

## Encapsulation of bioactive compounds for the generation of nutraceuticals



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### ABSTRACT

Numerous studies have been developed to improve the quality of life of society about the improvement and quality of food that promotes the maintenance and conservation of health in the face of chronic non-communicable diseases (NCDs), such as cardiovascular diseases, diabetes, and cancer. Thus,

attention has been focused on the introduction of functional foods and supplementation with nutraceuticals that may offer health benefits in addition to their nutritional properties in diets. Functional foods have their own characteristics due to the presence of bioactive compounds, which promote benefits for the body in addition to their nutritional value. Thus, studies on bioactive compounds and nutraceuticals have been increasing, given their benefits. Bioactive compounds are very unstable, so studies show that the best way for manipulation and efficacy in the body is to use them with a protective encapsulation, thus forming a nutraceutical. Polymeric systems are used for encapsulation, which promote a better delivery of these bioactive compounds.

**Keywords:** Bioactive compounds, Nutraceuticals, Polymeric encapsulation, Functional foods.

## 1 INTRODUCTION

The search for improvement in the quality of life has had a growing space in society, more and more the population has been seeking to eat healthier, perform physical exercises and, with this, generate changes for healthier habits. Given the importance of a healthier diet, we are looking for foods that contain compounds that bring health benefits, which are called functional foods. These foods have beneficial health properties due to the presence of bioactive compounds, in addition to their nutritional value already evaluated. Thus, the field of studies on functional foods has been growing widely in recent decades, in which the main bioactives of foods and their health benefits have been studied about the control/prevention of chronic non-communicable diseases (NCDs) (REZA AND KRISTEN, 2015).

The food industry has been investing in formulations to improve the characteristics of marketed products with the addition of vitamins to foods, as well as the formulation of nutraceutical compounds (ASUNÇÃO *et al.*, 2014). Thus, bioactive compounds have stood out for their characteristics, such as antioxidant, anti-inflammatory, and anticancer properties, among others.



The encapsulation of bioactives is necessary for the protection of the compound, since they present great instability, degrading easily with the variation of temperature, humidity, and pH (CARMO *et al.*, 2015).

Encapsulation techniques are widely used in the food industry and are economically viable, but they need the improvement of new technologies to obtain better results (ASUNÇÃO *et al.*, 2014).

Based on the above, the objective of this article is to carry out a recent survey on the encapsulation of bioactives for the maintenance and preservation of health and the development of nutraceuticals for food supplementation.

## 2 BIOACTIVE COMPOUNDS

Most plant extracts have good properties that help maintain and improve human health, but they are not widely used because they have high volatility and instability to UV light (BAKRY *et al.*, 2016; BASER, BUCHBAUER, 2015; MARTINS *et al.*, 2017), thus requiring an encapsulation to remain stable, potentially improving its activity (BAKRY *et al.*, 2016; VEIGA *et al.*, 2019).

The use of bioactive compounds in the food industry is currently limited due to their low solubility in water, low bioavailability, pH sensitivity and easy degradation in aggressive environments such as the gastric environment (MONTES *et al.*, 2019).

Given the great instability of bioactive compounds, their use by the food industry is currently very limited. As a solution to this problem, several technological and nanotechnological approaches have emerged, with different encapsulation systems to increase the therapeutic efficacy of bioactive compounds (MONTES *et al.*, 2019).

Examples of commonly found encapsulated bioactive compounds are essential oils, such as tuna oil, fatty acids, sunflower oil, lycopene, fiber, among others. The type of encapsulation selected is defined according to the end use of the compound, as there are several types and systems of encapsulation.

There are several methods for encapsulation, due to the differences found in each molecule of the bioactive compounds, which are differentiated by molar mass, chemical structure, solubility, among other characteristics that affect the chemical and physical requirements when encapsulation occurs (SILVA *et al.*, 2015).

The choice of the most suitable method depends on the type of material, the application and the desired release mechanism for its action. One of the classifications of encapsulation is the size of the encapsulated particle, which can be nanoparticles, microparticles or macroparticles.

According to Carneiro (2011), the type of wall material used will influence both the stability and the protective capacity of the powdered product. The ideal wall material should have properties of being a good film former at the interface; have low viscosity at high concentrations of solids;



exhibit low hygroscopicity; release the encapsulated material when desirable in the final product; have low cost; have high availability and offer good protection to the encapsulate.

An example is the great difficulty encountered in the encapsulation of highly lipophilic substances that, with processing time, storage and commercial use, end up suffering oxidation (developing rancidity and altering sensory characteristics) and having considerable losses in their chemical composition (GANGURDE *et al.*, 2016).

### 3 ENCAPSULATION

Polymeric systems are the most promising and versatile encapsulation bases, standing out in the market; their efficacy depends strictly on the properties of the polymer used for this purpose (GANGURDE *et al.*, 2016; PUTTASIDDAIAH *et al.*, 2022).

The encapsulation forms a physical barrier, in which the isolated compound is preserved and wrapped to a membrane, usually polymeric, which under specific conditions, occurs when this membrane ruptures in specific places, thus releasing the compound in question (CARMO *et al.*, 2015). In addition to the physical barrier factor, encapsulation promotes and controls the effectiveness of the compounds to be released, being able to expand their range of application and ensure the optimal daily dosage of delivery.

This is a widely used practice in the food industry due to the protection provided to the bioactive in terms of thermal degradation, microbiological stability, in addition to providing an adequate concentration (SHISHIR *et al.*, 2018).

According to Carmo *et al.* (2015), encapsulation is defined as the joining of particles in a coating material, which allows the formation of a physical barrier between the encapsulate and the medium, thus protecting the encapsulated compound from the adversities of the medium, such as temperature variation, pH, humidity and oxidation. The encapsulation consists of an encapsulating layer, usually of polymeric origin, acting as a protective film with active characteristics for such property, isolating the substance in question from the external environment. This film can undergo specific stimuli in places directed to the release of the substance (CARMO *et al.*, 2015).

Encapsulation can also have multiple benefits, such as improving the bioavailability of the encapsulated bioactive; use of pH-sensitive polymers, which modifies the characteristics of the capsule wall material, promoting better bioavailability, and also allows the delivery of bioactives to a specific site, which could enhance its pharmacological activity.

With the development of nanotechnology, it is also possible to develop nanoencapsulation for bioactive compounds, with better properties and efficiency. It can contribute more efficiently in the economic and nutritional areas, ensuring better stability, solubility, efficacy, protection, and bioavailability (SINGH *et al.*, 2023).



In the literature, there are some studies on the encapsulation and nanoencapsulation of bioactive compounds using polymers for the formulation of nutraceutical products.

Nguyen and Jeong (2018) proposed the encapsulation of quercetin through the *electrospray* method for the preparation of poly(lactic-co-glycolic acid) (PLGA) microspheres. Quercetin is found in several plants and has many biological effects (DAVIS et al., 2009), *such as anticarcinogenic, anti-inflammatory, antiviral, and antioxidant effects* (AGUIRRE et al., 2018).

For the fabrication of the microspheres, the authors used different ratios of quercetin and PLGA in different proportions of the mixture of acetone (ACE) with dimethylformamide (DMF); the experiments were carried out at room temperature and *electrospray* parameters, including flow rate, applied voltage and tip-collector distance, were evaluated (NGUYEN; JEONG, 2018).

PLGA and quercetin are highly soluble in acetone and dimethylformamide, which enables the use of these solvents to produce quercetin-charged microspheres (BOHR *et al.*, 2012).

The use of acetone as the only solvent resulted in microspheres with diverse morphologies that exhibited a flattened pattern. The results obtained by the authors from the formulation of PLGA microspheres suggested that quercetin-laden particles offer better long-term delivery to easily access therapeutic targets *in vivo*.

Figueiredo et al. (2020) developed a study on the encapsulation of camu-camu extract (*Myrciaria dubia*), a fruit of Amazonian origin, standing out for its high nutritional value and content of bioactive compounds, being called the "king of vitamin C" or "superfruit" (AGUIAR; SOUZA, 2016). In addition, camu-camu extract powder can also be applied for pharmacological and cosmetic purposes since its high antioxidant potential has been associated with the contents of ascorbic acid and phenolic compounds (FUJITA *et al.*, 2017).

Figueiredo et al. aimed to synthesize microparticles containing camu-camu extract by encapsulating it with different biopolymers. After camu-camu extraction, the authors used maltodextrin (MD), inulin (IN) and oligofructose (OL) for encapsulation in the spray-drying process. The wettability of the powders was evaluated, which is the ability of the powder particles to rehydrate in water. Thus, rapid wettability is considered a desirable characteristic of powdered food products (SARABANDI et al., 2017). The encapsulation made with OL and IN showed a shorter wetting time, differing significantly from the treatment with MD. The particle size of powdered products is associated with important characteristics such as susceptibility to spoilage, fluidity, appearance and dispersibility of particles (BOTREL *et al.*, 2014). Significant differences were observed for the size of the particles with the different biopolymers, and the particles with IN had a larger mean diameter. Silva and Meireles (2015) investigated the effect of the degree of polymerization (PD) of inulin on this process, and reported that this effect is probably due to agglomeration caused by the increase of



existing bond sites in surface particles, leading to particle-particle interactions, resulting in the formation of larger particles in the system.

The lowest stability found was with the use of prebiotic biopolymers (IN and OL), with degradation beginning at 225°C and with DM, the degradation process started at around 275°C. The analysis was also carried out with the pure extract of lyophilized camu-camu (CEL), where it was possible to observe a lower thermal stability, with the degradation temperature around 100°C, which demonstrates the importance and need for the encapsulation process. Figueiredo et al. (2020) concluded that the encapsulation process is advantageous, as it protects bioactive compounds, which can be applied in various food matrices such as dairy products, beverages, emulsions, candies, among others, incorporating antioxidant capacity, in addition to providing enrichment nutrients.

Salah et al. (2020) proposed the nanoencapsulation of anthocyanins extracted from red raspberry bagasse into  $\beta$ -lactoglobulin ( $\beta$ -Lg) for the generation of nutraceuticals and application in food and pharmacological matrices.

Anthocyanins (AC) are natural pigments responsible for coloring in many fruits and vegetables, possessing bio-functional properties (ZHANG *et al.*, 2020). Red raspberries are rich in anthocyanins (CHEN *et al.*, 2020; ZHANG *et al.*, 2021), and have antioxidant, anticancer, and antidiabetic functions, among others (LI *et al.*, 2020; WANG *et al.*, 2020). The use of AC in the food industry is restricted due to its rapid deterioration as a result of exposure to pH, temperature, oxygen, light, metal ions, among others (LIU *et al.*, 2020). The bioavailability of anthocyanins is also very low, mainly due to their degradation during gastrointestinal digestion processes (CHI *et al.*, 2019; MANSOUR *et al.*, 2020).

Natural polymers have been used as encapsulating material to improve the properties of polyphenols, including AC. Encapsulation techniques increase the efficiency of bioactives, increasing their solubility, bioavailability, stability and can control their release (LI *et al.*, 2015). Biopolymer-based nanoparticle delivery systems are being developed not only to encapsulate the bioactive compounds, but also to protect and transport them to the target system (HU *et al.*, 2017). Salah and collaborators proposed encapsulation by the coacervation method, which is a simple and straightforward process being combined with the ultrasonic process for manufacturing protein nanoparticles. The coacervation method is appropriate for thermosensitive bioactive compounds, as there is no need to remove oils or surfactants (ROHIWAL *et al.*, 2015). Other studies have shown that this method has also been used for encapsulation of many components, such as curcumin, quercetin, date palm seed, doxorubicin and scutellarin, to improve their bioavailability (CHAVOSHPOUR-NATANZI; SAHIHI, 2019; WEI *et al.*, 2014).

Encapsulation with  $\beta$ -Lg was done in samples varying the AC concentration and also with the empty particle. Encapsulation by coacervation and ultrasonic processing were performed, generating



nanoencapsulated particles. All samples produced showed a nanoscale size, demonstrating that the coacervation method combined with the ultrasonic process is a successful way of generating protein nanoparticles (JUN *et al.*, 2011). An aqueous ethanol solution was added to the system, and only H<sub>2</sub>O could also be added to inhibit the aggregation of particles due to their repulsive forces, resulting in the presence of negative charges on the protein molecules (BAGHERI *et al.*, 2013).

The authors concluded that the  $\beta$ -Lg nanoparticles loaded with anthocyanin (AC) were successful in the manufacturing process by coacervation and ultrasonication, generating monodisperse particles with sizes within the expected, presenting a good yield and a high encapsulation efficiency. When analyzing the thermal stability, it was observed that this was increased due to the protection offered by the encapsulation with the biopolymer used, thus being a promising technique for application in food matrices (SALAH *et al.*, 2020).

Meng *et al.* (2021) proposed the encapsulation of curcumin (Cur) in zein/carboxymethyl dextrin (CMD) nanoparticles in different proportions for its application in the food industry, given the great benefits of curcumin. As a polyphenolic compound, curcumin has physiological benefits with antioxidant, anti-inflammatory, anti-aging, and anticancer action, acting in the prevention of NCDs (PAN *et al.*, 2019). However, like other bioactive compounds, Cur is highly unstable, has high hydrophobicity and reduced oral bioavailability, thus requiring efficient encapsulation (PAN *et al.*, 2020).

The complex formed by carboxymethyl and dextrin associated with zein has the ability to increase the protection of biologically active components (SONG, *et al.*, 2017). This association promotes the improvement of some characteristics of dextrin, such as increased solubility in water and thermal stability (TAN *et al.*, 2013).

At the end of the analyses, the authors demonstrated that the encapsulation of Cur in zein/CMD nanoparticles is the most efficient form of encapsulation with an excellent thermal stability.

Gagliardi *et al.* (2021) proposed a comparison of polymeric nanoencapsulation systems of poly(lactic acid-glycolic co-acid) (PLGA) and zein, for the encapsulation of rutin, which is a bioflavonoid present in several foods, characterized by its antioxidant, anti-inflammatory, and anticancer activity. The nanoparticles were produced by the nanoprecipitation technique, being prepared with PLGA (75:25) using poloxamer-188 (PLX188) or polysorbate 80 as stabilizers to modulate the properties (COSCO *et al.*, 2019).

The particles encapsulated with SD-zein showed great stability at different temperatures, confirming the remarkable ability of the natural matrix to effectively retain the bioactive compound, and no physical destabilization was observed.



Thus, the authors concluded that rutin can be integrated into polymeric nanoparticles consisting of biomaterials and characterized by different physicochemical properties intended for different applications.

At the end of this survey, it can be concluded that studies on the encapsulation and generation of nutraceuticals from bioactive compounds of functional foods have been growing, due to the advancement of new technologies that have been developed and the great interest of the food industries, given the importance of bioactives in food for the prevention and maintenance of health.

There are several types of encapsulations, and those employing polymers are the most promising on the market, due to their good properties, including being biodegradable and biocompatible.

The most diverse forms of encapsulation are also observed, with specific materials for each system in question, especially with regard to nanoencapsulation, which is more promising and efficient. All the analyses carried out with the encapsulated systems demonstrate the best results for trapping the bioactive, in micro size and especially in nano size, with specific properties of each system for a release in a specific location. Several factors have been studied and proven to be efficient for encapsulation systems.

In this way, the efficiency of encapsulation for the protection of the bioactive and being possibly efficient for the formation of nutraceuticals has been proven by several studies, demonstrating that they are very promising for the scientific field, which can generate great benefits to society.



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