Trends in Food Science & Technology 70 (2017) 69–81

Contents lists available at ScienceDirect

Trends in Food Science & Technology

journal homepage: www.elsevier.com/locate/tifs

Whey and soy protein-based hydrogels and nano-hydrogels as bioactive delivery systems

Arash Abaee[a], Mehdi Mohammadian[b], Seid Mahdi Jafari[a,*]

[a] Department of Food Materials and Process Design Engineering, Gorgan University of Agricultural Sciences and Natural Resources, Gorgan, Iran
[b] Department of Food Science and Engineering, University College of Agriculture and Natural Resources, University of Tehran, Karaj, Iran

ARTICLE INFO

Keywords:
Hydrogels
Nano-gels
Globular proteins
Delivery systems
Whey proteins
Soy proteins

ABSTRACT

Background: Bioactive molecules are mostly amenable to degradation at processing, storage, and harsh digestion conditions. Hence, high-throughput encapsulation bodies must be designed in a way to protect them from destructive circumstances and to enhance their bioavailability.

Scope and approach: This review article focuses on versatile mechanisms for gelation of globular proteins and highlights the current studies on whey and soy protein hydrogels as two key animal and herbal proteins used in fabricating coating materials. Moreover, different categories of hydrogels, such as aerated hydrogels, hydrogels made from aggregated forms of proteins, hydrogels originated from food-grade materials, and hydrogels with nano scale dimensions are discussed.

Key findings and conclusions: The gelation and particulation method have dramatic effects on the liberation features as well as the bioactivity of the wrapped ingredients. Therefore, different approaches are needed to be considered in order to increase the bioavailability of nutraceuticals and drugs accommodated within protein hydrogels. Accordingly, there is a growing trend for developing innovative modes of gelation and immobilizing bioactive materials into the hydrogel network.

1. Introduction

Delivery systems are engineered as a means to retain the sensitive compounds from degradation against food processing operations, digestive enzymes plus unfavorable environmental conditions (e.g., oxidation, temperature, pH, and light), as well as for site-specific gastrointestinal delivery and controlled release of water-loving and water-fearing nutraceuticals (Faridi Esfanjani & Jafari, 2016; Katouzian & Jafari, 2016). Delivery systems can be classified to lipid-based networks (e.g., conventional emulsions, micro- and nanoemulsions, multiple emulsions, liposomes, solid lipid nanoparticles, and nano-structured lipid carriers), biopolymer-based systems (e.g., individual carbohydrate and protein carriers and their complexes), nature-inspired systems (e.g., caseins, cyclodextrins, and amylose helixes), and specialized equipment-based systems (e.g., electrospinning and electrospraying, and nano-spray dryer) (Jafari, 2017a,b). Among these systems, protein-based hydrogels are especially welcomed from different sectors due to their outstanding properties, such as high nutritional value, excellent functional properties, amphiphilic nature, biocompatibility, biodegradability, and lower toxicity in comparison with synthetic polymers (Snyders et al., 2007).

There are three gel-based delivery vehicles: hydrogels, organogels, and bigels. Hydrogels are three-dimensional solid networks fabricated by physically or chemically cross-linked hydrophilic polymeric structures that can entangle a lot of water or other biological liquid inside their network (Iemma et al., 2006). Hydrogels can be formulated in different physical states including microparticles, nanoparticles, coatings, and films (Ahmed, 2015; Hoare & Kohane, 2008). An organogel or oleogel is a thermoreversible semi-solid system composed of a liquid organic phase within a three-dimensional, cross-linked network (Vintiloiu & Leroux, 2008). Self-assembly is the main mechanism for the formation of the gel network in organogels in which mostly low molecular weight compounds are capable of gelling organic solvents (Marangoni & Garti, 2015; Vintiloiu & Leroux, 2008). Bigels are other rapidly expanding delivery systems which are formulated via the combination of an organogel with a hydrogel at relatively high shear rates. With respect to their structure, bigels have the characteristics of both hydrogels and organogel and have spawning novel applications in the delivery of bioactive compounds (Lupi et al., 2015, 2016; Sagiri et al., 2015; Singh et al., 2014).

* Corresponding author.
E-mail address: smjafari@gau.ac.ir (S.M. Jafari).

http://dx.doi.org/10.1016/j.tifs.2017.10.011
Received 18 June 2017; Received in revised form 2 October 2017; Accepted 20 October 2017
Available online 25 October 2017
0924-2244/

2. Preparation and formation of hydrogels

Biopolymer-derived hydrogels have recently captured considerable attention as promising delivery practices for nutraceuticals and drugs. Natural carbohydrates and proteins are proper nominees for engineering delivery systems owing to their ability for gelation, amenability to modifications, structural diversity, biodegradability, and biocompatibility (Mokhtari, Jafari, & Assadpour, 2017). Food globular proteins, owing to their aggregation and gelation properties, can wrap bioactive compounds inside their network and are reliable delivery systems due to their inherent biocompatibility, biodegradability, high nutritional value, and tunable swelling and liberation characteristics (Chen, Remondetto, & Subirade, 2006).

Globular proteins are able to produce heat and cold-set gels (Zhang, Zhang, Chen, Tong, & McClements, 2015). Heating of protein aqueous solutions triggers molecular unfolding and disruption of proteins, thereby leading to exposure of hydrophobic patches as well as to formation of disulfide bonds. Finally, heat-set gels will be formed by the aggregation of the unfolded protein moieties along with the participation of intermolecular β-sheet architectures (Caillard, Remondetto, Mateescu, & Subirade, 2008; Oztop, McCarthy, McCarthy, & Rosenberg, 2014). In the case of whey protein heat-induced gels, gel network is basically formed through covalent bonds (inter- and intramolecular disulfide bonds) and a broad array of non-covalent interactions such as hydrogen bonding, ionic, and hydrophobic interactions (Oztop, McCarthy, McCarthy, & Rosenberg, 2012; Oztop et al., 2014). On the contrary, globular proteins yield gels via the cold-gelation approach. Having a uniform architecture, high strength, and the ability to gel at ambient temperatures, cold-set gels are unique candidates for designing functional foods in which heat sensitive nutraceuticals are preserved (Nicolai, Britten, & Schmitt, 2011; Martin & De Jong, 2012a; Veerman, Baptist, Sagis, & van der Linden, 2003). It is important to bear in mind that the applications of heat-set gels are limited to the formulations that do not contain heat-sensitive bioactive ingredients due to the requirement of heat treatment for these types of hydrogels (Chen et al., 2006).

Cold-set gelation of food globular proteins occurs in two stages, which initiates by heating the protein solution at neutral pH (above isoelectric point) below the protein gelling extent and at low ionic strength steering the reaction to denaturation and imperfect unfolding of proteins. This follows by acidification to reach the isoelectric pH of protein (acid-induced cold gelation) or supplementation with salts (salt-induced cold gelation) so that the inter-protein repulsion is lowered (mono, di and polyvalent cations) and/or to generate cross-linkages (only di and polyvalent cations) among protein clusters (Kuhn, Cavallieri, & Da Cunha, 2010). $CaCl_2$ and NaCl are applied to the cold gelation of globular proteins (Kuhn, Cavallieri, & Da Cunha, 2011). Alternative cations, such as Fe^{2+} (Martin & De Jong, 2012a; Remondetto, Paquin, & Subirade, 2002) and Mg^{2+} (da Silva, Delgado & Goncalves, 2010) also have been utilized to fabricate whey protein cold-set gels with improved nutritional value and functionality. One main advantage of cold-induced gelation over other methods is the exposure of different functional groups within the protein molecules as a result of denaturation which can create various interactions between bioactive ingredient and polypeptide chains such as hydrogen-bonding, electrostatic, and hydrophobic interactions. These newly-formed bonds between bioactive compounds and proteins can be exploited to design targeted delivery systems (Chen et al., 2006). Moreover, a greater control over the resulting shape, structure and texture of the produced gel is allowed by the cold-induced approach of gelation (Egan, O'Riordan, O'Sullivan, & Jacquier, 2014).

Hydrogels prepared from globular proteins such as whey proteins, vegetable globulins, soy proteins, egg white proteins, pea proteins, wheat proteins plus other origins are discussed in detail within the literature. In addition, the physicochemical and industrial significance hydrogels prepared from animal and herbal resources (i.e., whey and soy proteins) and their role in the delivery of nutraceuticals and bioactive ingredients such as vitamins, minerals, drugs, etc., have been reviewed brilliantly.

2.1. Nano-scale hydrogels as delivery systems

According to the recent advancements in nanotechnology, scholars are eager to apply nanotechnology in designing delivery systems for confinement, protection, and site-specific liberation of bioactive materials (Jafari & McClements, 2017; Joye, Davidov-Pardo, & McClements, 2014). Delivery of drugs and nutraceuticals by the means of nanotechnology, results in the improvement of their bioavailability as well as increasing their residence time in the gastrointestinal tract (Ghasemi, Jafari, Assadpour, & Khomeiri, 2017). One striking feature of nanocarriers is their ability to permeate into the living tissues and enter the epithelial cell lining fenestration and to arrive at the intended cells. Among the distinctive natural or synthetic polymer-based nanoparticulate entities employed in the food industry, protein-based nanohydrogels have demonstrated practical applications due to their non-toxicity, biodegradability, and miniscule size with a large interior network for multivalent bioconjugation, which offers enough space for entrapment of functional components (Chen et al., 2006). Protein gelation has been suggested for the fabrication of micron- (below 100 μm) and nano-sized (below about 0.1 μm) fragments (Stokes, 2012). For instance, nanogels can be formulated by heating a uniform solution of soy proteins (Chen, Lin, Sun, & Zhao, 2014) or by heating of micro-emulsified whey protein solutions (Zhang & Zhong, 2010).

Ding and Yao (2013) fabricated soy protein/soy polysaccharide complex nanogels to convey folic acid to the intestine. Nanogels were made through electrostatic binding of soy proteins with soy polysaccharides and folic acid at pH = 4.0 and the denaturation of proteins via thermal processing. It was suggested that soy protein/soy polysaccharide nanogels are able to preserve folic acid against harsh storage and processing situations in the preparation of food and beverage formulations. Moreover, Feng et al. (2015) developed soy β-conglycinin − dextran core − shell nanogels via the Maillard reaction followed by a self-assembly procedure. Dextran is able to impart steric hindrance at the shell of the nanoparticles, thereby stabilizing the nanoparticles. Authors claimed that these nanoparticles have the application for the delivery of water-insoluble molecules owing to the hydrophobic attraction between β-conglycinins and bioactive compounds.

In another study, Sadeghi, Madadlou, and Yarmand (2014) fabricated nutraceutical-carrying whey protein nanoparticles by micro-emulsification-cold gelation mode. Aqueous extract of date palm pit was entrapped in a water-in-oil microemulsion containing heat-degraded whey proteins and glucono delta-lactone (GDL) in its aqueous state. As a result, at the isoelectric pH of whey proteins, the nanodroplets formed gel structure once the hydrolysis of GDL took place.

3. Factors affecting formation of globular protein hydrogels

Several techniques have been employed to fabricate hydrogels from biopolymers including cold and heat gelation strategies (Chen et al., 2006). From another perspective, food protein gelation procedures can be divided into three classes: physical (heat, high pressure), chemical (pH, ionic), and biochemical (enzymatic action) techniques (Norton, Espinosa, Watson, Spyropoulos, & Norton, 2015). Gelation plus the matrix and textural attributes of formulated food globular protein-based hydrogels can be regulated through different factors, such as type of ion, temperature, pH, ionic strength and extent of added ion and chemical bonding agents used for gelation (Nicolai et al., 2011).

3.1. Type and concentration of ions

The ultimate gel architecture depends on the added amount of ions added to the heat denatured protein solutions (Fig. 1); hydrogels with fine-stranded (consisted of cross-linked flexible strands) are formed as a