispersive liquid-liquid microextraction with liquid chromatography-tandem mass spectrometry. *Talanta*, 121: 97-104.

Vettor M, Bourgeois S, Fessi H, Pelletier J, Perugini P, Pavanetto F, Bolzinger MA. (2010) Skin absorption studies of octyl-methoxycinnamate loaded poly(D,L-lactide) nanoparticles: estimation of the UV filter distribution and release behaviour in skin layers. *Journal of Microencapsulation*, 27(3): 253-62.

Wesselingh JA, Kill S, Vild ME. (2007) Design & Development of Biological, Chemical, Food and Pharmaceutical Products, In: Wiley (Ed.), Chichester, UK.

Wiechers J. (2005) Optimizing skin delivery of active ingredients from emulsions: from theory to practice. In: Rosen M.R. (ed), *Delivery System Handbook for Personal Care and Cosmetic Products-Technology, Applications, and Formulations*, Chapter 20, Norwich, New York: William Andrew, Inc.

Wiechers J. (2008) *Science and Applications of Skin Delivery Systems*. Allured Publishing Corporation, USA.

Wille JJ. (2006) Thixogel: a starch matrix encapsulation technology for topical drug and cosmetic delivery. In: Wille, J.J. (ed.), *Skin Delivery Systems: Transdermals, Dermatologicals and Cosmetic Actives*, 223–245, Oxford: Blackwell Publishing.



Wilson N, Shah NP. (2007) Review Paper: Microencapsulation of Vitamins. *ASEAN Food Journal*, 14 (1): 1-14.

Wisuitiprot W, Somsiri A, Ingkaninan K, Waranuch N. In vitro human skin permeation and cutaneous metabolism of catechins from green tea extract and green tea extract-loaded chitosan microparticles. *International Journal of Cosmetic Science*, 33(6): 572-9.

Yamamoto I, Tai A, Fujinami Y, Sasaki K, Okazaki S. (2002) Synthesis and characterization of a series of novel monoacylated ascorbic acid derivatives, 6-O-acyl-2-O-alpha-D-glucopyranosyl-L-ascorbic acids, as skin antioxidants. *Journal of Medicinal Chemistry*, 45(2): 462-8.

Yang JH, Lee SY, Han YS, Park KC, Choy JH. (2003) Efficient Transdermal Penetration and Improved Stability of L-Ascorbic Acid. *Bulletin of the Korean Chemical Society*, 24(4): 499-503.

Yasutami S, Hiromichi I, Hideya A, Atsuko R, Naoto O, Naomichi B, Taketoshi M. (2004) Skin Whitening Effect of Linoleic Acid Is Enhanced by Liposomal Formulations. *Biological and Pharmaceutical Bulletin*, 27(4): 591—594.

Yin WS, Yates MZ. (2009) Encapsulation and sustained release from biodegradable microcapsules made by emulsification/freeze drying and spray/freeze drying. *Journal of Colloid and Interface Science*, 336(1): 155–161.

Yusuf N, Irby C, Katiyar SK, Elmets CA. (2007) Photoprotective effects of green tea polyphenols. *Photodermatology, Photoimmunology & Photomedicine*, 23: 48–56.

Table 1. Usual methods for encapsulation and respective particle sizes. (Ghosh, 2006)

Type of Method	Method	Particle size (µm)	References
Chemical process	Emulsion Polymerization	0.5–1000	Fairhurst et al., 2008; Ghosh, 2006; Hirech, 2003
	Suspension Polymerization	0.5–1000	
	Interfacial Polymerization	0.5–1000	
Physico-chemical process	Coacervation/Phase separation	1–1000	Ciriminna et al., 2013; Di Marco et al., 2010; Chen et al., 2009; Cocero et al., 2009; Martins et al., 2009; Nguyen-Ngoc et al., 2007; Gander et al., 2006; Kas et al., 2000; Madan, 1978
	Solvent evaporation/extraction	0.5–1000	
	Sol-gel encapsulation	2–20	
	Supercritical fluid-assisted microencapsulation	0.5-500	
	Layer-by-layer assembly	0.5–20	
Physico-mechanical process	Spray-drying	1–500	Shinde et al., 2014; Anwar et al., 2010; Fairhurst et al., 2008; Lakkis et al., 2007
	Spray-cooling	20 – 500	
	Co-extrusion	250–2500	
	Spinning disk	5–1500	
	Fluidized-bed coating	20–1500	
	Melt solidification	5-1000	
	Polymer precipitation	5-1000	

**Table 2.** Some examples of encapsulation of cosmetic ingredients for topical application.

Class / Function	Name Molecular formula CAS Number	Encapsulation Materials	Encapsulation Method	Principal Results	Reference
Vitamin / Antioxidant	Retinol (Vitamin A) C <sub>20</sub> H <sub>30</sub> O 68-26-8 Retinyl palmitate (Vitamin A palmitate) C <sub>36</sub> H <sub>60</sub> O <sub>2</sub> 79-81-2	Glyceryl behenate SLN	Melt solidification	Particle size: 224 nm Release after 6h: 3400 ng out of 500 µg Retinol SLN incorporated in o/w cream showed better localizing action results	Jenning et al. (2000)
	Retinol (Vitamin A) C <sub>20</sub> H <sub>30</sub> O 68-26-8	Precursor: Tetraethyl orthosilicate Stabilizer: Hydroxypropyl cellulose Surfactants: Tween 20; Span 80 External oil phase: N-decyl alcohol Catalysts: HCl; NH <sub>3</sub>	Sol-gel encapsulation	Particle size: 15-40 µm Encapsulation efficiency: 45% (max) Microspheres entrapping retinol were best formed with NH <sub>4</sub> OH as a catalyst for TEOS ratio R <sub>w</sub> = 4	Myung-Han et al. (2001)
	Retinol (Vitamin A) C <sub>20</sub> H <sub>30</sub> O 68-26-8	Shell: Chitosan Solvent: Ethanol	Solvent evaporation	Particle size: 50–200 nm Zeta potential: 50-75 mV Encapsulation efficiency: > 60% Retinol solubility increased 1600-fold	Dong-Gon et al. (2006)
	Retinyl acetate (Vitamin A acetate) C <sub>22</sub> H <sub>32</sub> O <sub>2</sub> 127-47-9	Shell: LA-Chitosan	Sonication	Particle size: 100–500 nm Encapsulation efficiency: 90% (max)	Chen-Guang et al. (2003)
	Ascorbic acid (Vitamin C) C <sub>6</sub> H <sub>8</sub> O <sub>6</sub> 50-81-7	ZnO/SiO <sub>2</sub>	Coprecipitation	Particle size: 0.5 µm Sustained releasing of vitamin C	Yang et al. (2003)
	α-Tocopherol (Vitamin E) C <sub>29</sub> H <sub>50</sub> O <sub>2</sub> 59-2-9	Shell: Gliadin Solvent: Ethanol/water (62/38 v/v)	Desolvation	Particle size: 900 nm Encapsulation efficiency: > 77%	Duclairoir et al. (2002)
Phenol / Antioxidant	Catechin C <sub>15</sub> H <sub>14</sub> O <sub>6</sub> 7295-85-4	Shell: Chitosan Solvent: Acetone	Water-in-silicone emulsion	Particle size: 1.9 µm Encapsulation efficiency: 50% Improvement of the ability of catechins to permeate skin	Wisuitiprot et al. (2011)
Purine, Alkaloid / Antioxidant, Anti- cellulite	Caffeine C <sub>8</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> 58-08-2	Alginate	Emulsification/Internal gelation	Particle size: 45 µm Encapsulation efficiency: 51% Encapsulation of caffeine is suitable for its transdermal delivery	Cangueiro et al. (2011)

Flavonol / Antioxidant, Anti- inflammatory	Quercetin C <sub>15</sub> H <sub>10</sub> O <sub>7</sub> 117-39-5	Shell: Tristearin Emulsifier: Phosphatidylcholine	Melt emulsification	Particle size: 10-45 µm Encapsulation efficiency: 62% Light-induced decomposition of quercetin in the cream was decreased	Scalia et al. (2009)
Caffeic acid ester / Antioxidant Anti-bacterial, Anti- inflammatory	Rosmarinic acid C <sub>18</sub> H <sub>16</sub> O <sub>8</sub> 20283-92-5	Shell: Polycaprolactone Solvents: Methylene chloride, Acetone	Emulsion solvent evaporation	Particle size: 6-10 µm Encapsulation efficiency: 78% (max) Improved long-term stability	Kim et al. (2010)
Polyphenols / Antioxidant, Anti- inflammatory, Anti-aging	Yerba mate (Ilex paraguariensis)	Chitosan Triphosphosphate pentasodium	Ionic gelation Spray drying	Particle size: < 0.5 µm Encapsulation efficiency: > 87 % Sustained releasing of polyphenols Maintenance of the antioxidant activity of polyphenols	Harris et al. (2011)
Polyphenol / Antioxidant, Anti- irritating, Anti- inflammatory, Anti-aging	Resvestarol C <sub>14</sub> H <sub>12</sub> O <sub>3</sub> 501-36-0	Transfersomes with surfactants Ethanol-containing lipid vesicles	Thin film hydration	Particle size: 80-120 nm Encapsulation efficiency: > 70% Ethanol-containing vesicles based on sulfur polymer cement were able to promote permeation through the skin	Scognamiglio et al. (2013)
Flavonoid / Antioxidant, Anti- irritating, Anti- inflammatory, Whitening agent	Glabridin 59870-68-7 C <sub>20</sub> H <sub>20</sub> O <sub>4</sub>	Cyclodextrin	Solvent evaporation	—	Capsutech Ltd. (2007)
Bioflavonoid / Antioxidant, Emollient	Rutin (Vitamin P) C <sub>27</sub> H <sub>30</sub> O <sub>16</sub> 153-18-4	Shell: Ethylcellulose Solvent: Isopropyl alcohol Stabilizer: Twen-80	Desolvation; Solvent Evaporation	Encapsulation efficiency: 65% Loading capacity: 5-45 mg Release after 24h: 14-60 mg	Banjare et al. (2012)
Bioflavonoid / Antioxidant, Emollient	Rutin (Vitamin P) C <sub>27</sub> H <sub>30</sub> O <sub>16</sub> 153-18-4	Shell: MCM-41 and NH <sub>2</sub> -MCM-41 silica Solvent: Methanol	Solvent Evaporation	Encapsulation efficiency: 18% Greater accumulation in the skin for rutin complexed with NH <sub>2</sub> -MCM-41	Berlier et al. (2013)
Provitamin / Humectant, Emoll ient, Moisturizer	D-Panthenol (Provitamin B5) C <sub>9</sub> H <sub>19</sub> NO <sub>4</sub> 81-13-0	Liposome or Phospholipid vesicles (ex.: BROOKOSOME™ DP)	—	—	Maybelline Intermediate Company (1999)
Vitamin, Fatty acid / Emollient, Thickening agent, Antioxidant, Anti- inflammatory, Whitening agent	Linoleic acid (Vitamin F) C <sub>18</sub> H <sub>32</sub> O <sub>2</sub> 60-33-3	Liposomes of unhydrogenated soybean, Phospholipids and Phosphatidylcholine	High pressure homogenizer	Liposomal LA showed a whitening effect more effective than non-liposomal LA	Yasutami et al. (2004)

Carotenoid/ Antioxidant, Pigment	Lycopene C <sub>40</sub> H <sub>56</sub> 502-65-8	Ascorbic acid-6-palmitate, Cholesterol and Dicetyl phosphate	Solvent evaporation	Particle size: 200–300 nm Encapsulation efficiency: 90% (max)	Luxsuwong et al. (2014)
Sun filter	Benzophenone-3 C <sub>13</sub> H <sub>10</sub> O 119-61-9	Cetyl palmitate SLN Poly(ε-caprolactone)	Hot high pressure homogenization; Precipitation	The sun protection factor increased when benzophenone-3 was encapsulated in both nanostructures	Marcato et al. (2008)
	Benzophenone-3 C <sub>13</sub> H <sub>10</sub> O 119-61-9	Carnauba wax and Isodecyl oleate NLCs Stabilizer: Tween 80	Hot high pressure homogenization	Particle size: 0.3–8 μm Encapsulation efficiency: 90% (max)	Lacerda et al. (2010)
	Octyl methoxycinnamate C <sub>18</sub> H <sub>26</sub> O <sub>3</sub> 466-77-3	Shell: Poly(ε-caprolactone) Solvent: Acetone Stabilizers: Poloxamer 188; Tween 85	Solvent evaporation	Particle size: 250–450 nm Encapsulation efficiency: 45-90%	Alvarez-Román et al. (2001)
	Octyl methoxycinnamate C <sub>18</sub> H <sub>26</sub> O <sub>3</sub> 5466-77-3 Avobenzone C <sub>20</sub> H <sub>22</sub> O <sub>3</sub> 70356-09-1	Shell: Stearic acid, Glyceryl behenate Surfactant: Hydrogenate phosphatidylcholine	Melt emulsification	Particle size: 4-36 μm Encapsulation efficiency: >85% Reduced percutaneous penetration of UV filters achieved by the lipid microcapsules (opposed to nano)	Scalia et al. (2010)
UV filter, Pigment	Titanium dioxide TiO <sub>2</sub> 13463-67-7	Liposomes	Liposome Entrapment	The encapsulation of the micropigment into liposomes does not result in a better stability but it causes a deeper penetration into the skin	Bennat et al. (2001)
Tanning agent	Dihydroxyacetone (DHA) C <sub>3</sub> H <sub>6</sub> O <sub>3</sub> 96-26-4	Water-insoluble polymer such as oily fats	—	—	Duran (1995)
Essential oil / Fragrance	<i>Mentha piperita</i>	Shell: Chitosan Glycolic acid Coacervating agent: TTP, NaOH	Coacervation	Particle size: 1-1.5 μm Encapsulation efficiency: > 60%	Anchisi et al. (2006)
Fragrances	Camphor, Citronellal, Eucalyptol, Limonene, Menthol	Shell: Ethylcellulose, hydroxypropyl Methylcellulose and Poly(vinyl alcohol) Solvent: Ethanol	Solvent evaporation	Particle size: < 450 nm Encapsulation efficiency: > 60% Loading capacity: > 40%	Aurapan et al. (2010)
Moisturizer	Urea CH <sub>4</sub> N <sub>2</sub> O 57-13-6	Shell: Poly (D, L-lactic-co-glycolic acid) (PLGA) Solvent: Ethanol, Dichloromethane	Solvent evaporation	Particle size: 1-5 μm Encapsulation efficiency: 40% creams with microparticulated urea had slower release than free urea creams	Haddadi et al. (2008)

$\alpha$ -Hydroxy acid/ Moisturizer	Glycolic acid C <sub>2</sub> H <sub>4</sub> O <sub>3</sub> 79-14-1	Liposomes Chitosan Liposomes modified by chitosan	Reverse phase evaporation method	Particle size: 2-25 $\mu$ m Encapsulation efficiency: 65% (max) Liposomes are suitable to modulate glycolic acid release	Perugini et al. (2000)
Anti-acne	Salicylic Acid C <sub>7</sub> H <sub>6</sub> O <sub>3</sub> 69-72-7	Lecithin and Cholesterol	Thin film hydration	Particle size: 0.2–0.8 $\mu$ m Encapsulation efficiency: 43%	Bhalerao et al. (2003)
Anti-bacterial, Anti-acne	Benzoyl peroxide C <sub>14</sub> H <sub>10</sub> O <sub>4</sub> 94-36-0	Shell: Ethylcellulose Emulsifier: Polyvinyl alcohol	Emulsion solvent diffusion	Particle size: 420-310 $\mu$ m Encapsulation efficiency: 90%	Jelvehgari et al. (2006)
	Benzoyl peroxide C <sub>14</sub> H <sub>10</sub> O <sub>4</sub> 94-36-0	Shell: Ethylcellulose, Solvent: Dichloromethane Emulsifier: Polyvinyl alcohol	Emulsion solvent diffusion	Particle size: 300-600 $\mu$ m Encapsulation efficiency: 60-98%	Nokhodchi et al. (2005)

max: maximum obtained

Jenning et al. (2000), Yang et al. (2003) and Marcato et al. (2008) did not refer the encapsulation efficiency

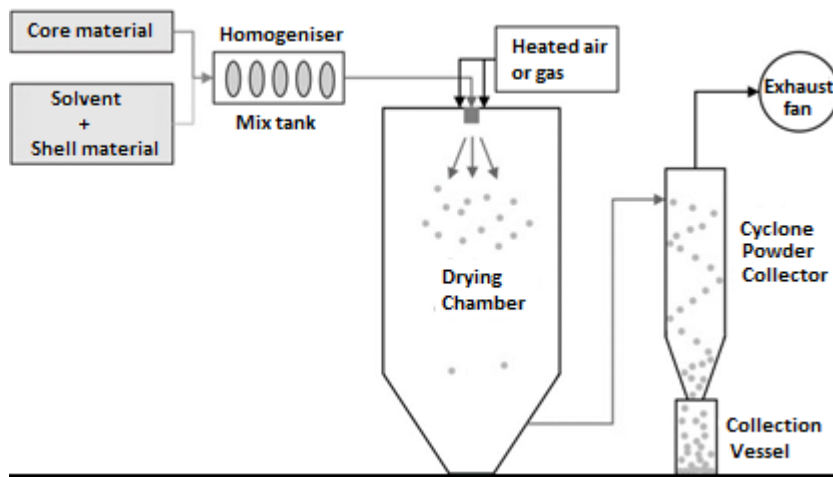
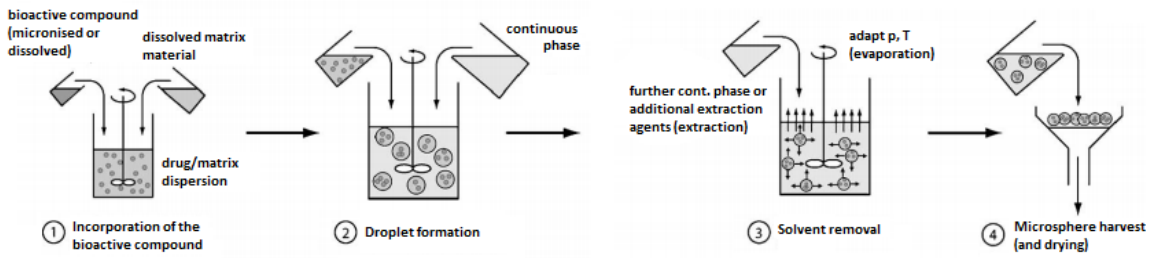
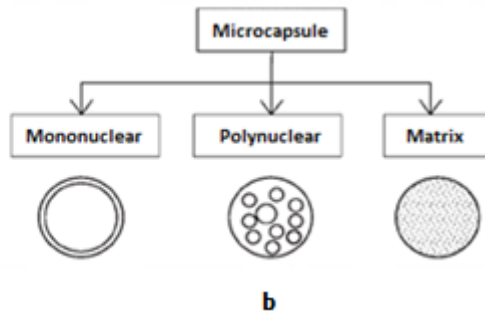
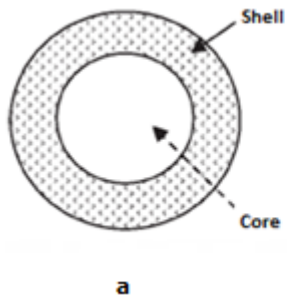


Figure 1. (a) Scheme of a microcapsule. (b) Morphology of microcapsules. (Adapted from Ghosh, 2006)

Figure 2. Schematic overview over the four principal process steps in microsphere preparation by solvent extraction/evaporation. (Adapted from Freitas et al., 2005)

Figure 3. Schematic illustration of the process of micro-encapsulation by spray-drying. (Adapted from Chávarri, 2012).