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Review

Biodegradable polymers as wall materials to the synthesis of bioactive compound nanocapsules

Priscilla Pereira dos Santos [a, b], Simone Hickmann Flôres [a], Alessandro de Oliveira Rios [a], Renan Campos Chisté [b, c, *]

[a] Institute of Food Science and Technology, Federal University of Rio Grande do Sul (UFRGS), 91501-970, Porto Alegre, Rio Grande do Sul, Brazil
[b] UCIBIO, REQUIMTE, Department of Chemical Sciences, Faculty of Pharmacy, University of Porto, (FFUP), 4050-313, Porto, Portugal
[c] Faculty of Food Engineering (FEA), Institute of Technology (ITEC), Federal University of Pará (UFPA), 66075-110, Belém, Pará, Brazil

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ABSTRACT

Background: Nanoparticles have been synthetized using polymers as wall materials to protect bioactive compounds against external factors (light, heat and oxygen), increasing the stability and improving the bioavailability of nanoencapsulated compounds.
Scope and approach: The encapsulation processes and type of polymers (natural or synthetic) exert a direct impact on the synthesis of bioactive compound nanocapsules, which reflect in parameters, such as size, zeta potential, encapsulation efficiency, aqueous solubility, aqueous stability, surface permeability, desired bioactive compounds release profile and wall resistance; and these characteristics might limit its use by food, pharmaceutical and cosmetic industries. This review summarizes researches on nanocapsules synthesis (advantages and limitations of different techniques) and focuses on the importance of different biodegradable polymers as wall materials for obtaining stable and safe nanocapsules.
Key findings and conclusions: Different wall materials can be used to synthesize bioactive compound nanocapsules; however, biodegradable polymeric nanocapsules have proven to be one of the most stable structures during storage and showed high efficiency to control the release of encapsulated compounds and due to these characteristics, they have been focus of various studies for future applications in health and food-related areas.

1. Introduction

Nanotechnology has been considered one of the main technology of the 21st century and it promises a revolution in the pharmaceutical, medical and food fields. This technology involves design, synthesis, characterization and application of particles or systems with dimensions less than 1 μm (Hoyt & Mason, 2008).

The nanotechnology is currently applied in a great number of commercial products (cosmetics and sunscreens, drugs, dental fillings, food), as well as in water filtration and catalytic systems (Brayner, 2008). In drug delivery systems, the use of polymeric nanoparticles improves the stability, absorption, and therapeutic concentration of drugs within the target tissue (Kayser, Lemke, & Hernandez-Trejo, 2005). In addition, nanotechnology can also improve thermal and storage stabilities, water solubility and bioavailability of bioactive compounds for food application (Huang, Yu, & Ru, 2010), innovating the macroscale characteristics of foods, such as texture, taste, coloring strength and industrial processes (Ezhilarasi, Karthik, Chhanwal, & Anandharamakrishnan, 2012).

Bioactive compounds can be nanoencapsulated by different types of nano-sized vehicles, such as nanoemulsion, liposomes or nanocapsules. Nanoemulsion, which corresponds to preparation of oil-in-water (O/W) emulsion, improves solubility and bioavailability of bioactive compounds due to the reduction of incomplete dissolution of lipids (Yin, Chu, Kobayashi, & Nakajima, 2009), while liposomes are prepared with lipids and phospholipids, providing protection to the compound encapsulated in their core (Soppimath, Aminabhavi, Kulkarni, & Rudzinski, 2001). However, liposomes have low encapsulation efficiency and fast leakage rate of water-soluble drugs in the blood; and nanoemulsions have very low storage stability (Sharma, Bansal, Visht, Sharma, & Kulkarni, 2010; Soppimath et al., 2001). Considering this context, biodegradable

* Corresponding author. Faculty of Food Engineering (FEA), Institute of Technology (ITEC), Federal University of Pará (UFPA), Rua Augusto Corrêa, 01-Guamá, CEP 66075-110, Belém, Pará, Brazil.
E-mail address: rcchiste@ufpa.br (R.C. Chisté).

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polymeric nanocapsules have attracted the attention for innumerous applications due to its high stability, high encapsulation efficiency and controlled release of encapsulated compounds (Singh, Pandey, Tewari, & Agarwal, 2011).

Polymeric nanocapsules are prepared with natural or synthetic polymers as wall materials and they can be used to nanoencapsulate drugs and bioactive compounds. The use of "generally recognized as safe" (GRAS) materials is important to produce safe nanocapsules under the conditions of its intended use, along with nutritional quality and stability to food or pharmaceutical applications. These GRAS materials generally exhibit controlled-release behavior and some examples were already referred in the literature, such as polysaccharides from plants (gum Arabic) or microbial (Xanthan gum) origin. Moreover, food proteins (whey protein), emulsifiers, such as lecithin, Tweens, Spans (Huang et al., 2010) and synthetic polymers such as poly(lactic acid) (PLA) and it copolymers, poly(lactide-co-glycolide) (PLGA); and poly(ε-caprolactone) (PCL) are also frequently used due to their biocompatibility and biodegradability characteristics (Hans & Lowman, 2002).

Thus, the purpose of this review was to gather information concerning the techniques of nanocapsules synthesis and the most frequent biodegradable polymers used as wall material for obtaining polymeric nanocapsules of bioactive compounds. Furthermore, the readers may figure out how these polymers can affect the characteristics of the synthesized nanocapsules.

2. Synthesis of polymeric nanocapsules

Nanocapsules are vesicular system in which specific compounds, solubilized in an aqueous or oil core, are covered by a single polymeric membrane (wall material) (Couvreur, Barratt, Fattal, & Vauthier, 2002). After synthesis, the evaluation of the nanocapsules stability is crucial mainly in relation to important parameters, such as size, polydispersity index (PDI), zeta potential, morphology, pH and release profile.

Size and size distribution of nanocapsules are essential due to their ability to modify physicochemical and pharmaceutical behaviors of encapsulated compounds (Yegin & Lamprecht, 2006). Nanoparticles size, also denominated mean diameter or z-average, can be determined by several methods, such as laser diffraction (LD) and coulter counter; however, the most used technique is dynamic light scattering (DLS) (Venturini et al., 2011; Yegin & Lamprecht, 2006), which allows the description of particle size distribution and destabilization phenomena. The size distribution is indicated as PDI that represents the particles uniformity in suspension, in which PDI values between 0.1 and 0.25 indicate a narrow size distribution and PDI values higher than 0.5 indicate a broad distribution (Wu, Zhang, & Watanabe, 2011).

Zeta potential is a physical property that is exhibited by particles in suspension, macromolecule or material surface; it corresponds to the electrical potential of nanoparticles as influenced by the nanocapsule composition and the medium in which they are dispersed (Lobato et al., 2013; Wu et al., 2011). This parameter is widely used to indicate suspension stability in colloidal dispersions, where zeta potential values higher than 30 mV and lower than −30 mV promote high stability and prevent particles aggregation (Mohanraj & Chen, 2006).

Morphology is also another important parameter for the characterization of nanocapsules and many types of electron microscopy are usually applied to observe nanoparticle morphology and structure. As an example, currently, transmission electron microscopy (TEM) is the most used technique, which is performed after freeze–fracture of nanocapsules that allow to obtain information about structure, polymer porosity and wall thickness estimative (Couvreur et al., 2002).

The above-mentioned parameters should be evaluated after the preparation of nanocapsules and monitored during storage of the suspension. However, nanocapsules stability depends on the composition and chosen technique for the synthesis and, as consequence, the most efficient technique to prepare nanocapsules will depend on both the physicochemical characteristics of polymer and also the bioactive compound to be nanoencapsulated (Reis, Neufeld, Ribeiro, & Veiga, 2006). Furthermore, the choice of the organic solvent used during nanocapsules synthesis is also very important due to the possibility of providing risk to human health, limiting the application of nanocapsules.

According to the formulation, the nanocapsules can be synthesized by two different methods (Fig. 1): interfacial polymerization of monomers and preformed polymer (Couvreur, Dubernet, & Puisieux, 1995).

2.1. Nanocapsule synthesis by polymerization of monomers

In this method, monomers of cyanoacrylate are polymerized to form nanoparticles in aqueous solution. Polymerization of monomers was applied for the first time to obtain structures denominated "nanoparts" constituted of polyoxyethylene 4-lauryl ether to the application as adjuvants (enhancers of the immune response) in immunology (Birrenbach & Speiser, 1976). However, the term "nanocapsules" was introduced for this structure by Couvrier, Tulkenst, Roland, Trouet, and Speiser (1977), which synthetized nanocapsules of polyacrylamide aiming to allow access of some compounds for lysosomes.

Monomer polymerization can be classified into emulsion and interfacial polymerization, where the first is one of the fastest techniques for obtaining nanoparticle and the second one was reported to present high drug encapsulation efficiency (Reis et al., 2006).

Briefly, the monomer is added in an aqueous solution containing surfactant (polymerization medium) under vigorous mechanical stirring to polymerize at room temperature (Fig. 2) (Rollot, Couvreur, Roblot-Treupel, & Puisieux, 1986). During polymerization process, stabilizers and surfactants are added in the formulation and the type and concentration of these constituents are responsible for particle size and molecular mass of nanocapsules obtained; the solvents are used to disperse the oil in aqueous phase and serve as vehicle for monomers (Mohanraj & Chen, 2006; Soppimath et al., 2001). The compound of interest is incorporated either by solubilization in the polymerization medium or by adsorption after completed polymerization (Soppimath et al., 2001). After the concentration under reduced pressure at room temperature, the suspension has to be purified to remove stabilizers and surfactants by ultracentrifugation and, then, the particles are suspended in surfactant-free medium (Mohanraj & Chen, 2006).

The monomer that is used in the synthesis of nanocapsules should present fast polymerization rate between the organic phase and aqueous phase. As an example, poly-(alkylcyanoacrylate) presents very fast polymerization rate and it is biodegradable and biocompatible (Krauel, Pitaksuteepong, Davies, & Rades, 2004; Reis et al., 2006; Soppimath et al., 2001). Furthermore, polymerization must be carried out in acidic medium and further pH increase to produce high molecular mass, as well as stable nanocapsules (Soppimath et al., 2001).

Nanocapsules obtained by polymerization of monomers were developed to the application with pharmaceutical compounds, such as endocytizable and lysosomotropic drugs (Birrenbach & Speiser, 1976; Couvreur, Tulkenst, Roland, Trouet, & Speiser, 1977). Moreover, researches regarding nanocapsules prepared by polymerization of monomers for the application in textile