Natural Polymers As Nanocapsule Carriers

Danijela Rajić, Srđan Vuković, Svetlana Pelemiš, Milesa Srećković

***Abstract*— Natural polymers obtained from renewable sources have recently been increasingly considered as suitable carriers, in the form of nanocapsules, for various active components. They enable the formation of a system for the delivery of active substances so that it is possible to encapsulate, protect, and release bioactive substances in drugs and food. Encapsulation of active components also enables the protection of sensitive and easily volatile components. Particular attention is paid to their application in the food industry for the production of functional foods, which, in addition to being nutritional, also have a certain therapeutic effect. In the pharmaceutical industry, more and more research is being devoted to them in the area of long-release drugs. Nanocapsules outperform most other colloidal carriers because of their small size, greater encapsulation potential, greater encapsulation power, and targeted action. Most of the existing carriers based on natural proteins used in the food and pharmaceutical industries are hydrophilic, so the encapsulation of hydrophobic active substances is a special challenge. This paper presents an overview of natural polymers used as suitable carriers and the possibilities of their use in the synthesis of nanocapsules for various uses.**

***Index Terms*— natural polymers; renewable sources; nanocapsule carriers; drugs; active components.**

I. Introduction

Natural polymers derived from food are considered desirable materials for constructing delivery systems to encapsulate, protect, and release bioactive components in nutraceuticals, pharmaceuticals and food [1]. Food proteins are of particular interest in the design of delivery systems, due to their high nutritional value, abundant sources, structural versatility and considerable functional properties [2, 3]. Nanoparticles constructed of food proteins have suitable physicochemical properties and functional attributes, which allow them to entrap both hydrophilic and hydrophobic bioactive compounds. They are increasingly being applied as delivery systems in the food industry to improve the stability and oral bioavailability of bioactive components [4]. Nanocapsules have an advantage over most of the other colloidal carriers due to their smaller size, higher encapsulation efficiency, more effective penetration ability and targetability [5]. Nanobiotechnology have wide range of application [6]. Nanocapsules were first developed around 1970. They were initially devised as carrier for vaccines and anticancer. Over the past few decades, there has been considerable interest in developing biodegradable nanocapsules (liposome, virus like particle (VLP), protein, etc.) as effective food and drug delivery device [2].

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Nanocapsules have become an important area of research in the field of food and drug delivery vehicles [7].Scientific community working at the interface of chemistry and biology is always on the lookout for biopolymers from natural and sustainable sources to generate newer structures which could be used for applications ranging from product structuring to the in vivo delivery of bioactives. Since, most of the biopolymers approved and been used for food and pharmaceutical applications (such as gelatin, casein, dextran, etc.) are water soluble in nature; it becomes necessary to involve steps of physical and chemical alterations like cross-linking and hydrophobic modifications in order to generate colloidal particles from these materials [8].

Nanocapsules have an advantage over hydrogels, organogels, liposome, and microparticles due to their smaller particle size, higher encapsulation efficiency, more effective penetration ability and targetability. Nanocapsules are usually fabricated from varieties of natural polymers, mainly including food- grade proteins and polysaccharides, because they are biocompatible, biodegradable, and non-toxic properties, such as soy protein lactoferrin, gelatin, chitosan and alginate [5]. Nanocapsules generally vary in size from 10 to 1000 nm [9,10]. Recently protein nanoparticles have been shown efficacy as biodegradable carrier which can incorporate variety of drugs in relatively non-specific fashion [11]. The food or drug is dissolved, entrapped, encapsulated or attached to a nanoparticles matrix and depending upon the method of preparation, nanoparticles, nanospheres or nanocapsule can be obtained. Nanocapsules are vesicular systems in which the drug is confined to a cavity surrounded by a unique polymer membrane, while nanospheres are matrix systems in which the drug is physically and uniformly dispersed [7,9]. Figure 1 shows the schematic diagram of nanocapsulated and nanosphere particles loaded with food or drug.

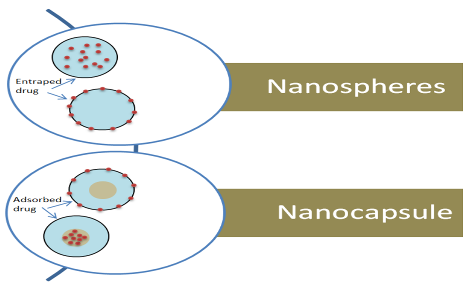

Fig. 1. Schematic diagram of nanospheres and nanocapsules

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Among these colloidal system those based on protein may be vary promising since they are biodegradable and non-antigenic relatively easy to prepared and their size distribution can be monitored easily [12]. A wide variety of drugs can be delivered using nanoparticulate carriers via a number of routes. Food-borne diseases are becoming one of the serious problems faced by humans along with environmental contamination and because of that technological innovations in food safety related to consumer confidence and human health are becoming extremely urgent [13].

II. PLANT PROTEINS

Among various natural or synthetic polymer-based particulate systems potentially available to food applications, plant protein-based micro- and nanoparticles are preferably used for nutrient or drug delivery because they offer advantages over other materials in terms of biodegradability, abundant renewable sources, safety status in vivo, and many useful functional properties [14-18]. Additionally, they also exhibit high loading capacity of various bioactives due to their amphiphilic structure, multiple binding sites, and a variety of possible binding mechanisms include electrostatic attractions, hydrophobic interactions, hydrogen and covalent bonding. Due to the known characteristics of microencapsulation, easy surface modification and scale-up feasibilities, particulate systems in micron and nanometre scales provide better opportunities for targeted delivery of bioactive ingredients [16, 19, 20]. The plant proteins most commonly used in the production of nanocapsules are zein, soy, and wheat proteins, and they will be discussed in this paper.

A. Zein

Zein is a protein classified within the group of prolamins. It is attractive for use in nanotechnology as a polymer matrix and is classified as Generally Recognized As Safe (GRAS) by the U.S. Food and Drug Administration (FDA). In addition, zein has promising characteristics, such as biocompatibility, biodegradability, and low toxicity. It is widely used in that it can encapsulate generally different insoluble compounds in water to provide stability and control of release when is in the GastroIntestinal Tract (GIT) [14, 21]. Zein is the main form of protein storage contained in the endosperm tissue of corn and comprises almost 80% of the whole protein content in the corn. In the past, zein was considered more of a by-product of corn processing industries; the consensus indicated zein to be a low-valued material without important potential technological uses. However, due to several recent methodologies and developing processes allowing applications in different fields, nowadays, there is new thought related to zein and zein-based materials towards considering them as more valuable materials. Potential applications of zein include uses as biodegradable plastics, fibers, adhesives, coatings, ceramics, inks, cosmetics, textiles and chewing gum [14, 22, 23, 24].

B. Soy proteins

Soy proteins, the by-product of soy oil processing, is now one of the most widely used protein ingredients in food processing. When different processing methods are conducted, soy protein aggregates with different structures and functionalities could be formed along different pathways [25]. In addition to zein, soy protein-based particles are also promising candidates as delivery systems for nutraceuticals or drugs. Due to the ligand binding properties, soy proteins can serve as an effective carrier for various bioactive molecules. They can bind these molecules to form complexes in nanoscale through physical interactions, mainly hydrophobic interactions, hydrogen bonds and van der Waals attraction. Recent studies suggest that soy proteins have the potential to be used as carriers for both hydrophobic and hydrophilic bioactive compounds, such as vitamin B12, cranberry polyphenols, curcumin, resveratrol (RES), and polyphenols from Concord grape pomace, to improve their water solubility, stability and bioavailability [14].

C. Wheat gliadins

Nanocapsules made from gliadin, a component of wheat gluten, have been prepared for nutrient/drug delivery and controlled release applications. For example, gliadin nanocapsules has been used as carriers for all-trans-retinoic acid (RA) [26]. Gliadin nanocapsules (450–475 nm) were showed to be a suitable delivery and controlled release system for nutrients and drugs with different polarity (hydrophobic and amphiphilic). It was found that the amounts of the entrapped drug increased with an increase in the drug hydrophobicity, confirming a strong interaction between gliadins and apolar compounds. Their essential feature is low price and availability [14, 26].

III. PREPARATION METHODS

Protein nanocapsules can be obtained by different methods [11]. Protein nanocapsules have been extensively studied as suitable for drug delivery since they are biodegradable, non-toxic and non antigenic, because of their defined primary structure and high content of charged amino acids (that is, lysine). The protein-based nanocapsules could allow the electrostatic adsorption of positively or negatively charged molecules without the requirements of other compounds. In addition, protein nanocapsules can be easily prepared under soft condition, by coacervation or controlled desolvation processes [2]. Among the available potential colloidal drug carrier systems covering the size range described, protein-based nanocapsules play an important role [11]. Biopolymers, such as proteins, are commonly used to encapsulate oil-in-water emulsions. Simple and complex coacervation, spray drying and heat denaturation represent three major microencapsulation techniques based on proteins. Their principles are quite similar: emulsification of the core material (oil) is followed by microcapsules wall formation induced by environmental conditions changing. Concerning simple coacervation method, the protein precipitation around oil droplets is obtained by changing pH and temperature or by the "salting-out" technique. Widespread presence of microcapsules based on animal proteins such as gelatin, casein or albumin contrasts with a very limited use of plant proteins. Wheat gliadin was one of the rare plant storage proteins used for encapsulation of dispersed oil phase by simple coacervation method. The microparticles made from soy protein isolate (SPI) were mainly fabricated by using spray-drying, coacervation, and cold gelation techniques [11, 14, 27]. The table 1 provides an overview of nanoparticle types and methods of their preparation.

TABLE I
OVERVIEW OF PLANT-PROTEIN BASED NANOCAPSULES AND TYPE OF PREPARATION [14]

Type of particles	Preparation
Zein microparticles	Spray drying or supercritical antisolvent method
Zein microparticles	Spray or freeze drying
Zein nanoparticles	Liquid–liquid dispersion method
Zein nanoparticles	Phase separation or liquid–liquid dispersion method
Zein nanoparticles	Liquid–liquid dispersion method or electrospraying
Zein nanoparticles	Supercritical anti-solvent
Zein nanoparticles	Liquid–liquid dispersion method or electrospraying
Zein-chitosan complex nanoparticles	Low-energy phase separation method
SPI-zein complex microparticles	Ca^{2+}-induced cold gelation method
SPI/FA-conjugated SPI nanoparticles	Ethanol desolvation method
SPI nanoparticles	Ca^{2+}-induced cold gelation method
Soy protein nanocomplex	Ligand binding properties
SPI-CMCS complex nanoparticles	Ca^{2+} induced co-gelation method
Soy protein-soy polysaccharide complex nanogels	High-pressure homogenization and heating procedures
Soy lipophilic protein nanoparticles	Ultrasonic treatment
Gliadin nanoparticles	Antisolvent precipitation method

IV. CONCLUSION

Natural polymers show great potential for developing promising delivery vehicles to incorporate and protect various bioactive ingredients, and control their release behaviour under the different conditions. It could be used to produce a wide range of delivery systems, such as micro- and nanoparticles, fibers, films and hydrogels, all of which can be tailored for the design of innovative functional foods. As the interest in functional foods is rapidly growing, the development of advanced plant protein-based delivery systems will expand the possible applications. Nanocapsules outperform most other colloidal carriers because of their small size, greater encapsulation potential, greater encapsulation power, and targeted action. Nevertheless, the delivery of functional ingredients in the complex food systems is rather challenging as it is essential to evaluate not only the impact of complex food matrix on the storage stability and bioavailability of the encapsulated ingredients, but also the effect of the delivery systems on the food product functionality, such as stability, texture, taste, appearance and bioavailability of the ingredients.

The work also has a wide application from forensics to herritology.

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