CHAPTER SEVEN

Polysaccharide-based nanotechnology approaches to deliver bioactive compounds for food applications

Thiécla Katiane Osvaldt Rosales[a,b] **and João Paulo Fabi**[a,c,d,*]
[a]Department of Food Science and Experimental Nutrition, School of Pharmaceutical Sciences, University of São Paulo, São Paulo, SP, Brazil
[b]Instituto de Pesquisa Energéticas e Nucleares—IPEN, São Paulo, SP, Brazil
[c]Food Research Center (FoRC), School of Pharmaceutical Sciences, University of São Paulo, São Paulo, SP, Brazil
[d]Food and Nutrition Research Center (NAPAN), School of Pharmaceutical Sciences, University of São Paulo, São Paulo, SP, Brazil
*Corresponding author: e-mail address: jpfabi@usp.br

Contents

Advances in Chemical Engineering, Volume 62
ISSN 0065-2377
https://doi.org/10.1016/bs.ache.2023.08.001

Abstract

Nanoencapsulation based on natural polysaccharides effectively protects and improves the bioavailability of different bioactive compounds. Food polysaccharides have essential functional properties to compose targeted delivery nanosystems in the intestine. This chapter describes the characteristics of the leading natural polysaccharides used as nanocarriers for application in food products. Also, it demonstrates the principal methodologies used for elaboration and applicability, indicating the characterization methods mechanisms for the formation and targeted release. The essential biomaterials for this purpose are chitosan, cellulose, and pectin, which can be used alone or combined with proteins to form nano-gels with multiple functionalities. Several methodologies can be used for preparation, such as molecular self-organization and ionic gelation. Nanoencapsulated bioactives based on these polysaccharides can be protected, maintain functional properties, thus increasing the absorption and bioavailability. Biocompatibility, biodegradability, and non-toxicity are the highlighted advantages of these biopolymers. In addition, they can be extracted from sustainable sources, such as industrial by-products. Several studies have proven the advantages and relevancy of biomaterials for protection against the environment, factors intrinsic to human digestion, and enhancing the beneficial effects of biologically active compounds. Nanoencapsulation based on polysaccharides effectively enables the inclusion of these compounds in foods or to develop new dietary supplements.

1. Introduction

Bioactive compounds have attracted substantial interest in recent decades due to their health-promoting properties and possible technological applicability, mainly in adding these compounds to food and developing food supplements (Siddiqui et al., 2023). Polyphenolic compounds, carotenoids, vitamins, and some minerals are associated with the reduction of non-communicable chronic diseases, such as cardiovascular, neurological, diabetes, and various types of cancer (Comunian et al., 2021; Henriques et al., 2020; Rajoka et al., 2021).

Despite the broad applicability and the potential benefits attributed to the ingestion of these compounds, there is a limitation to their full biological use. Molecular instability, solubility, bioaccessibility, absorption, and bioavailability are inefficient for most of them thus limiting technological applications (Rashwan et al., 2022; Tarone et al., 2020). In this regard, nanoencapsulation is adequate for the protection of bioactive and conducive to developing precisely foods designed for controlled delivery and bioaccessibility of functional components in specific target tissues in the human body (Dima et al., 2020a,b).

Nanotechnology applied to food and nutraceuticals is an emerging field (Otchere et al., 2023). The use by the food and pharmaceutical industries to formulate systems for the protection, delivery, and controlled release of various bioactive compounds has been expanding in recent decades, as well as the search for effective biomaterials for the construction of nano-systems (Baliyan et al., 2020; Gonçalves et al., 2022). Identifying biomaterials for protection, targeting, and responsive delivery to biological stimuli is essential for effective formulations (De Anda-Flores et al., 2021).

Food polysaccharides are biopolymers that have gained relevant importance in elaborating nanoparticles to form delivery systems for bioactive compounds and drugs directed to the intestine (da Silva and Fabi, 2022; Rosales and Fabi, 2023b,c; Shen et al., 2022). There is growing interest in the excellent functionalities of natural polysaccharides due to the safe, healthiness, low-cost, and efficient development of nanoformulations for application in food products (Dacoba et al., 2019; Zhang et al., 2021a,b). Food polysaccharides-based nanomaterials exhibit many advantages as pharmaceutic forms for sustained and controlled delivery systems. They are biocompatible and biodegradable polymers, with vast sources for extraction—mainly the by-products of the food industry, such as fruit peels (Comunian et al., 2021; Rosales and Fabi, 2023b).

The protection of bioactivity and improvement of efficiency in the use of bioactive compounds applied in food using nanostructures based on polysaccharides—due to the complexity of interactions and influencing factors—must be described and discussed in depth to support future studies in developing new nano-foods and pharmaceutical formulations to improve human health (Anal et al., 2019; Shen et al., 2022). Thus, this chapter proposes an extensive review that emphasizes the progress of research in the formulation of nanostructures based on food-derived polysaccharides through different techniques and contributes with a discussion about their application of nano-encapsulated bioactive compounds as functional ingredients. In addition, this chapter describes the main approaches commonly used to elaborate nano-complexes of polysaccharides loading bioactive compounds, highlighting the main properties of biopolymers—pectin, cellulose, and chitosan—and the characterization methods and applicability in the food and pharmaceutical segments.

2. Nanoencapsulation of bioactive compounds is promising to improve their absorption, stability, and functionality

Bioactive compounds are plant components (small parts), such as fruits, nuts, cereals, and others, that perform various biological functions in reducing the risks of chronic non-communicable diseases (Bao et al., 2019; Tran et al., 2020). The consumption of bioactive compounds has been attributed to significant improvements in disease markers such as antioxidant, anti-inflammatory, and anti-aging effects, which decrease risks of development of cancer, diabetes, obesity, and cardiovascular and neuroendocrine disorders. Examples of phytochemicals are polyphenols, flavonoids, carotenoids, terpenes, alkaloids, fatty acids or oils (e.g., α-linolenic acid and linoleic acid), vitamins (e.g., folic acid and cholecalciferol), and some bioactive peptides (Gonçalves et al., 2018; Wei and Huang, 2019; Wijaya et al., 2020; Zhang et al., 2021a,b).

The regular consumption of bioactive molecules is associated with beneficial effects for human health through the modulation of important physiological and cellular activities, making them attractive for enriching a range of foods and developing new nutraceutical formulations (Câmara et al., 2020; Gonçalves et al., 2018; Shishir et al., 2018; Siddiqui et al., 2023). Some compounds are cited in the literature for their specific biological action—such as curcumin, a natural compound extracted from saffron—and the biological effects related to the antineoplastic, antioxidant, and anti-inflammatory activity (Sanidad et al., 2019). Carotenoids such as lycopene are studied due to their antioxidant action and anticancer properties attributed to regular consumption (Akbari-Alavijeh et al., 2020; El Gharras, 2009). Anthocyanins from blue, red, and purple vegetables (blackberry, strawberry, blueberry, and red cabbage) are important antioxidant and anticancer compounds (Joseph et al., 2014; Rodriguez-Amaya, 2016; Viegas et al., 2019). Also, resveratrol, mainly present in grapes, has positive cardiovascular effects, cardio-protectors, and antioxidant action (Fraga et al., 2019).

However, despite its wide occurrence in several sources, molecular instability leads to limited bioavailability. Many of these bioactives are labile, and they have moderate or low solubility in water or lipids, show chemical and thermal instabilities (factors such as pH, oxygen, and some metals). They also show high excretion, poorly absorbed, limited bioaccessibility, inefficient biological use, and considerable loss of bioefficacy after ingestion. In addition, due to the complexity of the food matrix where these compounds are inserted, many other components influence their stability and bioaccessibility, such as the presence of dietary fibers and some minerals. Furthermore, the functionality of most bioactive compounds can be lost during food processing and storage (Azad et al., 2021; Fleschhut et al., 2006; Zhang et al., 2022). For these reasons, the effective supplementation of these compounds and their inclusion in the food and pharmaceutical industries are challenging (Bao et al., 2019; Duda-Chodak et al., 2015).

For the protection and maintenance of the stability of these compounds and to maximize their biological use, forming intermolecular complexes with biomacromolecules in nanostructures can be considered a viable alternative. Bioactive compounds stabilized in nanostructures may be more biologically efficient and included for food fortification and dietary supplement development (de Souza Simões et al., 2017; Jafari and McClements, 2017). The limitations for the oral administration of several natural compounds susceptible to external factors and factors inherent to digestion can be overcome by developing nanostructures using the functional design of targeted delivery and release vehicles (Debele et al., 2016).

The application of nanoparticles as delivery systems for bioactive compounds has been widely explored in recent decades. Nanostructured biopolymers can protect, deliver and release several bioactive compounds in the intestine (Bealer et al., 2020; Matalanis et al., 2011). Nanotechnology ($10 < d < 1000$ nm) can effectively overcome this intense degradation, promote excellent absorption and bioavailability, use their properties, maintain a stable structure, and enable broad applicability in food/pharmaceutical formulations (Fathi et al., 2014; Salarbashi et al., 2020). Naturally occurring biopolymers have been researched to encapsulate various phytochemicals and drugs. In this regard, the food and pharmaceutical industry has shown great interest in enabling the use of bioactive in all stages, from production and food storage to ingestion (Baliyan et al., 2020). Nanoencapsulation can be described as trapping a central compound in the internal phase of another immiscible substance, called a carrier or wall material, in a solid or liquid state. Nanostructures are options for protecting bioactive substances and accurately releasing them in biological systems (Assadpour and Jafari, 2019a; Sadeghi et al., 2017).

The nanoencapsulation process is a tool to promote the stability, water solubility, bioaccessibility, and bioavailability of natural bioactive compounds (Gonçalves et al., 2018). Nanostructures can attenuate the degradation resulting from human digestion, minimizing the effects along the gastrointestinal tract. The encapsulation of biologically active molecules is a promising method for obtaining stable and directed particles specific to the body (Shen et al., 2022). Targeted delivery systems based on polysaccharides can release the encapsulated bioactive compounds in their interior through an external stimulus. Among the various characteristics of polysaccharides (in addition to those already described) is the potential to release charged bioactive (encapsulated material) in specific sites (cells, tissues, and organs) is of notable importance to elaborate nanostructures with a design designed to direct delivery of the compound in certain metabolic situations and various diseases, promoting more effective therapeutic results (Li et al., 2021; Rashidinejad et al., 2021; Rezaei et al., 2022). Oral therapy systems to enhance the biological use of these bioactive are aimed at adverse treatments in various diseases, such as some types of cancer (Bao et al., 2019). Protecting bioactive factors intrinsic to human digestion may increase the biological system's bioaccessibility, absorption, and bioavailability. Targeted delivery and controlled release are essential to decrease degradation and loss of functional properties. Controlled release occurs with biological stimuli such as temperature, humidity, pH, light, and enzymatic hydrolysis (Faridi Esfanjani et al., 2018; Manzoor et al., 2020; Rashidinejad et al., 2021).

The nanoencapsulation process is effective in increasing the stability of different bioactive compounds. This technological process can protect unstable and susceptible molecules from environmental conditions during processing and storage, avoiding degradation and loss of functionality and maintaining the sensorial characteristics of the encapsulated compounds. The food industry is exploring bioactive compounds' protection and controlled release; these attributes are necessary for the processing period and food storage used in food formulation or packaging (Rosales and Fabi, 2022; Sekhon, 2010). Bioactive compounds within nanostructures can improve some undesirable sensory characteristics, such as unpleasant flavors, and improve some food characteristics, such as the use of carotenoids, and polyphenols (e.g., anthocyanins), to add color in many foods. They can also prevent oxidative reactions thus preserving bioactivity and nanoparticles could control the release of bioactive agents. Furthermore, nanoencapsulation of these compounds can improve foods' quality, stability, and shelf-life (Fasolin et al., 2021; Rashidinejad et al., 2021; Rezaei et al., 2019, 2022). Polysaccharides and proteins are the two main food macromolecules most used in nanostructures to encapsulate different bioactive compounds (Wusigale et al., 2020).

3. Polysaccharides-based nanoparticles as bioactive compounds delivery systems

Food biopolymers, especially the polysaccharides, have many excellent properties for forming nanostructures. Polysaccharides are biodegradable, biocompatible, and ideal for the nanocarrier of active molecules (Adrian et al., 2019). Among the various biomaterials for application in food, polysaccharides (alone or in combination with proteins) are promising to form encapsulation and colloidal delivery nanosystems (Akbari-Alavijeh et al., 2020). Polysaccharides are a complex of polymeric biopolymers isolated from plant, animal, microbial, and algal sources constructed from monosaccharides (composed of at least 10 monosaccharides) linked by glycosidic bonds. Most of them are biomaterials distributed in abundance in nature; they are soluble in water, with low cost, and with consolidated techniques for extraction and isolation (Antonov et al., 2019; Bordenave et al., 2014; Mudgil and Barak, 2013; Persin et al., 2011).

Polysaccharides with negative or positive charges (due to pH and molecular structure) are effectively used to create new nanostructures. The abundance in nature, sustainable techniques for extraction, and essential attributes such as support of the circular economy (extracted from by-products), biodegradability, biocompatibility, bioactivity, low toxicity, and good solubility are indicative of the promising application in nanostructures (Hosseini et al., 2017; Lara-Espinoza et al., 2018). They are sustainable biomaterials with ample sources for extraction. Food industry by-products, such as fruit peels and seeds, can be used as a source for extracting bioactive compounds (such as polyphenols) and biopolymers such as pectin (citrus peel, apple, chayote, passion fruit), chitosan (shrimp and crab waste) and cellulose (wheat bran and apple peel) (Rosales and Fabi, 2023b,c; Suleria et al., 2020). The materials used to form intestinal delivery nanosystems must consider the ability of the biopolymer to have resistance, flexibility, and mucoadhesiveness, and it must be responsive to different biological stimuli. In this regard, polysaccharides have flexible, degradable, fermentable, and hydrophilic structures, resist to digestion factors, and pass intact through the gastrointestinal tract (Muvva et al., 2020; Nasrollahzadeh et al., 2021).

The composition of the polysaccharides regarding the monosaccharide units classifies these biopolymers as homopolysaccharides (only a single type of monomer) or heteropolysaccharides (two or more different types). Their properties are defined according to their chemical structure and other reactive functional groups, chemical composition, and molecular weight ranges (Barclay et al., 2019; Nasrollahzadeh et al., 2021). In addition, they have unique and specific bioactivity and the formation of delivery systems for bioactive compounds and drugs (Barclay et al., 2019; Luo and Wang, 2014; Wusigale et al., 2020). Furthermore, some particular polysaccharides have important biological activities, such as the ability to modulate the immune system, intestinal homeostasis, glycemic control, and blood cholesterol, and reduce the risks of developing some types of cancer (Ahmad et al., 2022; Keizman et al., 2021; Posocco et al., 2015; Wang et al., 2022).

The polysaccharides commonly used in industry for various purposes and safe are starch, cellulose, β-glucan, and glycogen (homopolysaccharides) and gum arabic, arabinoxylans, chitosan, pectin, and xanthan gum (heteropolysaccharides). The structure of polysaccharides is diverse, with different compositions, chain lengths, and functional groups. To form nanoparticles, the hydrophilic groups (hydroxyl, carboxyl, and aldehyde) in the molecule and responsible for creating non-covalent bonds with other molecules of similar character (Barclay et al., 2019). Hydrophilic functional groups, such as aldehyde, carboxyl, hydroxyl, and amino, are distributed along their molecular structure when homogenized with other biopolymers and can establish an intermolecular interaction, generating a bio-adhesive state. This interaction allows the formation of a trapping system of active molecules for targeted delivery (Antonov et al., 2019; Zhang et al., 2021a,b). Current literature indicates that food polysaccharides are frequently used food biopolymers for manufacturing nanostructures to encapsulate and deliver bioactive compounds. Polysaccharides are abundant in nature, have adequate water solubility, non-toxicity and low-cost processing, show high surface/volume ratio, good dispersibility and bioaccessibility, and can effectively targeted or control the release of the encapsulated bioactive compound. In addition, they have several reactive functional groups in their structure (e.g., carboxylic acid, hydroxyl, and amino groups), which contributes to their structural and functional diversity and the capacity for intermolecular interaction. Polysaccharides can interact and form protein-polysaccharide complexes through hydrogen bonding and hydrophobic interactions, suitable for specific applications in delivering bioactive compounds and drugs (Akbari-Alavijeh et al., 2020; Carrasco-Sandoval et al., 2021; Esmaili et al., 2019; Lu et al., 2019). For intestinal delivery, many physical, chemical, enzymatic, and mucoadhesive barriers along the gastrointestinal tract need to be overcome.

Polysaccharides are sustainable biomaterials with ample sources for extraction. Food industry by-products, such as fruit peels and seeds, can be used as a source for extracting bioactive compounds (such as polyphenols) and biopolymers such as pectin (citrus peel, apple, chayote, passion fruit), chitosan (shrimp and crab waste) and cellulose (wheat bran and apple peel) (Colodel et al., 2020; Rosales and Fabi, 2023b,c; Suleria et al., 2020).

Nanoencapsulation of bioactive compounds through polysaccharide-protein nano complex may enable the elaboration of nanostructures with essential characteristics to be added in food formulations, such as stability, biodegradability, biocompatibility, effectively controlled release, and site-specific delivery (Shen et al., 2022). Some disadvantages of using some polysaccharides for the targeted delivery of bioactive reported in the literature are the broad and mixed molecular weights, the quite variable composition between the different types, and some insolubility. Limitations that can be circumvented by molecular modification techniques in some cases and thus make the application feasible (Wen and Oh, 2014). Food-derived polysaccharides and their combination with proteins are promising biomaterials to form complex nanoencapsulation systems (Rosales and Fabi, 2023b,c).

4. Polysaccharide-protein nanocomplexes for the encapsulation of bioactive compounds

Nanocomplexes based on polysaccharides and proteins are promising vehicles for biologically active compounds. Interactions between proteins and polysaccharides provide different nano-system functionalities to protect active molecules (Zhang et al., 2021a). Several investigations and critical literature reviews have indicated that nanoparticles based on polysaccharides combined with proteins have highlighted the potential to encapsulate, protect, deliver, and release bioactive compounds (Abaee et al., 2017; Jafari et al., 2017).

Proteins are typical large biomolecules involved in diverse biological systems (cell structure, catalyze metabolic reactions, and DNA replication). They have potential applications in the food industry as agents to promote the sensory perception of food products (aroma, taste, flavor, color, and texture). Proteins have different active functional properties, for example, the retention of water, fat and the formation of gels, foams, and emulsions, contributing to quality-related attributes. Proteins are biopolymers built with different amino acids linked by peptide bonds. These biopolymers are found in other foods based on vegetables, animals, algae, and fungi (Arroyo-Maya and McClements, 2015).

The molecular structure (primary, secondary, tertiary, and quaternary), amino acid composition, and processing conditions influence the functionality of these macromolecules. In addition, free amino, sulfhydryl, and hydrophobic groups are in the protein structure, and the electrical charges are distributed on the protein's surface (depending on the amino acid composition). Natural proteins have functionalities differentiated to be added in foods (e.g., water-soluble, rheological, emulsifying, foaming, and gelling properties); these characteristics are related to the interaction potential of this biopolymer with polysaccharides (Munin and Edwards-Lévy, 2011; Tang, 2019; Wusigale et al., 2020).

Under certain conditions, these biopolymers can stabilize chemically unstable compounds and enable the formation of safe, biocompatible, biodegradable, and effective nanostructures for specific delivery and release in target organs (Dima et al., 2020b). Their structural and conformational characteristics directly influence the formation of the protein-polysaccharide complex. The association of food proteins to polysaccharides depends on factors such as groups of constituent amino acids, density or distribution of charges, electrostatic interactions, hydrogen bonds, hydrophilicity, and hydrophobicity. Environmental factors such as pH, ionic strength, type of solvent, and temperature also directly influence these interactions (Wusigale et al., 2020; Zhang et al., 2021a,b). The protein-polysaccharide nano complex occurs due to two main interactions: non-covalent complexation (predominantly electrostatic, hydrophobic interactions, and hydrogen bonds) and covalent interactions (Bordenave et al., 2014; Dridi and Bordenave, 2021). In a specific way, when heated under controlled solution parameters (biopolymer concentration, pH, ionic strength, and temperature/retention time), proteins can have their structure suitable for hydrophobic interactions. After thermal denaturation, proteins can bind to exposed non-polar groups and form more stable nanostructures (Mohammadian et al., 2020).

The link between polysaccharides and proteins is highly ordered nanostructures, resulting in initial complexes with different functional properties and promising compared to the individual biopolymers. Proteins from different sources have been applied in the encapsulation of bioactives, such as vegetable proteins (soy, pea, zein, peanuts, wheat gluten) and animal proteins (lysozyme, whey protein, casein, gelatin, albumin, and collagen) (Lin et al., 2015; Stenger et al., 2017; Tang, 2019; Wu et al., 2020; Wusigale et al., 2020). In forming nanogel, the protein plays a fundamental role in nano-encapsulating active molecules for target delivery (Stenger et al., 2017).

5. Different functionality of polysaccharide-derived nanogels

Nanogels are biopolymer-based nanocarriers that protect and increase bioavailability (Zhang et al., 2021a,b). They are versatile nano-vehicle systems for encapsulating hydrophilic and hydrophobic compounds with high load capacity and response to specific biological stimuli (Rezaei et al., 2019). Nanogels can be defined as nanometer-sized structured hydrogel particles. Formed from hydrophilic or amphiphilic polymers chemically or physically-crosslinked into networks (Bourbon and Cerqueira, 2016; Zhang et al., 2015). Nanogels have different characteristics, such as retaining water while maintaining their three-dimensional conformation (Bourbon and Cerqueira, 2016).

They can be classified according to (1) origin: natural, synthetic, and hybrid hydrogel; (2) synthesis methods: homopolymer, copolymer, multipolymer, and interpenetrating polymer network hydrogel; (3) electrical charge: neutral, cationic, anionic, ampholytic and hydrophobically modified; (4) pore size: non-porous, microporous and super-porous hydrogel; (5) physical properties: conventional and environmentally susceptible "smart"; (6) configuration: amorphous, crystalline and semi-crystalline; (7) degradability: biodegradable and non-biodegradable; and (8) crosslinking: physical and chemical crosslinking. The network of interactions formed in nanogels can capture different bioactive substances for protection and controlled release (Debele et al., 2016; Singhal and Gupta, 2016). Thus, it is of great interest to the food and pharmaceutical industries since nanogels based on polysaccharides can be added to food formulations (nano-foods and fortified foods) or pharmaceutical applications (nutraceuticals and dietary supplements) (de Britto et al., 2014; Feng et al., 2019).

Nanogels based on polysaccharides have advantages over other methodologies, such as the swelling property when in an aqueous solution in the gastrointestinal tract and its high loading capacity of bioactive compounds. The biodegradability, low toxicity, and non-inclusion of potentially toxic compounds (some emulsifiers and surfactants) indicate safety for oral ingestion and non-immunogenicity. Nanogels elaborated by molecular self-organization based on polysaccharides (isolated or combined with other biopolymers) and without potentially toxic crosslinking agents are free of adverse reactions and safe for human consumption (Hamman, 2010; Zhang et al., 2021a,b). Nanogels can also show gelling, foaming, and emulsifying properties (Adrian et al., 2019; Muvva et al., 2020; Rezaei et al., 2019; Zhang et al., 2021a,b). The structure and conformation of biopolymers influence the multifunctional characteristics of nanogels (Fathi et al., 2018). Nanogels have the potential to direct the delivery of bioactive compounds and induce their passive or active absorption in different types of metabolic situations, contributing to more effective therapeutic results and reaching certain intestinal regions, such as more distal portions of the intestine. Nanogels can be designed to maintain encapsulation stability and sustained release of bioactive substances throughout the entire digestive tract, with more excellent cell permeability, mucoadhesiveness, and greater permanence in the intestine (Fasolin et al., 2021; Rezaei et al., 2019).

Nanogels based on biopolymers (proteins and polysaccharides) by self-assembly can form nanostructures through a complex network of interactions. The molecular self-organization of nanogels is based on the spontaneous organization of structures by non-covalent bonding, mainly hydrogen bonds and hydrophobic and electrostatic interactions (Fathi et al., 2018).

Non-covalent interactions include electrostatic, hydrophobic, hydrogen bonding, and steric exclusion interactions in addition to covalent interactions, such as enzymatic crosslinking, chemical crosslinking, and Maillard reaction. In this regard, various methods can be used to form polysaccharide nanogels: coacervation, thermal denaturation, emulsification, injection or extrusion, shearing, and spray cooling are examples applied (Hamidi et al., 2008; Neamtu et al., 2017; Wei and Huang, 2019). For covalent crosslinking, agents such as genipin, 1-ethyl-3-(3-dimethyl aminopropyl)-carbodiimide, and glutaraldehyde are cited for maintaining or increasing the stability of nanogels; however, despite being practical, they are potentially toxic for addition to food products. However, nanogels of proteins and polysaccharides by self-assembly technique (without the addition of reticulate agents), formed by gelling methods and thermal denaturation, are considered safe and effective options for nanostructures to encapsulate active compounds due to the absence of potentially toxic agents (Neamtu et al., 2017; Wei and Huang, 2019; Zhao et al., 2020). The applications of nanogels are vast, as a variety of bioactive substances can be encapsulated. The most reported compounds in the literature are phenolic compounds, carotenoids, vitamins, some minerals, and drugs with anticancer action for the targeted treatment (de Britto et al., 2014; Fasolin et al., 2019).

6. Pectin as wall materials for the nanoencapsulation of bioactive compounds

Pectin is one of the naturally occurring and abundant plant polysaccharides. It is an ideal biomaterial for the nanoencapsulation of different compounds and releases in the intestine (Rosales and Fabi, 2023a). Pectin is a structural part of the plant cell wall. It is constituted by heterogeneous complexes of polysaccharides (not derived from starch), representing 10–30% of the total weight of the fruit (Lara-Espinoza et al., 2018; Sriamornsak, 2011). Pectins are anionic biopolymers of α-D-galactopyranuronic acid—Gal*p*A (galacturonic acid) linked by α-1,4 glycosidic bonds (about 70% of the structure) (Mohnen, 2008; Ninan et al., 2013). Pectin (low/medium degree of esterification) at neutral pH is negatively charged, and pK_a is pH ~3.6. The predominant net negative charge makes interacting with positively charged ions or molecules, such as calcium salts and proteins, possible. This interaction is ideal for unstable compounds' physical and chemical entrapment (Bauer, 2012; Mohnen, 2008; Ninan et al., 2013; Reichembach et al., 2021).

Some characteristics of pectin as a biomaterial should be highlighted; they produce highly viscous gels or solutions ideal for emulsifying and thickening, with broad technological applicability (Moreira et al., 2014; Viebke et al., 2014). In addition, resistance, absence of toxicity, biocompatibility, biodegradability, the possibility of extraction, and sustainable sources (citrus peel, apple, chayote peel, and Passiflora fruit albedo) are essential characteristics (Rosales and Fabi, 2023b,c).

Pectin resists the acid pH of the stomach and the action of digestive enzymes, reaching the distal portions of the intestine. These polysaccharides have systemic beneficial properties for the human body due to the fermentation of the pectic structure by the intestinal microbiota and consequent production of short-chain fatty acids (butyrate, propionate, and acetate)—energy substrate of intestinal cells for growth and with direct and indirect effects (do Prado et al., 2019; Duda-Chodak et al., 2015; Fathi et al., 2014). Pectin can gradually release the bioactive in the intestine to be absorbed alone, or the pectin-based nanostructure can be absorbed and release the content inside the cell (Fathi et al., 2014; Khotimchenko, 2020; Nguyen et al., 2011).

The scientific literature has reported that pectin as a nanocarrier can maximize the absorption of active molecules intact in the small intestine; in addition, it can transport to the large intestine a more significant number of compounds to be metabolized by the local microbiota. Although some studies indicate that there may be swelling and consequent premature release of pectic matrices, combining with other macromolecules and adding salts can circumvent this undesirable effect (Khotimchenko, 2020; Morris et al., 2010; Rosales and Fabi, 2023a). Pectin composing nanostructures has several advantages; in addition to protection, this polysaccharide is biocompatible, responds to biological stimuli, can intensify cell permeation, and inhibits enzymes, reducing encapsulated active compounds' degradation (Fernandes et al., 2020; Gottesmann et al., 2020; Morris et al., 2010; Tomas, 2022). In this sense, many studies have explored this potential to encapsulate various bioactive, such as polyphenolic compounds (Esmaili et al., 2019; Luo et al., 2015; Rosales et al., 2021).

7. Nanoencapsulation of bioactive compounds within nanocarriers produced by cellulose and its derivatives

Cellulose and its derivatives are considered suitable biomaterials for the nanoencapsulation of many natural bioactive compounds. Cellulose is an essential and abundant polysaccharide distributed in nature (Zhai et al., 2018). It is a structural component of the cell wall of plants (microfibrils for the structure of the cell). It is a polysaccharide (homopolymer) composed of glucose in long linear chains, units linked by β-1,4 glycoside connections, with groups of three hydroxyl groups for the glucose fraction. It generally has a high molecular weight (Lampugnani et al., 2018; Pérez and Samain, 2010). Intermolecular interactions, cross-link polymerization, chain elongation, and side-chain functional group effects such as hydroxyl, methyl, and hydroxypropyl ether occur among structural groups (Kamel et al., 2008; Pérez and Samain, 2010).

Cellulose and its derivates are biocompatible and biodegradable and have been extensively investigated for many technological applications in the most diverse industrial segments (Assis et al., 2021). Despite its applicability, a significant limitation of using natural cellulose is its insolubility in water. However, hydrolysis of higher molecular weight cellulose to smaller fragments can lead to higher solubility (Calvini et al., 2006; Pandey et al., 2014). The chemical alteration of cellulose forms its soluble derivatives (e.g., carboxymethylcellulose, methylcellulose, hydroxypropyl cellulose, hydroxy propylmethyl-cellulose, and hydroxy ethyl-cellulose). These derivatives have improved properties for targeted delivery and increased biocompatibility, adhesion, water retention, thickening, and emulsifying ability. For this reason, they are best applied to form nanostructures for targeted delivery (Cordeiro et al., 2021; Nurkeeva et al., 2003; Sun et al., 2020; Wang et al., 2011). Cellulose and derivatives are biocompatible, resistant to gastric pH, and responsive to stimuli to gradually release nano-encapsulated compounds, thereby protecting against environmental adversities (enzymes, pH, microbiota, and interaction with other food components) (Bai et al., 2012; Gopinath et al., 2018; Pandey et al., 2014; Sarkar et al., 2017; Zhai et al., 2018).

8. Chitosan-based nanoencapsulation strategy to improve the molecular stability of bioactive compounds

Chitosan-based nanostructures can stabilize unstable compounds efficiently and safely, with broad technological applicability in the food industry (Guadarrama-escobar et al., 2023; Quadrado and Fajardo, 2020; Rinaudo, 2006). Studies indicate that bioavailability can be optimized using chitosan as a nanocarrier, leading to more effective therapeutic effects for several bioactive molecules. Chitosan is an amphiphilic and cationic polysaccharide (neutral and acidic pH) that forms gels in diverse types of solutions (Liang et al., 2014; Park et al., 2010). Chitosan is a biomaterial with critical nanotechnological applications such as biodegradability, non-toxic, and soluble in organic and inorganic acids. Chitosan is achieved after alkalinization and deacetylation of chitin, a component insoluble in water and organic solvents (Rinaudo, 2006).

For application in nanostructures, the degree of deacetylation and the molecular weight has a direct influence; the greater the degree of deacetylation, the higher the solubility of that polysaccharide (Kumar et al., 2004; Leiva et al., 2015). The interaction with other biopolymers and bioactive compounds occurs due to functional groups in the chitosan structure, mainly free amino acids and primary and secondary hydroxyl groups. The hydroxyl groups of chitosan can undergo several chemical reactions, such as etherification, esterification, crosslinking, graft copolymerization, and *O*-acetylation, and they are applied to modify the functional groups thus forming several new compounds (Luo and Wang, 2014; Park et al., 2010). The main chemical alterations are alkylation, acylation, hydroxy alkylation, carboxy alkylation, phosphorylation, sulphation, oligomerization, enzymatic modifications, and co-polymerizations (Goodarzi et al., 2013; Park et al., 2010).

To form nanostructures, chitosan needs to be covalently crosslinked, in which to the electrostatic interaction and ionotropic gelation occur it requires chitosan (negative charge) and another biopolymer of opposite charge (positive) for the interaction (Park et al., 2010; Takeuchi et al., 2005). The often use of chitosan and its derivatives to form nanostructures for encapsulation and controlled delivery is due to the main characteristics of this biopolymer, such as the ability to adhere to the intestinal mucosa, inducing more excellent absorption and bioavailability. One of the highlighted factors is the interaction between mucin, a glycoprotein of the intestinal epithelium (mucus), and the structure of chitosan (formed by residues of *N*-acetyl neuraminic acid, sulfated galactose and hydrophobic fucose containing methyl groups) (Park et al., 2010; Sogias et al., 2008; Takeuchi et al., 2005).

9. Other polysaccharides form nanostructures

Other food polysaccharides (different extraction sources) can also manufacture nanoparticles to encapsulate and deliver bioactive compounds. Some natural polysaccharide gums (e.g., guar, xanthan, carrageenan, and gums Arabic) are biopolymers that produce highly viscous aqueous solutions and form gels at low concentrations. Furthermore, intermolecular interactions form three-dimensional networks to protecting and delivering biologically active molecules. Gum Arabic, carboxymethylcellulose, carrageenan, and alginate have been used to prepare nanogels through nanospray drying to encapsulate different dietary nutrients. The nanostructure was formed due to complex interacting forces (hydrogen bonds, electrostatic and hydrophobic interactions) (Barclay et al., 2019; Zhou et al., 2016). Polysaccharides such as dextran (Jin et al., 2016), starch (Bianchini et al., 2022), and glycogen (Besford et al., 2020) are cited (less than the others) as promising to form nanostructures and to be applied in food.

10. Polysaccharide-based nanosystems: Mechanisms for controlled delivery and release of bioactive compounds

Nanosystems for polysaccharide-based controlled delivery constitute an area in constant development. The construction and release mechanisms are different according to the purpose of the nanoencapsulation and the food matrix into which it will be inserted (Karimi et al., 2016, 2017). Some factors influence the formation of polysaccharide-based nanostructures, such as the nature of the biopolymers involved and the conditions related to the environment. The types of interactions between polysaccharides and proteins are fundamental for the stability and control of the structure. In addition, inclusion in food matrices impacts the sensorial characteristics of the food, such as appearance, color, texture, flavor, and taste (Feng et al., 2019).

These factors are classified into two distinct categories: extrinsic and intrinsic factors. The external ones are related to physical-chemical parameters, such as pH, ionic strength, proportion and concentration of biopolymers, presence of crosslinkers or surfactants, temperature, agitation, and pressure. The intrinsic ones are the physicochemical parameters of the biopolymers, such as type of biopolymer, charges, molecular weight, flexibility, hydrophobicity, and hydrophilicity (Abaee et al., 2017; Wei and Huang, 2019; Zhang et al., 2021a,b).

The formation of physically crosslinked nanostructures (oppositely charged biopolymers) is mainly driven by electrostatic interaction. Among the various factors involved, pH plays a crucial role in modulating this process. This environmental factor influences the ionization of functional groups such as carboxyl and amino groups presented in polysaccharides and protein, respectively (Esmaili et al., 2019; Moreira et al., 2014).

Self-assembly-driven nanocomplexes made with biopolymers is pH dependent. The pH of the solution must be controlled to be between the pK_a of carboxylic acids and the isoelectric point (pI) of proteins. In this situation, there will be deprotonation of the carboxyl groups and protonation of the amino groups, with difference between charges (cationic and anionic) being the driving force for the electrostatic interaction. For example, the binding between pectin and lysozyme—positively charged chains of lysozyme and the negatively charged chains of pectin—occurs at neutral pH since lysozyme (ionized amino groups, NH^{+3}) has a pI of around 10.7, and the pK_a of carboxylic acids (COO^-) of pectin is around pH 3.2. The formed nanoparticles showed greater complexity, naturally ordered, highly organized, and biological functionalities distinct from the isolated compounds (Lin et al., 2015; Neufeld and Bianco-Peled, 2017).

Another crucial factor for forming polysaccharide nanostructures is ionic strength, determined by the concentration of salts in the nano-system. The concentration and nature of the ions are important factors for the gelation process. When they are in high concentrations, the ions can interact with the free ionic groups on the surface of the biopolymers, causing a reduction in the electrostatic interaction. Some studies have tested different concentrations of monovalent (NaCl) and divalent ($CaCl_2$) cations and ionic strength related to resistance, stability, and water retention capacity (Antonov et al., 2019; Schmidt et al., 2009).

Different forces (non-covalent complexation and covalent interactions) form nano-complexes (polysaccharide-polysaccharide and polysaccharide-protein) to nanoencapsulate bioactive compounds. The approaches of bottom-to-top (such as liquid antisolvent precipitation, pH control encapsulation, ionic heating or gelling, and self-assembly) and top-to-bottom methods (nanoemulsion) are among the example of the approaches in the encapsulation of bioactive. Depending on the objective of bioactive compounds nanoencapsulation, the right choice of biomaterials, equipment, and method must be made. Each approach has unique advantages in elaborating stable nanostructures with controlled release and effective functional properties. The pH, ionic strength, mixing ratio and concentration of biopolymers, and charge density and biopolymer type play a crucial role in forming polysaccharide-based nanogels. It is necessary to carefully adjust these parameters to obtain stable nanostructures with release control. Also, controlling environmental factors is essential to nano-complexes with desirable properties for specific food applications (da Silva and Fabi, 2022; da Silva et al., 2023).

In addition to these factors, the proportion between the homogenized components and the final concentration of biopolymers are essential to be studied and adjusted. The ratio and concentration of biopolymers directly influence the control of a charge balance, the interaction between them, and the controlled release in the body. Mathematical models are indicated to calculate and obtain the maximum interaction between the constituent compounds, maximizing the responses, such as encapsulation efficiency, size, and homogeneity. The balance between electrical charges leads to a balance between electrostatic interactions (attractive and repulsive), forming nanostructures with more excellent stability (Antonov et al., 2019; Dridi and Bordenave, 2021; Neufeld and Bianco-Peled, 2017). The density and charge distribution of biopolymers affects the gelling process and the molar ratio for the nanostructure formation directly. Furthermore, the nature and characteristics of the biopolymer significantly influence the electrostatic interaction between biomolecules with opposite charges. Structurally, polysaccharides have different side chains (depending on the composition of the monosaccharide units), which can cause steric hindrance, reducing interactions and the formation of physically crosslinked polymeric networks (Antonov et al., 2021; Le et al., 2017; Warnakulasuriya and Nickerson, 2018).

In addition to the factors already discussed, temperature, agitation, and time are extrinsic factors related to forming physically crosslinked networks between biopolymers. For example, when polysaccharides are complex to globular proteins, the ability to form gels can be stimulated. Proteins have hydrophobic active groups located on their inner face and hydrophilic groups on the exposed surface of the molecule for the most part. Heating to certain temperatures can modify the native structure of proteins which affects covalent and non-covalent interactions (hydrophobic, hydrogen bonding, and electrostatic interactions). Heating can weaken hydrogen bonds, sulfhydryl (-SH) and disulfide (S-S) bridges, disposing of active groups for intermolecular interactions and forming more stable structures. The time and speed of agitation contribute to the intermolecular interaction influencing the physically crosslinked networks. These parameters must be carefully analyzed and optimized according to the objectives of nanoencapsulation, as they directly affect the protection and targeted delivery of the encapsulated bioactive compound (Abaee et al., 2017; Jiang et al., 2019; Lu et al., 2019; Xu et al., 2018).

11. Formation of polysaccharide-based nanoparticles

The nanoparticles are formed depending on the polysaccharides' molecular structure and structural properties. Also, the purpose of nanoencapsulation must be carefully defined in the matrix for addition, the arrangement of equipment, and the final application (Debele et al., 2016; Luo and Wang, 2014). The main techniques for preparing polysaccharide nanostructures are briefly discussed below.

Complexations of polyelectrolytes are formed through electrostatic interactions between charged groups in oppositely charged compounds. The driving force behind the formation is increased entropy due to the release of ions. The state-of-the-art of the technique has the characteristic of polymers with opposite charges, that driven by intermolecular electrostatic interaction, will form nanostructures. The interaction and stability are influenced by several factors: chemical structure, molecular weight and electric charge density, polyelectrolyte ratio, pH, temperature, and ionic strength (Boddohi et al., 2009; Lu et al., 2012; Szczęch and Szczepanowicz, 2020). The main advantage of the nanoparticles produced by this technique are cost-effectiveness, ease of use, no need for expensive equipment, and they are formed by simple mixing (opposite charges in solution and electrically charged) (Hamman, 2010).

Describing another technique, nanoemulsification can be described as a mixture of immiscible liquids with the addition of an interface agent (surfactants and co-surfactants). This process provides an efficient matrix for stabilizing, protecting, and targeting different types of compounds. Nanoemulsification is a process used to increase some bioactive compounds' solubility and kinetic stability (Akhavan et al., 2018; Cao et al., 2021; Garavand et al., 2021).

Nanoprecipitation is a technique of forming structures by a process that occurs with biopolymers and the addition of non-solvent to a polymeric solution. The method corresponds to forming nanocomplexes with polymeric aggregates that encapsulate bioactive compounds. The methodology includes several steps, such as supersaturation, nucleation, growth by condensation, and coagulation to construct nanostructures (Chen et al., 2019; Martínez Rivas et al., 2017).

The self-assembly technique results in polysaccharide nanocarriers that can stabilize and protect many bioactive compounds. This technique is widely used and is responsive to biological stimuli, such as human digestion and interaction with human cell membranes. The method is free of potentially toxic products, easy preparation, and can be used for safe food products. The homogenization of biopolymers is usually done in aqueous solution. The nanostructure formation occurs through the electrostatic interaction between compounds with opposite charges. The molecules are naturally ordered and different attractive forces are involved, such as hydrogen bonds, hydrophobic interaction, and *Van der Waals* (Antonov et al., 2019; Gummel et al., 2006; Zhang et al., 2021b; Zhao et al., 2020). The formation of nanostructures by molecular self-assembly, biopolymers of opposite charges homogenized to encapsulate different types of bioactive compounds, is exemplified in the scheme of Fig. 1.

Complex coacervation can be an option to encapsulate bioactive compounds. This technique can favor stability and high encapsulation efficiency and can be added to foods. For formation, the process constitutes the interaction of different biopolymers with opposite charges to form complexes that can trap an active molecule (Antonov et al., 2019; Ban and Kim, 2022; Singh and Yethiraj, 2020).

The ionic gelation technique uses biopolymers with different electrical charges interacting in an aqueous solution forming spherical particles to protect bioactive molecules. The methodology consists of adding a

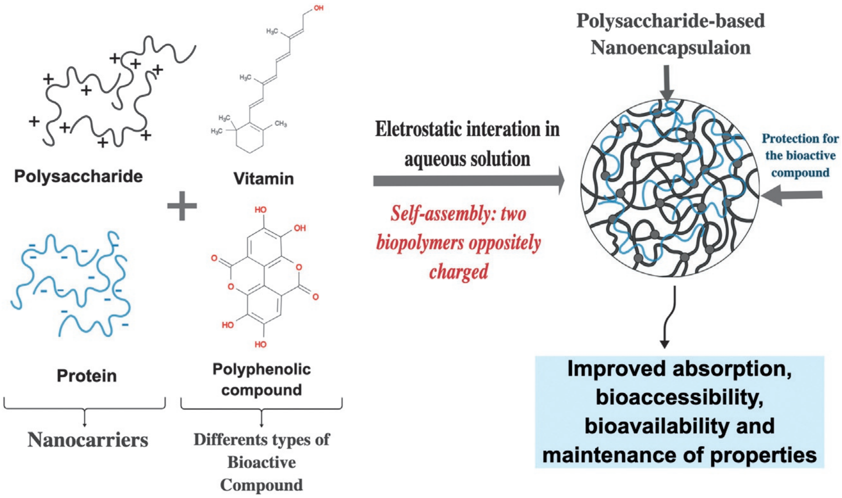

Fig. 1 Nanocapsules can be formed by coating polysaccharides (combined with proteins) and protecting the bioactive compound (vitamins or polyphenolics compounds). The figure was created with Mind the Graph (https://mindthegraph.com) (accessed on 04 Jun 2023).

polysaccharide dissolved in acid and added to a polycationic solution without potentially toxic products. They are safe and effective, with good encapsulation efficiency (Ahirrao et al., 2014; Antonov et al., 2019; Dogan Ergin et al., 2021).

The ionic cross-linking technique is a process to stabilize labile compounds under environmental conditions. The methodology involves forming polyelectrolyte complexes by binding divalent cations (Mg^{2+}, Ca^{2+}, and Ba^{2+}). Crosslinking is based on crosslinking through the interaction between tripolyphosphate anions and protonated amine groups of biopolymers (Andersen et al., 2015; Dogan Ergin et al., 2021; Prabaharan and Mano, 2005).

The characterization of nanoparticles is fundamental to obtaining stable and safe formulations for human consumption. Analysis of colloidal stability, investigation of aspects of formation mechanisms, morphological properties, interaction, and encapsulation efficiencies are essential. However, in vitro, assays to analyze cytotoxicity, viability, and cell death are indicated to attest safety evidence. In addition, animal toxicity analyses must be considered for insertion into food (Esmaili et al., 2019; Mourdikoudis and Pallares, 2018).

11.1 Mechanisms for the release of nano-encapsulated active ingredients

A crucial step is a release to obtain the bioavailability of bioactive compounds. The controlled and targeted release mechanism depends on several factors, such as the stability of the nanostructure, the specific location of the substance during a sustained period (sustained release), external stimuli (such as pH and microbiota), physical-chemical characteristics, and compatibility of the nanostructure, and its interactions with different biological systems (Zhang et al., 2021a,b).

The controlled release of active substances from nanostructures—such as nanogels—can occur through three primary mechanisms: diffusion, swelling, and chemical. The most common mechanism of release of bioactive compounds from nanostructures is diffusion (Zhang et al., 2015). Another release mechanism in aqueous media is swelling (an increase in the volume of the nanostructure). The balance between osmotic pressure and polymer elasticity establishes the physical dimensions of nanostructures. The ionization of pH-susceptible functional groups in the medium increases the nanostructure's osmotic pressure, resulting in swelling. Some characteristics, such as the chemical composition of the nanostructure (mainly biopolymers), the hydrophilicity of crosslinkers and the degree of crosslinking, and environmental factors (such as external pH), influence this process (Soni et al., 2016; Zhang et al., 2015). Degradation is a process for controlled release triggered by an ordered sequence of processes: (a) surface erosion, (b) mass erosion or fragmentation, and (c) release of active compounds. Physical and chemical phenomena are involved in the degradation, such as the diffusion of molecules inside or outside the particles, degradation of biopolymers, and finally, the breaking of cross-links and release of the contents. This process is critical to designing targeted systems that respond directly to specific environmental stimuli (enzyme-induced, electrostatic-induced, hydrophobic-induced, and temperature-induced) (Assadpour and Jafari, 2019b; Zhang et al., 2015).

11.2 Characterization and stability analysis of nanoparticles to be added to food matrices

After forming nanostructures based on polysaccharides, the analysis, and characterization are crucial factors for including in food matrices (Esmaili et al., 2019). Some techniques are indicated for this purpose: size analysis, polydispersity index, degree of association, conformation, interactions, and encapsulation efficiency. In general, the central characterization analyses commonly used are (a) determination of the particle size through dynamic light scattering analysis (DLS), which is fundamental to select methodologies that generate particles with adequate diameter and potentially safe. Very small particles (around >10 nm) can cause adverse reactions in the body. In addition, the polydispersity index is essential to obtain homogeneous nanostructures; an index <0.2 are considered uniform (monodisperse) and ideal for targeted release and better interaction with biological systems (Joye et al., 2014; Stetefeld et al., 2016).

Stability and aggregation propensity can be determined by analyzing the zeta potential (electrokinetic potential), which is the plane of particle shear in suspension, macromolecule, and colloidal systems under an electric field. Used to determine the surface charge of nanoparticles, values more than +30 mV or less than −30 mV are considered strongly cationic and strongly anionic, respectively: the higher the zeta potential in module, the greater the possibility of being stable due to electrostatically repulsion. In this way, the pH and ionic concentration directly affect the stability (Bhattacharjee, 2016; Honary and Zahir, 2013). The interaction between the constituent compounds of the nanostructures can be determined through infrared spectroscopy. This technique provides a structural characterization of the nano-complex and relates to intermolecular interactions, revealing the composition of the constituent functional groups (Gharanjig et al., 2022; Karoyo and Wilson, 2017).

Also, observing the morphology of nanoparticles is essential to identify the external features. Scanning and transmission microscopy can be used to observe pore size, homogeneity, morphology, and the presence of aggregates, visualizing structures to verify probable stability and agreement with other techniques, such as DLS (Vladár and Hodoroaba, 2020). Thermal analyses are essential to observe samples' thermal behavior and physical properties (pure and in mixtures) and can indicate interaction between molecules (due to the polymerization process). Through the differential scanning calorimeter, it is possible the measurement of energy absorbed (endothermic process) or released (exothermic process) of the samples, indicating whether there was a thermal phase transition, and to observe the properties. Data on glass transition, melting, denaturation, decomposition temperature, and unfolding enthalpy are important ones to be considered (Esmaili et al., 2019; Li et al., 2016; Neufeld and Bianco-Peled, 2017). Other techniques are indicated to study the physicochemical properties, stability, morphology, and interaction of polysaccharide nanostructures, such as nuclear magnetic resonance, confocal laser scanning microscope, atomic force microscope, X-ray diffraction, titration calorimetry isotherm, rheology and in silico methods (Karoyo and Wilson, 2017; Zhang et al., 2021b).

12. Nanoencapsulation of bioactive compounds: Challenges and future perspectives

Notably, there is progress in research and the manufacture of nanostructures via polysaccharides and their interactions with other biopolymers to encapsulate bioactive compounds. The studies described in the literature support that these biopolymers (especially pectin, chitosan, and cellulose) are promising to stabilize bioactive compounds, thus carrying out targeted delivery in the intestine and enhancing absorption and bioactivity. Applying these polysaccharide-based nanostructures loaded with bioactive compounds enables the processing of functional and innovative products (Shen et al., 2022).

Nanoencapsulation of bioactive compounds is a growing topic in food science. Although much has been discovered in recent decades, many challenges must be overcome in developing nanostructures for biologically-targeted release (Walia et al., 2019). The ever-increasing search for sustainable and effective biomaterials in protecting biologically active substances indicates that food polysaccharides are potential materials to constitute biological delivery systems successfully. They can overcome the adversities of the external environment and enhance absorption, resulting in more excellent bioavailability. The stability of nanostructures during processing and storage is a concern that must be addressed by adequate characterization analysis to avoid the loss of biological activity of the bioactive compounds encapsulated (Manzoor et al., 2020; Paredes et al., 2016). Many studies indicate that pectin, chitosan, and cellulose are promising for this purpose. These natural, biodegradable, biocompatible, and widely used biopolymers have positively protected different bioactive compounds, such as carotenoids, phenolic compounds, vitamins, minerals, and various drugs. Optimization of production processes, including the proper selection of encapsulation methods and manufacturing techniques, is crucial to ensure the quality and effectiveness of nanogels. Table 1 describes a summary of studies over the last few decades using different polysaccharides and their combinations. Many other techniques are used for many purposes. The most cited ones are the maintenance of molecular stability, protection against degradation, maintenance of anti-oxidation and color properties, and improvement of

Table 1 Recent studies on applying polysaccharides (alone or combined with other biopolymers) to nano-encapsulate bioactive compounds.

Polysaccharide	Bioactive compound	Nanoencapsulation method	Size (nm)	Encapsulation efficiency (%)	Purpose of nanoencapsulation	References
Chitosan–Alginate	Anthocyanin	Ionic pre-gelation and complex polyelectrolyte	358.5–635.9	68.9	Improve stability and increase bioavailability	Bulatao et al. (2017)
Starch-CMC	Essential oil	Self-assembly	100	–	To improve antimicrobial properties	Mohsenabadi et al. (2018)
Chitosan/Alginate	Vitamin B2	Ionic gelation	104	56	Molecular protection and controlled release	Azevedo et al. (2014)
Chitosan-TPP	Curcumin	Emulsion solvent Evaporation	254–415	18–96	Protection and stability	Sowasod et al. (2008)
TPP-LWM Chitosan	Lutein	Ionotropic gelation	80–600	85	Bioavailability	Arunkumar et al. (2013)
Beta-lactoglobulin–Pectin	Vitamin D2	Polyelectrolyte complex	100	–	To improve stability	Ron et al. (2010)
Chitosan	Epigallocatechin-3-gallate	Polyelectrolytic complex	200	10	Treatment of prostate cancer	Khan et al. (2014)
Pectin–Lysozyme	β-Lactose	Self-assembly	81.20 ± 0.34	96	Inhibition of galectin-3 protein	da Silva et al. (2023)
Chitosan	Iron	Coacervation	830	–	Controlled delivery system	Min et al. (2016)
Pectin–WPI	Anthocyanin	Self-assembly	200	55	Improve stability	Arroyo-Maya and McClements (2015)

Continued

Table 1 Recent studies on applying polysaccharides (alone or combined with other biopolymers) to nano-encapsulate bioactive compounds.—cont'd

Polysaccharide	Bioactive compound	Nanoencapsulation method	Size (nm)	Encapsulation efficiency (%)	Purpose of nanoencapsulation	References
CMC	Vitamin E	Nanoprecipitation	207, 6–230, 2	88, 43–99, 66	To improve stability and bioactivity	Mirzaei-Mohkam et al. (2019)
Pectin-whey protein	D-limonene	Complex coacervate	160	88	To improve stability	Ghasemi et al. (2018)
CMC	Anthocyanin	Ionic gelation	63.15–219.53	–	Improve stability during digestion	He et al. (2017)
Chitosan	Vitamin C	Ionic gelation	170	12	Protection and maintenance of functional properties	Jang and Lee (2008)
Chitosan–β-Lactoglobulin	Anthocyanin	Ionic gelation	91.71–69.3	–	To improve the stability and bioavailability	Ge et al. (2019)
Chitosan	Vitamin C	Ionic gelation	300	15	Enrichment food products	Jiménez-Fernández et al. (2014)
Chitosan–β-Lactoglobulin	Anthocyanin	Ionic gelation	580.4	77.4	Storage and oxidant stability (in vitro simulated digestion)	Chen et al. (2023)
β-Chitosan	Catechins	Ionic gelation	208–591	50–89	Maintain bioactive activity	Zhang et al. (2016)
CMC–gelatin	Zeaxanthin	Complex coacervation	210.7	64.56	To improve stability	Zhang et al. (2021a)
Chitosan–β-Lactoglobulin	Epigallocatechin gallate	Ionic gelation	100–500	60	Control release in the gastrointestinal	Liang et al. (2016)
Chitosan	Catechins	Ionic gelation	169.0–201.4	24–53	Protection and stability	Hu et al. (2008)

Soybean-insoluble dietary fiber	Anthocyanin	Emulsification	300	–	Storage stability and color protection	He et al. (2022)
Chitosan	Anthocyanin	Ionotropic gelation	274–455	70	Antioxidant potential	Chatterjee et al. (2021)
Pectin–WPI	Phenolic compound (mixture)	Nanoemulsion	>675	96.64	Molecular stability	Mohammadi et al. (2016)
Cellulose–Pectin	Phenolic compound (mixture)	Nanoemulsion	200	–	Anti_microbial Activity	Hassan et al. (2022)
Chitosan	Anthocyanin	Ionic gelation	160 to ~1000	–	Antioxidant activity	Ko et al. (2017)
Zein-CMC	Quercetin and Reveratrol	Antisolvent precipitation	217	25.1	Thermal stability	Yanget al. (2023)
Pectin	Resveratrol	Antisolvent precipitation	120	–	Stability, Bioaccessibility	Huang et al. (2019)
Pectin-Chitosan	Neohesperidin	Polyelectrolyte complex	87–225	72	Antioxidant Properties, Released and Bioavailability	Shishir et al. (2019)
Pectin–Chitosan	Anthocyanins	Self-assembly	100–300	66.68	Molecular stability and control released	Zhao et al. (2020)
Pectin–Lysozyme	Anthocyanins	Self-assembly	198.5	73	Molecular stability	Rosales et al. (2021)
Starch	Catechin	–	322.7, 559.2, and 615.6	59.09, 48.30, and 55.00	Protection and controlled release	Ahmad et al. (2019)

TPP, Tripolyphosphate; LWM, Low molecular weight; CMC, Carboxymethyl cellulose; WPI, Whey protein isolate.

bioaccessibility and bioavailability. The results indicate the choice of polysaccharide as a nanocarrier was crucial for a successful outcome for these studies.

The scientific results show the practical applicability of several food polysaccharides to form nanocarriers to encapsulate bioactive compounds. One critical step after nanoparticle formation is to consider the safety for oral ingestion. For this, it is emphasized that in vitro and in vivo analyses must be carefully performed to guarantee the absence of toxicity. In this sense, there need to be more in vivo studies (humans and animals), which should be carried out more frequently, seeking an outstanding certification of efficacy to increase bioavailability and certify safety for human consumption. Another critical point is to achieve the controlled and sustained release of bioactive compounds encapsulated in biological systems, reaffirming the emerging need for more in vivo studies.

The targeted delivery and release of bioactives is influenced by several factors, such as the composition of the biopolymers, their interaction with the encapsulated compound and the biological system, and environmental conditions, especially factors intrinsic to human digestion (enzymes, pH, and microbiota). Thus, designing intelligent nanostructures to control bioactive release over time and be susceptible to biological stimuli is crucial (Dogan Ergin et al., 2021; Faridi Esfanjani et al., 2018).

The choice of preparation methodology must consider the specific needs of each application and know the characteristics of the compounds involved, as well as the food matrix which will be the vehicle. The current trend is avoiding toxic and dangerous components as crosslinkers to form nanocomplexes (Araújo et al., 2017; Ayala-fuentes and Chavez-santoscoy, 2021). Nanostructures based on environmentally safe, economical, and solvent-free techniques are indicated for the food industry. Foods enriched with nano-encapsulated bioactive, food supplements, and nutraceuticals are a strong trend in the food and pharmaceutical industries. Thus, studies contemplating this theme and identifying new materials and methodologies are strongly supported. Consumer demand for new products with functional claims indicates the need for in-depth investigations and the establishment of specific legislation for the inclusion of nanoparticles in food, as well as doses to limit safe intake in a nutrition and health guide (Gopi Krishna et al., 2021).

To value waste from food industries and strengthen the circular economy, polysaccharides, and bioactive compounds can be extracted from by-products of food industries. Food-derived biopolymers are versatile, resistant, and promising for applications as structured nanomaterials for encapsulating and delivering bioactive compounds. In addition, they have nutritional value and distinct physical-chemical and biological properties, are widely distributed in nature, show consolidated techniques (and environmentally safe) for extraction, and with numerous properties to generate new functionalities and benefits in protection and increase bioavailability (Comunian et al., 2021; Saini et al., 2019). However, observing the complex factors involved in forming polysaccharide-based nanostructures, such as the pH, types of biopolymers used, concentration, molar ratio, and ionic strength, is essential. Furthermore, detailed characterization is necessary to obtain stable nano-complexes. In addition to food and pharmaceutical products, it provides many benefits for preserving and maintaining the release of encapsulated bioactive compounds. It is a viable option for improving biological activity, reducing the risk of developing chronic diseases, and as an additional treatment in various metabolic situations (de Souza Simões et al., 2017; Salarbashi et al., 2020).

13. Conclusion

Nanostructures based on food-derived biopolymers are promising technological applications with broad applications in the food and pharmaceutical industries for food, nutraceuticals, and supplements. Many compounds can be encapsulated, protected, and effectively controlled for delivery. The interaction between protein-polysaccharide through self-assembly by electrostatic interaction and ionic gelation, especially, is a widely used, biodegradable, biocompatible for hydrophilic and hydrophobic compounds. Nanogels have versatile, functional attributes such as increased dispersion, increased solubility, preservation of chemical activity, improved bioaccessibility, bioavailability, and maintain the available properties of bioactive compounds. Many factors are involved in forming polysaccharide nanostructures, which must be carefully evaluated and carefully analyzed to preserve safety and efficacy to be included in products for human consumption.

Acknowledgment

The authors acknowledge The National Council for Scientific and Technological Development (CNPq) for T.K.O.R. scholarship (#151150/2023-0) and J.P.F. productivity scholarship (#307842/2022-3). The authors acknowledge the São Paulo Research Foundation (FAPESP) for T.K.O.R. scholarship (#2023/09620-3). The study was financially supported by grants #2013/07914-8, #2022/12834-2 and #2023/01396-7 from the São Paulo Research Foundation (FAPESP).

References

Abaee A, Mohammadian M, Jafari SM: Whey and soy protein-based hydrogels and nano-hydrogels as bioactive delivery systems, *Trends Food Sci Technol* 70(October):69–81, 2017. https://doi.org/10.1016/j.tifs.2017.10.011.

Adrian G, Mihai M, Vodnar DC: The use of chitosan, alginate, and pectin in the, *Polymers* 11:1837, 2019.

Ahirrao SP, Gide PS, Shrivastav B, Sharma P: Ionotropic gelation: a promising cross linking technique for hydrogels, *Res Rev: J Pharm Nanotechnol* 2(1):1–6, 2014.

Ahmad A, Gulraiz Y, Ilyas S, Bashir S: Polysaccharide based nano materials: health implications, *Food Hydrocoll Health* 2(June):100075, 2022. https://doi.org/10.1016/j.fhfh.2022.100075.

Ahmad M, Mudgil P, Gani A, Hamed F, Masoodi FA, Maqsood S: Nano-encapsulation of catechin in starch nanoparticles: characterization, release behavior and bioactivity retention during simulated in-vitro digestion, *Food Chem* 270(July 2018):95–104, 2019. https://doi.org/10.1016/j.foodchem.2018.07.024.

Akbari-Alavijeh S, Shaddel R, Jafari SM: Encapsulation of food bioactives and nutraceuticals by various chitosan-based nanocarriers, *Food Hydrocoll* 105(November 2019), 2020, 105774. https://doi.org/10.1016/j.foodhyd.2020.105774.

Akhavan S, Assadpour E, Katouzian I, Jafari SM: Lipid nano scale cargos for the protection and delivery of food bioactive ingredients and nutraceuticals, *Trends Food Sci Technol* 74(February):132–146, 2018. https://doi.org/10.1016/j.tifs.2018.02.001.

Anal AK, Shrestha S, Sadiq MB: Food hydrocolloids biopolymeric-based emulsions and their effects during processing, digestibility and bioaccessibility of bioactive compounds in food systems, *Food Hydrocoll* 87(July 2018):691–702, 2019. https://doi.org/10.1016/j.foodhyd.2018.09.008.

Andersen T, Auk-emblem P, Dornish M: 3D cell culture in alginate hydrogels, *Microarrays* 4(2):133–161, 2015. https://doi.org/10.3390/microarrays4020133.

Antonov YA, Celus M, Kyomugasho C, Hendrickx M, Moldenaers P, Cardinaels R: Complexation of pectins varying in overall charge with lysozyme in aqueous buffered solutions, *Food Hydrocoll* 94(March):268–278, 2019. https://doi.org/10.1016/j.foodhyd.2019.02.049.

Antonov YA, Zhuravleva IL, Celus M, et al.: Effect of overall charge and local charge density of pectin on the structure and thermal stability of lysozyme, *J Therm Anal Calorim*, 2021. https://doi.org/10.1007/s10973-021-10954-5.

Araújo F, das Neves J, Martins JP, Granja PL, Santos HA, Sarmento B: Functionalized materials for multistage platforms in the oral delivery of biopharmaceuticals, *Prog Mater Sci* 89:306–344, 2017. https://doi.org/10.1016/j.pmatsci.2017.05.001.

Arroyo-Maya IJ, McClements DJ: Biopolymer nanoparticles as potential delivery systems for anthocyanins: fabrication and properties, *Food Res Int* 69:1–8, 2015. https://doi.org/10.1016/j.foodres.2014.12.005.

Arunkumar R, Prashanth KVH, Baskaran V: Promising interaction between nano-encapsulated lutein with low molecular weight chitosan: Characterization and bioavailability of lutein in vitro and in vivo, *Food Chem* 141(1):327–337, 2013. https://doi.org/10.1016/j.foodchem.2013.02.108.

Assadpour E, Jafari SM: A systematic review on nanoencapsulation of food bioactive ingredients and nutraceuticals by various nanocarriers, *Crit Rev Food Sci Nutr* 59(19): 3129–3151, 2019a. https://doi.org/10.1080/10408398.2018.1484687.

Assadpour E, Jafari SM: An overview of biopolymer nanostructures for encapsulation of food ingredients, In *Biopolymer nanostructures for food encapsulation purposes*, 2019b, Elsevier Inc. https://doi.org/10.1016/B978-0-12-815663-6.00001-X.

Assis RQ, Pagno CH, Stoll L, Rios PDA, de Oliveira Rios A, Olivera FC: Active food packaging of cellulose acetate: Storage stability, protective effect on oxidation of riboflavin and release in food simulants, *Food Chem* 349(February), 2021, 129140. https://doi.org/10.1016/j.foodchem.2021.129140.

Ayala-fuentes JC, Chavez-santoscoy RA: Nanotechnology as a key to enhance the benefits and improve the bioavailability of flavonoids in the food industry, *Foods* 10(11):2701, 2021. https://doi.org/10.3390/foods10112701.

Azad MOK, Adnan M, Kang WS, Lim JD, Lim YS: A technical strategy to prolong anthocyanins thermal stability in formulated purple potato (Solanum tuberosum L. cv Bora valley) processed by hot-melt extrusion, *Int J Food Sci Technol*:1–10, 2021. https://doi.org/10.1111/ijfs.15485.

Azevedo MA, Bourbon AI, Vicente AA, Cerqueira MA: Alginate/chitosan nanoparticles for encapsulation and controlled release of vitamin B2, *Int J Biol Macromol* 71:141–146, 2014. https://doi.org/10.1016/j.ijbiomac.2014.05.036.

Bai Y, Zhang Z, Zhang A, et al.: Novel thermo- and pH-responsive hydroxypropyl cellulose- and poly (L-glutamic acid)-based microgels for oral insulin controlled release, *Carbohydr Polym* 89(4):1207–1214, 2012. https://doi.org/10.1016/j.carbpol.2012.03.095.

Baliyan N, Rani R, Kaur P, Yadava YK, Kumar L: Nanoencapsulation development for interactive foods, *Chem Sci Rev Lett* 9(36):1039–1057, 2020. https://doi.org/10.37273/chesci.CS205107155.

Ban E, Kim A: Coacervates: recent developments as nanostructure delivery platforms for therapeutic biomolecules, *Int J Pharm* 624(July), 2022, 122058. https://doi.org/10.1016/j.ijpharm.2022.122058.

Bao C, Jiang P, Chai J, et al.: The delivery of sensitive food bioactive ingredients: absorption mechanisms, influencing factors, encapsulation techniques and evaluation models, *Food Res Int* 120(September 2018):130–140, 2019. https://doi.org/10.1016/j.foodres.2019.02.024.

Barclay TG, Day CM, Petrovsky N, Garg S: Review of polysaccharide particle-based functional drug delivery, *Carbohydr Polym* 221(April):94–112, 2019. https://doi.org/10.1016/j.carbpol.2019.05.067.

Bauer S: Mass spectrometry for characterizing plant cell wall polysaccharides, *Front Plant Sci* 3(MAR):1–6, 2012. https://doi.org/10.3389/fpls.2012.00045.

Bealer EJ, Onissema-karimu S, Rivera-galletti A, Francis M, Wilkowski J, Hu X: Protein–polysaccharide composite materials: fabrication and applications, *Polymers* 12:464, 2020.

Besford QA, Cavalieri F, Caruso F: Glycogen as a building block for advanced biological materials, *Adv Mater* 32:1–23, 2020. https://doi.org/10.1002/adma.201904625.

Bhattacharjee S: Review article DLS and zeta potential—what they are and what they are not? *J Control Release* 235:337–351, 2016. https://doi.org/10.1016/j.jconrel.2016.06.017.

Bianchini E, Wilson S, Caicedo D, Betina C, Koop L: Starch-based materials encapsulating anthocyanins: A review, *J Polym Environ* 30:3547–3565, 2022. https://doi.org/10.1007/s10924-022-02474-6.

Boddohi S, Moore N, Johnson PA, Kipper MJ: Polysaccharide-based polyelectrolyte complex nanoparticles from chitosan*, heparin and hyaluronan*, *Biomacromolecules* 10(6):1402–1409, 2009. https://doi.org/10.1021/bm801513e.

Bordenave N, Hamaker BR, Ferruzzi MG: Nature and consequences of non-covalent interactions between flavonoids and macronutrients in foods, *Food Funct* 5(1):18–34, 2014. https://doi.org/10.1039/c3fo60263j.

Bourbon AI, Cerqueira MA: Encapsulation and controlled release of bioactive compounds in lactoferrin-glycomacropeptide nanohydrogels: curcumin and caffeine as model compounds, *J Food Eng* 180:110–119, 2016. https://doi.org/10.1016/j.jfoodeng.2016.02.016.

Bulatao RM, Samin JPA, Salazar JR, Monserate JJ: Encapsulation of anthocyanins from Black Rice (Oryza Sativa L.) Bran extract using chitosan-alginate nanoparticles, *J Food Res* 6(3):40, 2017. https://doi.org/10.5539/jfr.v6n3p40.

Calvini P, Gorassini A, Luciano G, Franceschi E: FTIR and WAXS analysis of periodate oxycellulose: evidence for a cluster mechanism of oxidation, *Vib Spectrosc* 40(2):177–183, 2006. https://doi.org/10.1016/j.vibspec.2005.08.004.

Câmara JS, Albuquerque BR, Aguiar J, et al.: Food bioactive compounds and emerging techniques for their extraction: polyphenols as a case study, *Foods* 10(1):37, 2020. https://doi.org/10.3390/foods10010037.

Cao N, Tang X, Gao RJ, et al.: Galectin-3 participates in PASMC migration and proliferation by interacting with TGF-β1, *Life Sci* 274(February), 2021. https://doi.org/10.1016/j.lfs.2021.119347.

Carrasco-Sandoval J, Aranda-Bustos M, Henríquez-Aedo K, López-Rubio A, Fabra MJ: Bioaccessibility of different types of phenolic compounds co-encapsulated in alginate/chitosan-coated zein nanoparticles, *LWT* 149(June), 2021. https://doi.org/10.1016/j.lwt.2021.112024.

Chatterjee NS, Dara PK, Perumcherry Raman S, et al.: Nanoencapsulation in low-molecular-weight chitosan improves in vivo antioxidant potential of black carrot anthocyanin, *J Sci Food Agric* 101(12):5264–5271, 2021. https://doi.org/10.1002/jsfa.11175.

Chen S, McClements DJ, Jian L, et al.: Core-Shell biopolymer nanoparticles for co-delivery of curcumin and piperine: sequential electrostatic deposition of hyaluronic acid and chitosan shells on the Zein Core, *ACS Appl Mater Interfaces* 11(41):38103–38115, 2019. https://doi.org/10.1021/acsami.9b11782.

Chen C, Li Z, Wang C, et al.: Stability and antioxidant activity of chitosan/β-lactoglobulin on anthocyanins from Aronia melanocarpa, *LWT- Food Sci Technol* 173, 2023, 114335. https://doi.org/10.1016/j.lwt.2022.114335.

Colodel C, Vriesmann LC, Teófilo RF, de Oliveira Petkowicz CL: Optimization of acid-extraction of pectic fraction from grape (Vitis vinifera cv. Chardonnay) pomace, a winery waste, *Int J Biol Macromol* 161:204–213, 2020. https://doi.org/10.1016/j.ijbiomac.2020.05.272.

Comunian TA, Silva MP, Souza CJF: The use of food by-products as a novel for functional foods: their use as ingredients and for the encapsulation process, *Trends Food Sci Technol* 108(January):269–280, 2021. https://doi.org/10.1016/j.tifs.2021.01.003.

Cordeiro AS, Farsakoglu Y, Crecente J, María C, Fuente D, González SF: Carboxymethyl-β-glucan/chitosan nanoparticles: new thermostable and efficient carriers for antigen delivery, *Drug Deliv Transl Res* 11:1689–1702, 2021. https://doi.org/10.1007/s13346-021-00968-9.

da Silva MP, Fabi JP: Food hydrocolloids for health food biopolymers-derived nanogels for encapsulation and delivery of biologically active compounds: a perspective review, *Food Hydrocoll Health* 2(July), 2022, 100079. https://doi.org/10.1016/j.fhfh.2022.100079.

da Silva MP, Rosales TKO, Pedrosa LDF, Fabi JP: Formulation of a new proof-of-concept pectin/lysozyme nanocomplex as potential β-lactose delivery matrix: structure and thermal stability analyses, *Food Hydrocoll* 134:1081011, 2023. https://doi.org/10.1016/j.foodhyd.2022.108011.

Dacoba TG, Omange RW, Li H, Crecente-Campo J, Luo M, Alonso MJ: Polysaccharide nanoparticles can efficiently modulate the immune response against an HIV peptide antigen, *ACS Nano* 13(5):4947–4959, 2019. https://doi.org/10.1021/acsnano.8b07662.

De Anda-Flores Y, Carvajal-Millan E, Campa-Mada A, et al.: Polysaccharide-based nanoparticles for colon-targeted drug delivery systems, *Polysaccharides* 2(3):626–647, 2021. https://doi.org/10.3390/polysaccharides2030038.

de Britto D, de Moura MR, Aouada FA, et al.: Entrapment characteristics of hydrosoluble vitamins loaded into chitosan and N,N,N-trimethyl chitosan nanoparticles, *Macromol Res* 22(12):1261–1267, 2014. https://doi.org/10.1007/s13233-014-2176-9.

de Souza Simões L, Madalena DA, Pinheiro AC, Teixeira JA, Vicente AA, Ramos ÓL: Micro- and nano bio-based delivery systems for food applications: in vitro behavior, *Adv Colloid Interface Sci* 243:23–45, 2017. https://doi.org/10.1016/j.cis.2017.02.010.

Debele TA, Mekuria SL, Tsai H: Polysaccharide based nanogels in the drug delivery system: application as the carrier of pharmaceutical agents, *Mater Sci Eng C* 68:964–981, 2016. https://doi.org/10.1016/j.msec.2016.05.121.

Dima C, Assadpour E, Dima S, Jafari SM: Bioactive-loaded nanocarriers for functional foods: from designing to bioavailability, *Curr Opin Food Sci* 33:21–29, 2020a. https://doi.org/10.1016/j.cofs.2019.11.006.

Dima C, Assadpour E, Dima S, Jafari SM: Bioavailability and bioaccessibility of food bioactive compounds; overview and assessment by in vitro methods, *Compr Rev Food Sci Food Saf* 19(6):2862–2884, 2020b. https://doi.org/10.1111/1541-4337.12623.

do Prado SBR, Castro-Alves VC, Ferreira GF, Fabi JP: Ingestion of non-digestible carbohydrates from plant-source foods and decreased risk of colorectal cancer: a review on the biological effects and the mechanisms of action, *Front Nutr* 6(May):1–17, 2019. https://doi.org/10.3389/fnut.2019.00072.

Dogan Ergin A, Bayindir ZS, Ozcelikay AT, Yuksel N: A novel delivery system for enhancing bioavailability of S-adenosyl-L-methionine: pectin nanoparticles-in-microparticles and their in vitro–in vivo evaluation, *J Drug Deliv Sci Technol* 61(September 2020), 2021, 102096. https://doi.org/10.1016/j.jddst.2020.102096.

Dridi W, Bordenave N: Influence of polysaccharide concentration on polyphenol-polysaccharide interactions, *Carbohydr Polym* 274(September), 2021, 118670. https://doi.org/10.1016/j.carbpol.2021.118670.

Duda-Chodak A, Tarko T, Satora P, Sroka P: Interaction of dietary compounds, especially polyphenols, with the intestinal microbiota: a review, *Eur J Nutr* 54(3):325–341, 2015. https://doi.org/10.1007/s00394-015-0852-y.

El Gharras H: Polyphenols: food sources, properties and applications - a review, *Int J Food Sci Technol* 44(12):2512–2518, 2009. https://doi.org/10.1111/j.1365-2621.2009.02077.x.

Esmaili SK, Ghanbarzadeh B, Ayaseh A, Pezeshki A, Hosseini M: Design, fabrication and characterization of pectin-coated gelatin nanoparticles as potential nano-carrier system, *J Food Biochem* 43(2):1–12, 2019. https://doi.org/10.1111/jfbc.12729.

Faridi Esfanjani A, Assadpour E, Jafari SM: Improving the bioavailability of phenolic compounds by loading them within lipid-based nanocarriers, *Trends Food Sci Technol* 76(April):56–66, 2018. https://doi.org/10.1016/j.tifs.2018.04.002.

Fasolin LH, Pereira RN, Pinheiro AC, Martins JT, Andrade CCP, Ramos OL: Emergent food proteins—towards sustainability, health and innovation, *Food Res Int* 125(April), 2019, 108586. https://doi.org/10.1016/j.foodres.2019.108586.

Fasolin LH, Martins AJ, Cerqueira MA, Vicente AA: Modulating process parameters to change physical properties of bigels for food applications, *Food Struct* 28, 2021, 100173. https://doi.org/10.1016/j.foostr.2020.100173.

Fathi M, Martín Á, McClements DJ: Nanoencapsulation of food ingredients using carbohydrate based delivery systems, *Trends Food Sci Technol* 39(1):18–39, 2014. https://doi.org/10.1016/j.tifs.2014.06.007.

Fathi M, Donsi F, McClements DJ: Protein-based delivery systems for the nanoencapsulation of food ingredients, *Compr Rev Food Sci Food Saf* 17(4):920–936, 2018. https://doi.org/10.1111/1541-4337.12360.

Feng J, Wu Y, Zhang L, et al.: Enhanced chemical stability, intestinal absorption, and intracellular antioxidant activity of cyanidin-3-O-glucoside by composite nanogel encapsulation, *J Agric Food Chem* 67(37):10432–10447, 2019. https://doi.org/10.1021/acs.jafc.9b04778.

Fernandes A, Oliveira J, Fonseca F, et al.: Molecular binding between anthocyanins and pectic polysaccharides—unveiling the role of pectic polysaccharides structure, *Food Hydrocoll* 102(December 2019), 2020. https://doi.org/10.1016/j.foodhyd.2019.105625.

Fleschhut J, Kratzer F, Rechkemmer G, Kulling SE: Stability and biotransformation of various dietary anthocyanins in vitro, *Eur J Nutr* 45(1):7–18, 2006. https://doi.org/10.1007/s00394-005-0557-8.

Fraga CG, Croft KD, Kennedy DO, Tomás-Barberán FA: The effects of polyphenols and other bioactives on human health, *Food Funct* 10(2):514–528, 2019. https://doi.org/10.1039/c8fo01997e.

Garavand F, Jalai-jivan M, Assadpour E, Mahdi S: Encapsulation of phenolic compounds within nano/microemulsion systems: a review, *Food Chem* 364(April), 2021, 130376. https://doi.org/10.1016/j.foodchem.2021.130376.

Ge J, Yue X, Wang S, et al.: Nanocomplexes composed of chitosan derivatives and β-lactoglobulin as a carrier for anthocyanins: preparation, stability and bioavailability in vitro, *Food Res Int* 116:336–345, 2019. https://doi.org/10.1016/j.foodres.2018.08.045.

Gharanjig H, Iri M, Hosseinnezhad M, Gharanjig K, Jafari SM: Enhanced thermal stability of anthocyanins through natural polysaccharides from Angum gum and cress seed gum, *J Food Sci* 87(2):585–598, 2022. https://doi.org/10.1111/1750-3841.16016.

Ghasemi S, Jafari SM, Assadpour E, Khomeiri M: Nanoencapsulation of D-limonene within nanocarriers produced by pectin-whey protein complexes, *Food Hydrocoll* 77:152–162, 2018. https://doi.org/10.1016/j.foodhyd.2017.09.030.

Gonçalves RFS, Martins JT, Duarte CMM, Vicente AA, Pinheiro AC: Advances in nutraceutical delivery systems: from formulation design for bioavailability enhancement to efficacy and safety evaluation, *Trends Food Sci Technol* 78(June):270–291, 2018. https://doi.org/10.1016/j.tifs.2018.06.011.

Gonçalves RFS, Madalena DA, Fernandes JM: Application of nanostructured delivery systems in food: from incorporation to detection and characterization, *Trends Food Sci Technol* 129(May):111–125, 2022. https://doi.org/10.1016/j.tifs.2022.09.016.

Goodarzi N, Varshochian R, Kamalinia G, Atyabi F, Dinarvand R: A review of polysaccharide cytotoxic drug conjugates for cancer therapy, *Carbohydr Polym* 92(2):1280–1293, 2013. https://doi.org/10.1016/j.carbpol.2012.10.036.

Gopi Krishna P, Kameswaran S, Sri Ranjani T, Gunavathi Y: Recent developments in nanoencapsulation of bioactive compounds of microbial sources and their biomedical applications, In *Recent developments in applied microbiology and biochemistry*, 2021, Elsevier Inc. https://doi.org/10.1016/b978-0-12-821406-0.00014-x.

Gopinath V, Saravanan S, Al-Maleki AR, Ramesh M, Vadivelu J: A review of natural polysaccharides for drug delivery applications: special focus on cellulose, starch and glycogen, *Biomed Pharmacother* 107(July):96–108, 2018. https://doi.org/10.1016/j.biopha.2018.07.136.

Gottesmann M, Goycoolea FM, Steinbacher T, Menogni T, Hensel A: Smart drug delivery against helicobacter pylori: pectin-coated, mucoadhesive liposomes with antiadhesive activity and antibiotic cargo, *Appl Microbiol Biotechnol* 104(13):5943–5957, 2020. https://doi.org/10.1007/s00253-020-10647-3.

Guadarrama-escobar OR, Serrano-castañeda P, Anguiano-almaz E, et al.: Chitosan nanoparticles as oral drug carriers, *Int J Mol Sci* 24:4289, 2023. https://doi.org/10.3390/ijms24054289.

Gummel J, Boué F, Demé B, Cousin F: Charge stoichiometry inside polyelectrolyte-protein complexes: a direct SANS measurement for the PSSNa-lysozyme system, *J Phys Chem B* 110(49):24837–24846, 2006. https://doi.org/10.1021/jp064383k.

Hamidi M, Azadi A, Rafiei P: Hydrogel nanoparticles in drug delivery, *Adv Drug Deliv Rev* 60(15):1638–1649, 2008. https://doi.org/10.1016/j.addr.2008.08.002.

Hamman JH: Chitosan based polyelectrolyte complexes as potential carrier materials in drug delivery systems, *Drugs* 8:1305–1322, 2010. https://doi.org/10.3390/md8041305.

Hassan E, Fadel S, Abou-elseoud W, Mahmoud M: Cellulose nanofibers/pectin/pomegranate extract nanocomposite as antibacterial and antioxidant films and coating for paper, *Polymers* 14:4605, 2022. https://doi.org/10.3390/polym14214605.

He B, Ge J, Yue P, et al.: Loading of anthocyanins on chitosan nanoparticles influences anthocyanin degradation in gastrointestinal fluids and stability in a beverage, *Food Chem* 221:1671–1677, 2017. https://doi.org/10.1016/j.foodchem.2016.10.120.

He Y, Chen D, Liu Y, et al.: Protective effect and mechanism of soybean insoluble dietary fiber on the color stability of Malvidin-3-O-glucoside, *Foods* 11:1474, 2022.

Henriques JF, Serra D, Dinis TCP, Almeida LM: The anti-neuroinflammatory role of anthocyanins and their metabolites for the prevention and treatment of brain disorders, *Int J Mol Sci* 21:8653, 2020. https://doi.org/10.3390/ijms21228653.

Honary S, Zahir F: Effect of zeta potential on the properties of Nano-drug delivery systems—a review (part 1), *Trop J Pharm Res* 12(April):255–264, 2013.

Hosseini SMH, Ghiasi F, Jahromi M: Nanocapsule formation by complexation of biopolymers, In *Nanoencapsulation technologies for the food and nutraceutical industries*, 2017, Elsevier Inc. https://doi.org/10.1016/B978-0-12-809436-5.00012-4.

Hu B, Pan C, Sun Y, et al.: Optimization of fabrication parameters to produce chitosan—tripolyphosphate nanoparticles for delivery of tea catechins, *J Agric Food Chem* 56(16):7451–7458, 2008. https://doi.org/10.1021/jf801111c.

Huang X, Liu Y, Zou Y, et al.: Encapsulation of resveratrol in zein/pectin core-shell nanoparticles: stability, bioaccessibility, and antioxidant capacity after simulated gastrointestinal digestion, *Food Hydrocoll* 93(February):261–269, 2019. https://doi.org/10.1016/j.foodhyd.2019.02.039.

Jafari SM, McClements DJ: Nanotechnology approaches for increasing nutrient bioavailability, In *Advances in food and nutrition research*, ed 4, vol. 81, 2017, Elsevier Inc. https://doi.org/10.1016/bs.afnr.2016.12.008.

Jafari SM, Esfanjani AF, Katouzian I: Safety of nanoencapsulated food ingredients, In *Nanoencapsulation of food bioactive ingredients*, 2017, Elsevier Inc. https://doi.org/10.1016/B978-0-12-809740-3.00010-6.

Jang K, Lee HG: Stability of chitosan nanoparticles for L-ascorbic acid during heat treatment in aqueous solution, *J Agric Food Chem* 56, 2008. https://doi.org/10.1021/jf073385e. https://doi.org/1936–1941.

Jiang L, Liu Y, Li L, Qi B, Ju M, Xu Y: Covalent conjugates of anthocyanins to soy protein: unravelling their structure features and in vitro gastrointestinal digestion fate, *Food Res Int* 120(October 2018):603–609, 2019. https://doi.org/10.1016/j.foodres.2018.11.011.

Jiménez-Fernández E, Ruyra A, Roher N, Zuasti E, Infante C, Fernández-Díaz C: Nanoparticles as a novel delivery system for vitamin C administration in aquaculture, *Aquaculture* 432:426–433, 2014. https://doi.org/10.1016/j.aquaculture.2014.03.006.

Jin B, Zhou X, Li X, Lin W, Chen G, Qiu R: Self-assembled modified soy protein/dextran nanogel induced by ultrasonication as a delivery vehicle for riboflavin, *Molecules* 21(3):282, 2016. https://doi.org/10.3390/molecules21030282.

Joseph SV, Edirisinghe I, Burton-freeman BM: Berries: anti-inflammatory effects in humans, *J Agric Food Chem* 62(18):3886–3903, 2014. https://doi.org/10.1021/jf4044056.

Joye IJ, Davidov-pardo G, Julian D: Nanotechnology for increased micronutrient bioavailability, *Trends Food Sci Technol* 40(2):168–182, 2014. https://doi.org/10.1016/j.tifs.2014.08.006.

Kamel S, Ali N, Jahangir K, Shah SM, El-Gendy AA: Pharmaceutical significance of cellulose: a review, *Express Polym Lett* 2(11):758–778, 2008. https://doi.org/10.3144/expresspolymlett.2008.90.

Karimi M, Eslami M, Sahandi-Zangabad P, et al.: pH-sensitive stimulus-responsive nanocarriers for targeted delivery of therapeutic agents, *Wiley Interdiscip Rev Nanomed Nanobiotechnol* 8(5):696–716, 2016. https://doi.org/10.1002/wnan.1389.

Karimi M, Sahandi Zangabad P, Baghaee-Ravari S, Ghazadeh M, Mirshekari H, Hamblin MR: Smart nanostructures for cargo delivery: uncaging and activating by light, *J Am Chem Soc* 139(13):4584–4610, 2017. https://doi.org/10.1021/jacs.6b08313.

Karoyo AH, Wilson LD: Physicochemical properties and the gelation process of supramolecular hydrogels: a review, *Gels* 3(1):1–18, 2017. https://doi.org/10.3390/gels3010001.

Keizman D, Frenkel M, Peer A, et al.: Modified citrus pectin treatment in non-metastatic biochemically relapsed prostate cancer: results of a prospective phase II study, *Nutrients* 13(12):4295, 2021. https://doi.org/10.3390/nu13124295.

Khan N, Bharali DJ, Adhami VM, et al.: Oral administration of naturally occurring chitosan-based nanoformulated green tea polyphenol EGCG effectively inhibits prostate cancer cell growth in a xenograft model, *Carcinogenesis* 35(2):415–423, 2014. https://doi.org/10.1093/carcin/bgt321.

Khotimchenko M: Pectin polymers for colon-targeted antitumor drug delivery, *Int J Biol Macromol* 158:1110–1124, 2020. https://doi.org/10.1016/j.ijbiomac.2020.05.002.

Kumar MNVR, Muzzarelli RAA, Muzzarelli C, Sashiwa H, Domb AJ: Chitosan chemistry and pharmaceutical perspectives, *Chem Rev* 104(12):6017–6084, 2004. https://doi.org/10.1021/cr030441b.

Lampugnani ER, Khan GA, Somssich M, Persson S: Building a plant cell wall at a glance, *J Cell Sci* 131(2):jcs207373, 2018. https://doi.org/10.1242/jcs.207373.

Lara-Espinoza C, Carvajal-Millán E, Balandrán-Quintana R, López-Franco Y, Rascón-Chu A: Pectin and pectin-based composite materials: beyond food texture, *Molecules* 23(4), 2018. https://doi.org/10.3390/molecules23040942.

Le XT, Rioux LE, Turgeon SL: Formation and functional properties of protein–polysaccharide electrostatic hydrogels in comparison to protein or polysaccharide hydrogels, *Adv Colloid Interface Sci* 239:127–135, 2017. https://doi.org/10.1016/j.cis.2016.04.006.

Leiva A, Bonardd S, Pino M, Saldías C, Kortaberria G, Radić D: Improving the performance of chitosan in the synthesis and stabilization of gold nanoparticles, *Eur Polym J* 68:419–431, 2015. https://doi.org/10.1016/j.eurpolymj.2015.04.032.

Li C, Nie H, Chen Y, Xiang ZY, Li JB: Amide pectin: a carrier material for colon-targeted controlled drug release, *J Appl Polym Sci* 133(29):1–8, 2016. https://doi.org/10.1002/app.43697.

Li Y, He D, Li B, et al.: Engineering polyphenols with biological functions via polyphenol-protein interactions as additives for functional foods, *Trends Food Sci Technol* 110(February):470–482, 2021.

Liang J, Cao L, Zhang L, Wan X: Preparation*, characterization, and in vitro antitumor activity of folate conjugated chitosan coated EGCG nanoparticles*, *Food Sci Biotechnol* 23(2):569–575, 2014. https://doi.org/10.1007/s10068-014-0078-4.

Liang J, Yan H, Yang HJ, et al.: Synthesis and controlled-release properties of chitosan/β-lactoglobulin nanoparticles as carriers for oral administration of epigallocatechin gallate, *Food Sci Biotechnol* 25(6):1583–1590, 2016. https://doi.org/10.1007/s10068-016-0244-y.

Lin L, Xu W, Liang H, et al.: Construction of pH-sensitive lysozyme/pectin nanogel for tumor methotrexate delivery, *Colloids Surf B Biointerfaces* 126:459–466, 2015. https://doi.org/10.1016/j.colsurfb.2014.12.051.

Lu X, Gao H, Li C, et al.: Polyelectrolyte complex nanoparticles of amino poly (glycerol methacrylate)*s and insulin*, *Int J Pharm* 423:195–201, 2012. https://doi.org/10.1016/j.ijpharm.2011.12.017.

Lu X, Chen J, Guo Z, et al.: Using polysaccharides for the enhancement of functionality of foods: a review, *Trends Food Sci Technol* 86(October 2018):311–327, 2019. https://doi.org/10.1016/j.tifs.2019.02.024.

Luo Y, Wang Q: Recent development of chitosan-based polyelectrolyte complexes with natural polysaccharides for drug delivery, *Int J Biol Macromol* 64:353–367, 2014. https://doi.org/10.1016/j.ijbiomac.2013.12.017.

Luo Y, Pan K, Zhong Q: Casein/pectin nanocomplexes as potential oral delivery vehicles, *Int J Pharm* 486(1–2):59–68, 2015. https://doi.org/10.1016/j.ijpharm.2015.03.043.

Manzoor M, Singh J, Bandral JD, Gani A, Shams R: Food hydrocolloids: functional, nutraceutical and novel applications for delivery of bioactive compounds, *Int J Biol Macromol* 165:554–567, 2020. https://doi.org/10.1016/j.ijbiomac.2020.09.182.

Martínez Rivas CJ, Tarhini M, Badri W, et al.: Nanoprecipitation process: from encapsulation to drug delivery, *Int J Pharm* 532(1):66–81, 2017. https://doi.org/10.1016/j.ijpharm.2017.08.064.

Matalanis A, Jones OG, McClements DJ: Structured biopolymer-based delivery systems for encapsulation, protection, and release of lipophilic compounds, *Food Hydrocoll* 25(8):1865–1880, 2011. https://doi.org/10.1016/j.foodhyd.2011.04.014.

Min KA, Cho JH, Song YK, Kim CK: Iron casein succinylate-chitosan coacervate for the liquid oral delivery of iron with bioavailability and stability enhancement, *Arch Pharm Res* 39(1):94–102, 2016. https://doi.org/10.1007/s12272-015-0684-6.

Mirzaei-Mohkam A, Garavand F, Dehnad D, Keramat J, Nasirpour A: Optimisation, antioxidant attributes, stability and release behavior of carboxymethyl cellulose films incorporated with nanoencapsulated vitamin E, *Prog Org Coat* 134(March):333–341, 2019. https://doi.org/10.1016/j.porgcoat.2019.05.026.

Mohammadi A, Jafari SM, Assadpour E, Faridi Esfanjani A: Nano-encapsulation of olive leaf phenolic compounds through WPC-pectin complexes and evaluating their release rate, *Int J Biol Macromol* 82:816–822, 2016. https://doi.org/10.1016/j.ijbiomac.2015.10.025.

Mohammadian M, Waly MI, Moghadam M, Emam-djomeh Z, Salami M, Moosavi-movahedi AA: Food science and human wellness nanostructured food proteins as efficient systems for the encapsulation of bioactive compounds, *Food Sci Human Wellness* 9(3):199–213, 2020. https://doi.org/10.1016/j.fshw.2020.04.009.

Mohnen D: Pectin structure and biosynthesis, *Curr Opin Plant Biol* 11(3):266–277, 2008. https://doi.org/10.1016/j.pbi.2008.03.006.

Mohsenabadi N, Rajaei A, Tabatabaei M, Mohsenifar A: Physical and antimicrobial properties of starch-carboxy methyl cellulose film containing rosemary essential oils encapsulated in chitosan nanogel, *Int J Biol Macromol* 112:148–155, 2018. https://doi.org/10.1016/j.ijbiomac.2018.01.034.

Moreira HR, Munarin F, Gentilini R, et al.: Injectable pectin hydrogels produced by internal gelation: PH dependence of gelling and rheological properties, *Carbohydr Polym* 103(1):339–347, 2014. https://doi.org/10.1016/j.carbpol.2013.12.057.

Morris GA, Kök SM, Harding SE, Adams GG: Polysaccharide drug delivery systems based on pectin and chitosan, *Biotechnol Genet Eng Rev* 27(1):257–284, 2010. https://doi.org/10.1080/02648725.2010.10648153.

Mourdikoudis S, Pallares RM: Characterization techniques for nanoparticles: comparison and complementarity upon studying nanoparticle properties, *Nanoscale* 10:12871–12934, 2018. https://doi.org/10.1039/c8nr02278j.

Mudgil D, Barak S: Composition, properties and health benefits of indigestible carbohydrate polymers as dietary fiber: a review, *Int J Biol Macromol* 61:1–6, 2013. https://doi.org/10.1016/j.ijbiomac.2013.06.044.

Munin A, Edwards-Lévy F: Encapsulation of natural polyphenolic compounds; a review, *Pharmaceutics* 3(4):793–829, 2011. https://doi.org/10.3390/pharmaceutics3040793.

Muvva A, Chacko IA, Ghate V, Lewis SA: Modified pectins for colon-specific drug delivery, *Indian J Pharm Educ Res* 54(2), 2020. https://doi.org/10.5530/ijper.54.2s.57.

Nasrollahzadeh M, Sajjadi M, Iravani S, Varma RS: Starch, cellulose, pectin, gum, alginate, chitin and chitosan derived (nano)materials for sustainable water treatment: a review, *Carbohydr Polym* 251(September 2020), 2021, 116986. https://doi.org/10.1016/j.carbpol.2020.116986.

Neamtu I, Rusu AG, Diaconu A, et al.: Basic concepts and recent advances in nanogels as carriers for medical applications, *Drug Deliv* 24(1):539–557, 2017. https://doi.org/10.1080/10717544.2016.1276232.

Neufeld L, Bianco-Peled H: Pectin–chitosan physical hydrogels as potential drug delivery vehicles, *Int J Biol Macromol* 101:852–861, 2017. https://doi.org/10.1016/j.ijbiomac.2017.03.167.

Nguyen S, Alund SJ, Hiorth M, Kjøniksen AL, Smistad G: Studies on pectin coating of liposomes for drug delivery, *Colloids Surf B Biointerfaces* 88(2):664–673, 2011. https://doi.org/10.1016/j.colsurfb.2011.07.058.

Ninan N, Muthiah M, Park IK, Elain A, Thomas S, Grohens Y: Pectin/carboxymethyl cellulose/microfibrillated cellulose composite scaffolds for tissue engineering, *Carbohydr Polym* 98(1):877–885, 2013. https://doi.org/10.1016/j.carbpol.2013.06.067.

Nurkeeva ZS, Mun GA, Khutoryanskiy VV: Interpolymer complexes of water-soluble nonionic polysaccharides with polycarboxylic acids and their applications, *Macromol Biosci* 3(6):283–295, 2003. https://doi.org/10.1002/mabi.200390037.

Otchere E, Mckay BM, English MM, Aryee ANA: Current trends in nano-delivery systems for functional foods: a systematic review, *PeerJ* 11, 2023, e14980. https://doi.org/10.7717/peerj.14980.

Pandey M, Mohamad N, Amin MCIM: Bacterial cellulose/acrylamide pH-sensitive smart hydrogel: development, characterization, and toxicity studies in ICR mice model, *Mol Pharm* 11(10):3596–3608, 2014. https://doi.org/10.1021/mp500337r.

Paredes AJ, Asencio CM, Manuel LJ, Allemandi DA: Nanoencapsulation in the food industry: manufacture*, applications and characterization*, *J Food Bioeng Nanoprocess* 1(1): 56–79, 2016.

Park JH, Saravanakumar G, Kim K, Kwon IC: Targeted delivery of low molecular drugs using chitosan and its derivatives, *Adv Drug Deliv Rev* 62(1):28–41, 2010. https://doi.org/10.1016/j.addr.2009.10.003.

Pérez S, Samain D: Structure and engineering of celluloses, *Adv Carbohydr Chem Biochem* 64:25–116, 2010. https://doi.org/10.1016/S0065-2318(10)64003-6.

Persin Z, Stana-Kleinschek K, Foster TJ, Van Dam JEG, Boeriu CG, Navard P: Challenges and opportunities in polysaccharides research and technology: the EPNOE views for the next decade in the areas of materials, food and health care, *Carbohydr Polym* 84(1):22–32, 2011. https://doi.org/10.1016/j.carbpol.2010.11.044.

Posocco B, Dreussi E, De Santa J, et al.: Polysaccharides for the delivery of antitumor drugs, *Materials* 8(5):2569–2615, 2015. https://doi.org/10.3390/ma8052569.

Prabaharan M, Mano JF: Chitosan-based particles as controlled drug delivery systems, *Drug Deliv* 12(1):41–57, 2005. https://doi.org/10.1080/10717540590889781.

Quadrado RFN, Fajardo AR: Microparticles based on carboxymethyl starch/chitosan polyelectrolyte complex as vehicles for drug delivery systems, *Arab J Chem* 13(1):2183–2194, 2020. https://doi.org/10.1016/j.arabjc.2018.04.004.

Rajoka MSR, Thirumdas R, Mehwish HM, et al.: Role of food antioxidants in modulating gut microbial communities: novel understandings in intestinal oxidative stress damage and their impact on host health, *Antioxidants* 10(10):1–24, 2021. https://doi.org/10.3390/antiox10101563.

Rashidinejad A, Boostani S, Babazadeh A, et al.: Opportunities and challenges for the nanodelivery of green tea catechins in functional foods, *Food Res Int* 142(February), 2021, 110186. https://doi.org/10.1016/j.foodres.2021.110186.

Rashwan AK, Younes H, Karim N, et al.: Health properties of bioactive food compounds-loaded micro and nano-encapsulation systems: a review, *SVU-Int J Agric Sci* 4(2): 178–203, 2022. https://doi.org/10.21608/svuijas.2022.134530.1208.

Reichembach LH, Lúcia C, Petkowicz DO: Food hydrocolloids pectins from alternative sources and uses beyond sweets and jellies: an overview, *Food Hydrocoll* 118(December 2020), 2021, 106824. https://doi.org/10.1016/j.foodhyd.2021.106824.

Rezaei A, Fathi M, Jafari SM: Nanoencapsulation of hydrophobic and low-soluble food bioactive compounds within different nanocarriers, *Food Hydrocoll* 88(June 2018):146–162, 2019. https://doi.org/10.1016/j.foodhyd.2018.10.003.

Rezaei A, Rafieian F, Akbari-alavijeh S, Saeed M: Release of bioactive compounds from delivery systems by stimuli-responsive approaches; triggering factors, mechanisms, and applications, *Adv Colloid Interface Sci* 307(July), 2022, 102728.

Rinaudo M: Chitin and chitosan: properties and applications, *Prog Polym Sci* 31(7):603–632, 2006. https://doi.org/10.1016/j.progpolymsci.2006.06.001.

Rodriguez-Amaya DB: Natural food pigments and colorants, *Curr Opin Food Sci* 7:20–26, 2016. https://doi.org/10.1016/j.cofs.2015.08.004.

Ron N, Zimet P, Bargarum J, Livney YD: Beta-lactoglobulin-polysaccharide complexes as nanovehicles for hydrophobic nutraceuticals in non-fat foods and clear beverages, *Int Dairy J* 20(10):686–693, 2010. https://doi.org/10.1016/j.idairyj.2010.04.001.

Rosales TKO, Fabi JP: Nanoencapsulated anthocyanin as a functional ingredient: technological application and future perspectives, *Colloids Surf B Biointerfaces* 218(April), 2022. https://doi.org/10.1016/j.colsurfb.2022.112707.

Rosales TKO, Fabi JP: Pectin-based nanoencapsulation strategy to improve the bioavailability of bioactive compounds, *Int J Biol Macromol* 229(December 2022):11–21, 2023a. https://doi.org/10.1016/j.ijbiomac.2022.12.292.

Rosales TKO, Fabi JP: Valorization of polyphenolic compounds from food industry by-products for application in polysaccharide-based nanoparticles, *Front Nutr* 10, 2023b, 1144677. https://doi.org/10.3389/fnut.2023.1144677.

Rosales TKO, Fabi JP: Polysaccharides as natural nanoencapsulants for controlled, In: *Smart nanomaterials for bioencapsulation*, 2023c, Elsevier, pp 23–38.

Ko A, Lee JS, Sop Nam H, Gyu Lee H: Stabilization of black soybean anthocyanin by chitosan nanoencapsulation and copigmentation, *J Food Biochem* 41(2):e12316, 2017. https://doi.org/10.1111/jfbc.12316.

Rosales TKO, Pessoa da Silva M, Lourenço FR, Aymoto Hassimotto NM, Fabi JP: Nanoencapsulation of anthocyanins from blackberry (Rubus spp.) through pectin and lysozyme self-assembling, *Food Hydrocoll* 114(December 2020):1–50, 2021. https://doi.org/10.1016/j.foodhyd.2020.106563.

Sadeghi R, Mehryar L, Karimi M, Kokini J: Nanocapsule formation by individual biopolymer nanoparticles, In *Nanoencapsulation technologies for the food and nutraceutical industries*, 2017, Elsevier Inc. https://doi.org/10.1016/B978-0-12-809436-5.00011-2.

Saini A, Panesar PS, Bera MB: Valorization of fruits and vegetables waste through green extraction of bioactive compounds and their nanoemulsions-based delivery system, *Bioresour Bioprocess*, 2019. https://doi.org/10.1186/s40643-019-0261-9.

Salarbashi D, Bazeli J, Rad EF: An update on the new achievements in the nanocapsulation of anthocyanins, *Nanomed J* 0(2):87–97, 2020. https://doi.org/10.22038/nmj.2020.14628.

Sanidad KZ, Sukamtoh E, Xiao H, McClements DJ, Zhang G: Curcumin: recent advances in the development of strategies to improve oral bioavailability, *Annu Rev Food Sci Technol* 10:597–617, 2019. https://doi.org/10.1146/annurev-food-032818-121738.

Sarkar A, Zhang S, Murray B, Russell JA, Boxal S: Modulating in vitro gastric digestion of emulsions using composite whey protein-cellulose nanocrystal interfaces, *Colloids Surf B Biointerfaces* 158:137–146, 2017.

Schmidt I, Cousin F, Huchon C, Boué F, Axelos MAV: Spatial structure and composition of polysaccharide-protein complexes from small angle neutron scattering, *Biomacromolecules* 10(6):1346–1357, 2009. https://doi.org/10.1021/bm801147j.

Sekhon BS: Food nanotechnology—an overview, *Nanotechnol Sci Appl* 3(1):1–15, 2010.

Shen Y, Zhang N, Tian J, et al.: Advanced approaches for improving bioavailability and controlled release of anthocyanins, *J Control Release* 341(June 2021):285–299, 2022. https://doi.org/10.1016/j.jconrel.2021.11.031.

Shishir MRI, Xie L, Sun C, Zheng X, Chen W: Advances in micro and nano-encapsulation of bioactive compounds using biopolymer and lipid-based transporters, *Trends Food Sci Technol* 78(December 2017):34–60, 2018. https://doi.org/10.1016/j.tifs.2018.05.018.

Shishir MRI, Karim N, Gowd V, Xie J, Zheng X, Chen W: Pectin-chitosan conjugated nanoliposome as a promising delivery system for neohesperidin: characterization, release behavior, cellular uptake, and antioxidant property, *Food Hydrocoll* 95(December 2018): 432–444, 2019. https://doi.org/10.1016/j.foodhyd.2019.04.059.

Siddiqui AS, Anwar S, Yunusa MB, Nayik AG, Khaneghah MA: The potential of apricot seed and oil as functional food: composition, biological properties, health benefits & safety, *Food Biosci* 51(December 2022):102336, 2023.

Singh AN, Yethiraj A: Driving force for the complexation of charged polypeptides, *J Phys Chem B* 124(7):1285–1292, 2020. https://doi.org/10.1021/acs.jpcb.9b09553.

Singhal R, Gupta K: A review: tailor-made hydrogel structures (classifications and synthesis parameters), *Polym-Plast Technol Eng* 55:54–70, 2016. https://doi.org/10.1080/03602559.2015.1050520.

Sogias IA, Williams AC, Khutoryanskiy VV: Why is chitosan mucoadhesive? *Biomacromolecules* 9(7):1837–1842, 2008. https://doi.org/10.1021/bm800276d.

Soni KS, Desale SS, Bronich TK: Nanogels: an overview of properties, biomedical applications and obstacles to clinical translation, *J Control Release* 240:109–126, 2016. https://doi.org/10.1016/j.jconrel.2015.11.009.

Sowasod N, Charinpanitkul ST, Tanthapanichakoon W: Nanoencapsulation of curcumin in biodegradable chitosan via multiple emulsion/solvent evaporation, *Int J Pharm* 347:93–101, 2008.

Sriamornsak P: Application of pectin in oral drug delivery, *Drug Deliv* 8:1009–1023, 2011.

Stenger C, Zeeb B, Hinrichs J, Weiss J: Formation of concentrated biopolymer particles composed of oppositely charged WPI and pectin for food applications, *J Dispers Sci Technol* 38(9):1258–1265, 2017. https://doi.org/10.1080/01932691.2016.1234381.

Stetefeld J, Mckenna SA, Patel TR: Dynamic light scattering: a practical guide and applications in biomedical sciences, *Biophys Rev* 8:409–427, 2016. https://doi.org/10.1007/s12551-016-0218-6.

Suleria HAR, Barrow CJ, Dunshea FR: Screening and characterization of phenolic compounds and their antioxidant capacity in different fruit peels, *Foods* 9(9):1206, 2020. https://doi.org/10.3390/foods9091206.

Sun J, Chen J, Mei Z, et al.: Synthesis, structural characterization, and evaluation of cyanidin-3-O-glucoside-loaded chitosan nanoparticles, *Food Chem* 330(April), 2020, 127239. https://doi.org/10.1016/j.foodchem.2020.127239.

Szczęch M, Szczepanowicz K: Polymeric core-shell nanoparticles prepared by spontaneous emulsification solvent evaporation and functionalized by the layer-by-layer method, *Nanomaterials* 10(3):5–8, 2020. https://doi.org/10.3390/nano10030496.

Takeuchi H, Thongborisute J, Matsui Y, Sugihara H, Yamamoto H, Kawashima Y: Novel mucoadhesion tests for polymers and polymer-coated particles to design optimal mucoadhesive drug delivery systems, *Adv Drug Deliv Rev* 57(11):1583–1594, 2005. https://doi.org/10.1016/j.addr.2005.07.008.

Tang C: Food hydrocolloids nanostructured soy proteins: fabrication and applications as delivery systems for bioactives (a review), *Food Hydrocoll* 91(December 2018):92–116, 2019. https://doi.org/10.1016/j.foodhyd.2019.01.012.

Tarone AG, Cazarin CBB, Marostica Junior MR: Anthocyanins: new techniques and challenges in microencapsulation, *Food Res Int* 133(February), 2020. https://doi.org/10.1016/j.foodres.2020.109092.

Tomas M: Effect of dietary fiber addition on the content and in vitro bioaccessibility of antioxidants in red raspberry puree, *Food Chem* 375(June 2021), 2022, 131897. https://doi.org/10.1016/j.foodchem.2021.131897.

Tran N, Pham B, Le L: Bioactive compounds in anti-diabetic plants: from herbal medicine to modern drug discovery, *Biology* 9:252, 2020.

Viebke C, Al-Assaf S, Phillips GO: Food hydrocolloids and health claims, *Bioact Carbohydr Diet Fibre* 4(2):101–114, 2014. https://doi.org/10.1016/j.bcdf.2014.06.006.

Viegas O, Faria MA, Sousa JB, et al.: Delphinidin-3-O-glucoside inhibits angiogenesis via VEGFR2 downregulation and migration through actin disruption, *J Funct Foods* 54(September 2018):393–402, 2019. https://doi.org/10.1016/j.jff.2019.01.039.

Vladár AE, Hodoroaba V: Characterization of nanoparticles by scanning electron microscopy, In *Characterization of nanoparticles*, 2020, Elsevier Inc. https://doi.org/10.1016/B978-0-12-814182-3.00002-X.

Walia N, Dasgupta N, Ranjan S, Ramalingam C, Gandhi M: Methods for nanoemulsion and nanoencapsulation of food bioactives, *Environ Chem Lett* 17(4):1471–1483, 2019. https://doi.org/10.1007/s10311-019-00886-w.

Wang D, Tan J, Kang H, et al.: Synthesis, self-assembly and drug release behaviors of pH-responsive copolymers ethyl cellulose-graft-PDEAEMA through ATRP, *Carbohydr Polym* 84:195–202, 2011. https://doi.org/10.1016/j.carbpol.2010.11.023.

Wang L, Zhao L, Gong F-l, et al.: Modified citrus pectin inhibits breast cancer development in mice by targeting tumor-associated macrophage survival and polarization in hypoxic microenvironment, *Acta Pharmacol Sin* 43(6):1556–1567, 2022. https://doi.org/10.1038/s41401-021-00748-8.

Warnakulasuriya SN, Nickerson MT: Review on plant protein–polysaccharide complex coacervation, and the functionality and applicability of formed complexes, *J Sci Food Agric* 98(15):5559–5571, 2018. https://doi.org/10.1002/jsfa.9228.

Wei Z, Huang Q: Assembly of protein—polysaccharide complexes for delivery of bioactive ingredients: a perspective paper, *J Agric Food Chem* 67(5):1344–1352, 2019. https://doi.org/10.1021/acs.jafc.8b06063.

Wen Y, Oh JK: Recent strategies to develop polysaccharide-based nanomaterials for biomedical applications, *Macromol Rapid Commun* 35:1819–1832, 2014. https://doi.org/10.1002/marc.201400406.

Wijaya W, Zheng H, Zheng T, et al.: Improved bioaccessibility of polymethoxyflavones loaded into high internal phase emulsions stabilized by biopolymeric complexes: a dynamic digestion study via TNO's gastrointestinal model, *Curr Res Food Sci* 2:11–19, 2020. https://doi.org/10.1016/j.crfs.2019.11.007.

Wu CL, Chen QH, Li XY, et al.: Formation and characterisation of food protein–polysaccharide thermal complex particles: effects of pH, temperature and polysaccharide type, *Int J Food Sci Technol* 55(3):1368–1374, 2020. https://doi.org/10.1111/ijfs.14416.

Wusigale, Liang L, Luo Y: Casein and pectin: structures, interactions, and applications, *Trends Food Sci Technol* 97(September 2019):391–403, 2020. https://doi.org/10.1016/j.tifs.2020.01.027.

Xu W, Jin W, Wang Y, Li J, Huang K: Effect of physical interactions on structure of lysozyme in presence of three kinds of polysaccharides, *J Food Sci Technol* 55(8):3056–3064, 2018. https://doi.org/10.1007/s13197-018-3228-5.

Yang Z, Julian D, Peng X, et al.: Fabrication of zein—carboxymethyl cellulose nanoparticles for co-delivery of quercetin and resveratrol, *J Eng* 341, 2023. https://doi.org/10.1016/j.jfoodeng.2022.111322.

Zhai X, Lin D, Liu D, Yang X: Emulsions stabilized by nanofibers from bacterial cellulose: new potential food-grade pickering emulsions, *Food Res Int* 103(October 2017):12–20, 2018. https://doi.org/10.1016/j.foodres.2017.10.030.

Zhang Z, Li X, Sang S, et al.: Polyphenols as plant-based nutraceuticals: health effects, encapsulation, nano-delivery, and application, *Foods* 11(15):2189, 2022. https://doi.org/10.3390/foods11152189.

Zhang Z, Zhang R, Chen L, Tong Q, McClements DJ: Designing hydrogel particles for controlled or targeted release of lipophilic bioactive agents in the gastrointestinal tract, *Eur Polym J* 72:698–716, 2015. https://doi.org/10.1016/j.eurpolymj.2015.01.013.

Zhang H, Jung J, Zhao Y: Preparation, characterization and evaluation of antibacterial activity of catechins and catechins-Zn complex loaded β-chitosan nanoparticles of different particle sizes, *Carbohydr Polym* 137:82–91, 2016. https://doi.org/10.1016/j.carbpol.2015.10.036.

Zhang J, Jia G, Wanbin Z, et al.: Nanoencapsulation of zeaxanthin extracted from Lycium barbarum L. by complex coacervation with gelatin and CMC, *Food Hydrocoll* 112(December 2019), 2021a, 106280. https://doi.org/10.1016/j.foodhyd.2020.106280.

Zhang Q, Zhou Y, Yue W, Qin W, Dong H, Vasanthan T: Nanostructures of protein-polysaccharide complexes or conjugates for encapsulation of bioactive compounds, *Trends Food Sci Technol* 109(January):169–196, 2021b. https://doi.org/10.1016/j.tifs.2021.01.026.

Zhao X, Zhang X, Tie S, et al.: Food hydrocolloids facile synthesis of nano-nanocarriers from chitosan and pectin with improved stability and biocompatibility for anthocyanins delivery: an in vitro and in vivo study, *Food Hydrocoll* 109(June), 2020, 106114. https://doi.org/10.1016/j.foodhyd.2020.106114.

Zhou M, Wang T, Hu Q, Luo Y: Low density lipoprotein/pectin complex nanogels as potential oral delivery vehicles for curcumin, *Food Hydrocoll* 57:20–29, 2016. https://doi.org/10.1016/j.foodhyd.2016.01.010.