

Nanofood and Its Materials as Nutrient Delivery System (NDS)

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Incorporation of bioactive compounds such as vitamins, probiotics, bioactive peptides, and antioxidants into Nutrient Delivery System (NDS) for 'nanofood' provides simple way to develop novel functional foods that may have physiological benefits or reduce risks of diseases. As vital nutrient in nanofood, proteins possess unique functional properties including ability to form gels and emulsions, which allow them to be ideal nanofood materials for encapsulation of bioactive compounds. Based on protein physico-chemical properties, this review describes potential role of nanofood materials for development of NDS in hydrogel form, micro- or nano-particles. Applications of these nanofood materials to protect delivery-sensitive nutraceutical compounds are illustrated, and impacts of particle size on release properties are emphasized.

Key words: *Nanofood, nanofood-based materials, nutrient delivery system (NDS), hydrogel, nanoparticles*

Tomorrow we will design food by shaping molecules and atoms. Nanoscale biotech and nano-bio-info will have big impacts on the food and food-processing industries. The future belongs to new products, new processes with the goal to customize and personalize the products. Improving the safety and quality of food will be the first step.

Since Kim D. M. showed that a new type of food called firstly the name of 'nanofood',¹⁻⁶⁾ which means nanotechnology for food, and the encapsulated materials can be protected from moisture, heat or other extreme conditions, thus enhancing their stability and maintaining viability applications for this nanofood technique have increased in the food. Given how the word nanofood is often defined, one could say that a lot of our food is naturally made of nanoparticles. But industry needs guidelines on which new nanoparticles are safe to put in foods and food packaging. Current regulations address such substances by chemical makeup, not size - and size makes a difference in how ingredients behave inside the body. It may be unfortunate that the term nanofood is being used to described just about anything 1-100 nm in size, even natural materials ("Food proteins are globular particles between 10s to 100s nm in size") and more complex devices such as nanosensors, or even entire nanosystems. Perhaps it doesn't matter: we just need to come up with much more precise terminology for the huge range of things being created in that size range, many of which will be safe and beneficial food ingredients (and others, not).

On the one side, further breakthroughs in crop DNA

decoding and analyzing enable the industries to predict, control and improve the agricultural production. On the other side, with technology of manipulating the molecules and the atoms of food, the future food industry has a powerful method to design food with much more capability and precision, lower costs and sustainability.

Meanwhile, the combination of DNA and nanotechnology research generates the new nutrition delivery system, which brings the active agents more precisely and efficiently to the wanted parts of the human bodies and cells. Functional food will benefit firstly from the new technologies, followed by standard food, nutraceuticals and others.

Molecular technologies are disruptive technologies and change the conventional production faster than most scientists expect. It can make the products cheaper, the production more efficient, more safe and more sustainable using less water and chemicals. Producing less waste and using less energy. The impact for the food industry will be a change of 40 to 60 percent by 2015. The change is dramatic, the potentials are immense and the risks too. The main source of increasing the speed for these technologies within the next years is climate change, cost efficiency and population growth. But also new applications using food as drugs and nutrition.^{4,5)}

The emergence of dietary compounds with health benefits offers an excellent opportunity to improve public health. Known as nutraceuticals for nanofood, this category of compounds has received much attention in recent years from the scientific community, consumers, and nanofood manufacturers. The list of nutraceutical compounds (vitamins, probiotics, bioactive peptides, antioxidants and so on) is endless, and scientific evidences supporting the concept of health-promoting nanofood ingredients are growing

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steadily.^{1,2,4,7,9,10} Even though the nature of the involvement of nutraceutical substances in physiological functions is not yet fully understood, it is now well recognized that their addition to nanofood materials as simple means of decreasing disease risks holds much promise for benefits to society and that the scientific community should develop innovative functional nanofoods with the potential to produce physiological benefits or reduce the long-term risk of developing diseases.^{1,3,6,8,11,14}

The effectiveness of nutraceutical nanofood products in preventing diseases depends on preserving the bioavailability of the active ingredients. This represents a formidable challenge, given that only a small proportion of molecules remain available following oral administration, due to insufficient gastric residence time, low permeability, and/or solubility within the gut, as well as instability under conditions encountered during nanofood processing (temperature, oxygen, light) or in the gastro-intestinal (GI) tract (pH, enzymes, presence of other nutrients), all of which limit the activity and potential health benefits of nutraceutical molecules.^{1,4,7,15,20} The delivery of these molecules will therefore require nanofood formulators and manufacturers to provide protective mechanisms that maintain the active molecular form until the time of consumption and deliver this form to the physiological target within the organism. Polymer-based Nutrient Delivery Systems (NDS) that trap molecules of interest within networks have been developed extensively for the biomedical and pharmaceutical sectors to protect and transport bioactive compounds to target functions.^{3,7,19,21} In spite of the successful elaboration of many synthetic polymers as NDS, they cannot be used in nanofood applications that require compounds generally recognized as safe.

Nanofood biopolymers, specifically nanofood materials, are widely used generally recognized as safe. Numerous excellent articles highlight the functional properties of nanofood materials, including emulsification, gelation, foaming, and water-binding capacity as well as their applications as ingredients in the food industry.^{1,5,7,16,20,22,25} Among these functional properties, the gel-forming property is of special interest. Gels with diverse mechanical and nano-microstructural properties can be formed by controlling the assembly of nanofood molecular chains, thus offering the possibility of developing NDS biocompatible carriers for oral administration of sensitive nutraceuticals in a wide variety of nanofoods. Hydrogels are undoubtedly the most convenient and widely used matrix in nanofood applications. However, in the case of non-solid and semi-solid nanofoods, it is essential to decrease the matrix size to allow their incorporation without affecting the nanofood sensory qualities.^{4,7,20,21,26} More importantly, by decreasing the nanofood material size from micrometers to nanometers, new nanofood vehicles with improved delivery properties can be developed. To achieve this objective, two strategic approaches are currently used. The first one is the 'top down' approach, in which structures are generated by breaking up bulk nanofood materials; the second one is the 'bottom up' approach, which allows structures to be built

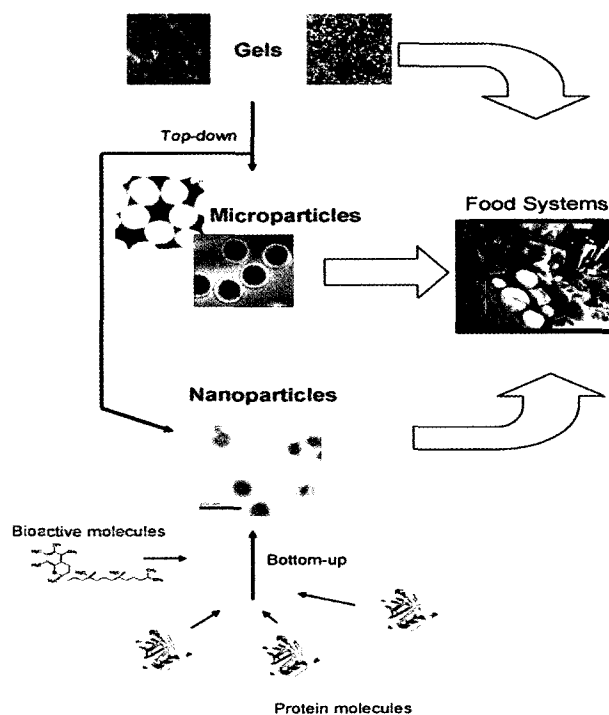


Fig. 1. Schematic representation of nanofood-based materials as nutrient delivery systems (NDS). (Source: Augustin, M.A. (2003) The role of microencapsulation in the development of functional dairy foods. *Australian J. Dairy Technol.* 58, 156-160.)

from nanofood molecules capable of self-assembly. Based on the knowledge of nanofood physicochemical properties, this review describes the potential role of nanofoods for the development of NDS (Fig. 1) and emphasizes the impact of particle size on their release properties.

Hydrogels for Nanofoods

Various strategies have been developed to protect and deliver bioactive molecules. One that has been the subject of numerous studies^{4,5,27,30} consists of trapping molecules of interest in hydrogels. A hydrogel is an infinite water-swollen network of hydrophilic polymers that can swell in water and hold a large amount of water while maintaining a network structure.³¹ A three-dimensional network is formed by cross-linking polymer chains through covalent bonds, hydrogen bonding, van der Waals interactions or physical entanglements.²⁸ Over the past decade, hydrogels have been studied extensively for biomedical and pharmaceutical applications due primarily to their ability to protect drugs from hostile environments and to deliver them in response to environmental stimuli such as pH and temperature.³¹ New synthetic methods have been used to prepare hydrogels for a wide range of drug delivery applications.^{29,31} Although successful as oral drug delivery systems, one of the inherent limitations of these hydrogels for nanofood applications is that they contain components that are not generally recognized as safe for consumption by healthy

individuals.

In the food industry, the use of nanofood materials to develop environment-sensitive hydrogels for nutraceutical delivery constitutes an interesting strategy. A fundamental advantage of this approach is that nutraceutical carrier gels can stabilize nanofood texture, which is a highly desirable characteristic in the manufacturing of nanofood products. Moreover, the presence of acidic (e.g. carboxylic) and basic (e.g. ammonium) groups in polypeptide chains, which either accept or release protons in response to changes in the pH of the medium (acidic in the stomach and neutral in the intestine), allows the release rate of molecules from hydrogels to be modulated by pH variations.³¹⁾

Gelation of nanofood materials, particularly globular proteins (e.g. egg white, soybean, and whey proteins), has attracted much attention over the years due to its physicochemical and industrial significances.^{22,23,32,33)} Gelation has traditionally been achieved through heat treatment. Thermal gels are produced by the unfolding of polypeptide chains with concomitant exposure of initially buried hydrophobic amino acid residues and subsequent self-aggregation of nano-sized protein molecules into a three-dimensional network that entraps water by capillary forces.³⁴⁾ Forces involved in the aggregation process include hydrophobic effects, van der Waals, hydrogen bonding, and covalent interactions.³³⁾ Depending on the preparation technique, gels can exhibit different nano-microstructural properties, which are strongly related to the aggregation of nano-sized molecular structure.³⁵⁾ However, the heat needed to produce these gels limits their application to formulations that do not contain heat-sensitive ingredients.

It has been shown that cold-induced gelation of globular whey proteins³⁶⁾ and, more recently, soybean proteins³⁷⁾ can be achieved by adding Ca^{2+} ions to a preheated protein suspension. This method requires a heating step, during which proteins are denatured and polymerized into soluble aggregates, followed by a cooling step and subsequent salt addition, which results in the formation of a network via Ca^{2+} -mediated interactions of soluble aggregates. A mechanism of cross-linking carboxyl groups with Ca^{2+} has been suggested for the gelation of pre-denatured whey proteins at ambient temperature³⁸⁾ with ionic strength playing a major role.³⁹⁾ The formation of cold-set gels opens interesting opportunities for nanofood materials as carriers of sensitive nutraceutical compounds and in the development of innovative functional nanofood ingredients. One advantage of this approach is exposure of multiple functional groups within the protein upon denaturing, which could be exploited to create different interactions between nutraceutical compounds and polypeptide chains such as hydrogen-bonding, hydrophobic interactions, and electrostatic interactions, which may, in turn, be applied to target nutraceutical delivery.

Recently, cold-set gels were obtained by adding a ferrous salt to solutions of denatured β -lactoglobulin (the major whey protein), addressing a mineral deficiency that concerns a large

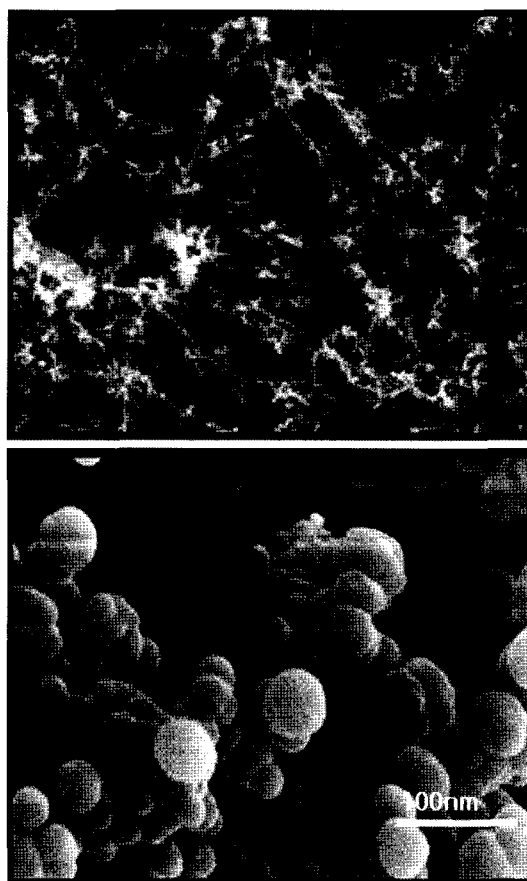


Fig. 2. Scanning electron micrographs of Fe-induced cold gels of β -lactoglobulin: filamentous gels (top) and particulate gels (bottom). (Source: Remondetto, G. E. and Subirade, M. (2003) Molecular mechanisms of Fe^{2+} -induced β -lactoglobulin cold gelation: An interactions story. *Biopolymers* 69, 461-469.)

number of people all over the world.⁴⁰⁾ Gel mechanical properties and nano-microstructural analyses showed that two types of gels could thus be obtained, depending on iron/protein ratio; at a lower iron concentration, 'filamentous' gels composed of more or less flexible linear strands making up a regular network characterized by elastic behavior and high resistance to rupture are formed, while at a higher iron concentration, 'particulate' gels composed of large and almost spherical aggregates characterized by less elastic behavior and lower rupture resistance are obtained (Fig. 2). These different nano-microstructural properties are strongly linked to aggregate molecular structure, as revealed by Fourier transform infrared spectroscopy and rheological data.³⁹⁾ The filamentous form is created by linear aggregation of structural units maintained by hydrophobic interactions, whereas the aggregate form is produced by random aggregation of structural units essentially controlled by van der Waals forces. Release studies showed that these nano-microstructures would have a major impact on iron delivery, due to their different sensitivities to environmental conditions such as pH and digestive enzymes and that filamentous gels show promise as matrices for transporting iron and promoting its

absorption.⁴¹⁾ Modulation of gel nano-microstructure and functional properties by cold gelation should allow tailoring of water-soluble delivery devices for nutraceutical and functional nanofood system development.

During the past few years, there has been growing interest in composite systems such as emulsion gels due to their practical applications in nanofood formulations.^{4,5,16)} Their flexibility and amphiphilic nature allow globular proteins such as whey proteins to be rapidly adsorb into the emulsion interface, where they self-aggregate and form continuous and homogeneous membranes around oil droplets through intermolecular β -sheet interactions.⁴²⁾ By coating oil droplets with charged layers, protein films provide an electrostatic barrier against flocculation and coalescence.^{12,14,17,43)}

Numerous works have demonstrated the ability of oil-in-water emulsions stabilized by whey protein isolates (WPI) to form gels by heat treatment, extending the possibilities for creating nanofoods with new and improved organoleptic properties.^{44,47)} Recently, it has been shown that β -lactoglobulin emulsions can be gelled at room temperature and that gel nano-microstructure can be modulated by varying the oil and calcium concentrations.⁴⁸⁾ Studies are presently underway in our laboratory on the suitability of such matrices as carriers for heat-sensitive and fat-soluble antioxidants. In particular, we have studied the influence of cold-set emulsion gel nano-microstructure on the controlled release of α -tocopherol, chosen as a bioactive compound model, under simulated GI conditions.⁴⁸⁾ Leung Sok Line *et al.* have thus demonstrated that cold-set β -lactoglobulin emulsion gels protect α -tocopherol under GI conditions and that α -tocopherol release is correlated with matrix degradation for both types of emulsion gels, which indicate that nano molecule delivery is regulated by gel biodegradation. Furthermore, degradation of these gels during the gastric step was only 20%, indicating the matrices are gastro-resistant. This point is thought to be related to the interaction of the dispersed oil droplets with the gel matrix, which strengthens the three-dimensional network.⁴⁸⁾ Even though the work is still in the early stage of development, the approach is promising.

Gelation of globular proteins has been the subject of numerous reviews, indicating both its scientific and commercial relevance.⁴⁹⁾ The ability of hydrogels made from such proteins to entrap both fat-soluble and water-soluble nanofood components of high health impact and to maintain the active forms of these components should contribute to the development of innovative functional solid nanofoods. Nevertheless, understanding the role of nutraceutical ingredients in gel molecular formation and studying their interactions within the protein network remain essential to anticipating their release profiles.

Nano- and Micro-particles for Nanofoods

In addition to hydrogel, polymer-based particulate systems have attracted considerable attention as active molecule

delivery devices.^{5,9,12,14,43,50,51)} Micro (sub-micro) particles are defined generally as particles less than about 1000 μm in size, consisting of solid, liquid or gaseous materials encapsulated within their polymeric matrix, adsorbed or conjugated onto the surface.^{1,3,4,7,16,52,53)} Used in the past to mask the unpleasant taste of certain ingredients or simply to convert liquids into solids, these particles are being increasingly used as delivery vehicles for nutraceutical compounds in foods.^{3,4,7,20,54)} A major advantage of their use is the ability to control the release rate of the incorporated materials and deliver them to the right place at the right time.⁵⁵⁾ This can be achieved by formulation to obtain the desired structure or precisely controlling the size. Particles may thus consist of a core composed of one to several types of ingredients surrounded by a wall or barrier of uniform or non-uniform thickness, either single-layered or multi-layered.⁵⁶⁾ Matrix degradation and, consequently, the release of contents can thus be regulated to occur at different times, for example, to mimic the administration schedules of different nutraceutical compounds. Recent technologies also provide a variety of possibilities to prepare particles of different sizes, in order to set polymer matrix degradation rate as well as active compound release rate, uptake, and distribution in the body.^{6,43,57-60)} Larger particles generally release encapsulated compounds more slowly and over longer time periods, while particle size reduction introduces several bio-adhesive improvement factors, including increased adhesive force and prolonged GI transit time, leading to a higher drug bioavailability.

In addition to being a vital nano-microstructures in nanofood, protein possesses many highly useful functional properties, as previously mentioned. These properties make proteins very good coating materials for the encapsulation of bioactive compounds. During the past two decades, interest in developing protein nano-micro particles as delivery systems has grown, and various kinds of animal proteins have been investigated, including gelatin,^{61,62)} collagen,^{14,43,63-65)} casein,^{66,67)} albumin,⁶⁸⁻⁷⁰⁾ and whey protein,⁷¹⁻⁷³⁾ in addition to plant proteins such as soy glycinin,⁷⁴⁾ and wheat gliadin.⁷⁵⁾ Multiple component matrices such as protein-polysaccharide^{76,77)} and protein-synthetic polymer⁷⁸⁾ particles have also been elaborated.

A wide variety of processes have been developed to prepare protein-based nano-micro particles. The most common techniques are spray-drying,^{1,4,5,7,16,17,79)} emulsifying-crosslinking,^{1,17,80)} and coacervation.⁸¹⁾ However, these techniques require heating or organic agents in at least one of the production steps, leading to destruction of some sensitive encapsulated nutrients as well as toxicity problems associated with residual organic agents.^{64,82)} The newly developed cold-gelation method described above provides an alternative way to develop protein nano-micro particles in the nanofood industry. No organic solvents are required for this method, and encapsulation is achieved under mild conditions, thereby minimizing destruction of sensitive nutraceutical compounds. More importantly, globular proteins such as whey proteins have the ability to denature, dissociate, and aggregate under different conditions of pH, ionic strength,

and temperature to form particles with sizes ranging from 40 nm to 2 μ m. These properties can be judiciously exploited to formulate active-nano molecule-loaded particles of specific size.

In the same way that the prefix 'micro' came into widespread use during the 1980s, the prefix 'nano' has been co-opted to describe the current generation of dimension-reducing. Technology for nanofood originally refers to the development of functional nanofood materials at a length scale of less than 100 nm.^{1,3,5,4,7} Although the applications of nano-scale particles in therapeutic systems have been well documented, and various systems have been designed for intelligent, modulated, and selective delivery of drugs to specific areas in the body in order to maximize drug action and minimize side effects, nanotechniques are relatively new in the nanofood industry. Due to their sub-cellular size, nanoparticles offer promising means of improving the bioavailability of nutraceutical compounds, especially poorly soluble substances such as functional lipids (e.g. carotenoids, phytosterols, ω -3 fatty acids), natural antioxidants, and numerous other compounds that are widely used as active ingredients in various food products. They can dramatically prolong compound residence time in the GI tract by decreasing the influence of intestinal clearance mechanisms and increasing the surface available to interact with the biological support.^{30,78,83} They can also penetrate deeply into tissues through fine capillaries, cross the epithelial lining fenestration (e.g. in the liver), and are generally taken up efficiently by cells,⁵⁵ thus allowing efficient delivery of active compounds to target sites in the body.

Among the various natural or synthetic polymer-based nanoparticulate systems potentially available to the nanofood industry, protein-based nanoparticles are particularly interesting, because they are relatively easy to prepare and their size distribution can be monitored.^{4,5,84} Various modifications allow them to form complexes with polysaccharides, lipids or other biopolymers, thanks to the consistent primary structure of proteins, and a wide variety of nutrients can be incorporated by relatively non-specific means. Protein-based nanoparticles can also conjugate nutrients via primary amino groups or sulfhydryl groups.^{19-21,85}

In order to improve nutraceutical compound bioavailability, the nanofood industry is currently attempting to increase the circulation time of conventional nano carriers in the GI tract, notably by surface-coating with a protein, which can profoundly modify the adhesive properties of nano carriers and their behavior in the GI tract, because some proteins are able to bind specifically to sugar residue-bearing sites located at the surface of epithelial cells.⁸⁶ Research has revealed that covalent binding of lectin to PVM/MA carriers decreases their terminal elimination rate in the GI mucosa, while BSA-coated nanoparticles display a high capacity to adhere especially to the stomach mucosa.⁷⁸ Protein-enriched surfaces can provide additional effects by mediating particle uptake by specific target-cell populations.⁸⁷

Protein coating of nanoparticles also provides additional protection of sensitive nutraceutical compounds in the GI tract. β -Lactoglobulin (β lg)-coated chitosan nanoparticles (around 100 nm) have been recently developed by our group via cold ionic gelation of chitosan and β lg mixtures with sodium tripolyphosphate.^{2,76} The coating ability of β lg, studied using native globular and heat-denatured forms, was found to be highly sensitive to formulation pH. Protein adsorption appears to be due to electrostatic, hydrophobic, and hydrogen-bonding interactions between β lg and chitosan. Release profiles for these nanoparticles were investigated in a simulated GI tract, using brilliant blue as the model molecule. Native β lg-coated nanoparticles exhibited the desirable property of retarding molecule release into the gastric environment. A pepsin degradation assay revealed that the native β lg coating resists acid and pepsin, unlike denatured β lg and denatured β lg cross-linked with Ca^{2+} . This desirable property is attributable to the hydrophobic amino acids of native β lg being hidden inside its calyx-like globular structure, given that pepsin preferentially attacks peptide bonds involving hydrophobic aromatic amino acids.⁸⁸ Under simulated intestinal conditions, the β lg coatings were degraded by pancreatin. Due to its muco-adhesive nature, the chitosan core should then adhere to the intestinal wall to facilitate the absorption of the nutraceutical compound. This study suggests that β lg, especially in its native configuration, is an interesting candidate for coating nanoparticles to protect carried nutrients from exposure to gastric fluids.

Recently acquired knowledge of whey protein physical chemistry has allowed us to build protein nanoparticles using the bottom-up approach. A monodisperse suspension of 40 nm whey protein nanospheres was obtained by modulating parameters affecting the thermal aggregation process (Fig. 3). Aggregates of submicron size can be obtained at relatively low calcium and protein concentrations and at a temperature around 55°C, which is well below the denaturation temperature of β -lactoglobulin (about 74°C). Dialyzed nanospheres had a zeta potential of -25 mV, this relatively high surface charge keeping the dispersion stable at 4°C for at least two months. Because covalent bonding, hydrogen bonding, hydrophobic interactions, and van der Waals forces are all involved in the formation of aggregated structures,²³ their respective contributions to the formation of gels was monitored macroscopically using turbidity measurements at 480 nm in the absence and presence of CaCl_2 (electrostatic bonding) and destabilizing agents (urea to prevent hydrogen bonding, SDS to block hydrophobic interactions, and 2-mercaptoethanol to prevent disulfide bridge formation). Based on observations thus made and on known mechanisms of β lg aggregation involving calcium or thiol/disulfide exchange,⁸⁹ the most probable mechanism leading to the formation of these nanoaggregates involves electrostatic interactions between protein and calcium, hydrophobic interactions between proteins, and the consolidation of the structure by intermolecular disulfide bonds.

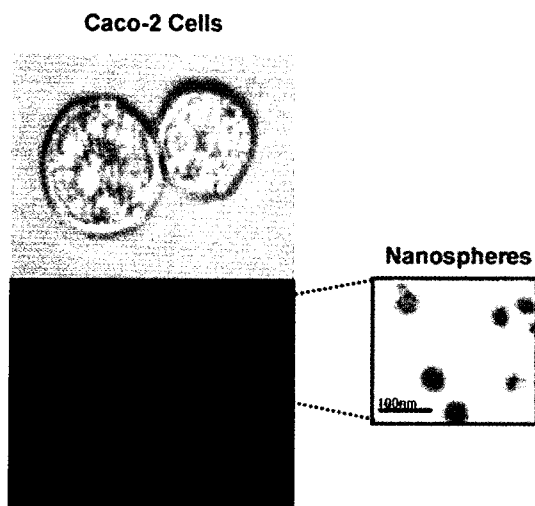


Fig. 3. Images of Caco-2 cells after incubation alone (top) and in the presence of FITC-labeled nanospheres (bottom). (Source: Clark, A. H. and Ross-Murphy, S. B., (1987) Structural and mechanical properties of biopolymer gels. *Advan. in Polymer Sci.* 83, 57-192.)

The potential of these nanospheres as carriers for oral administration of nutraceutical agents was studied *in vitro* by monitoring the interaction between fluorochrome-labeled nanospheres and cells of intestinal origin (Caco-2 cells). Fig 3 shows Caco-2 cells incubated without (top) and with (bottom) FITC-labeled nanospheres. FITC-labeled nanospheres can be clearly seen on the top half of the cells (i.e. area exposed) and are absent from the bottom half (i.e. area facing the flask). Interestingly, the nanospheres are not only able to adhere to the cell surface but are also visible within the cells. These experiments suggest that whey protein nanoparticles could be internalized by cells and degraded therein to release the nutraceutical compounds, significantly improving nutraceutical compound bioavailability while avoiding undesired toxic side effects of the free compounds.

As demonstrated by the above examples, new functions such as improved solubility, targetability, and adhesion to tissues arise from nanosizing. Nevertheless, the potential of nanofood science cannot be fully appreciated yet due to insufficient knowledge of the physicochemical aspects of nanoparticle systems organization and of the interactions between bioactive molecules and their carrier matrices. Further studies are needed to turn the concept of nanosizing into a realistic practical technique for the next generation of NDS for nanofood.

Future Trends

Nanofood and its materials show great promise for developing and engineering a range of new NDS matrices with the potential to incorporate nutraceutical compounds and provide controlled release via the oral route. Clear advantages of nanofood materials include their high nutritional value,

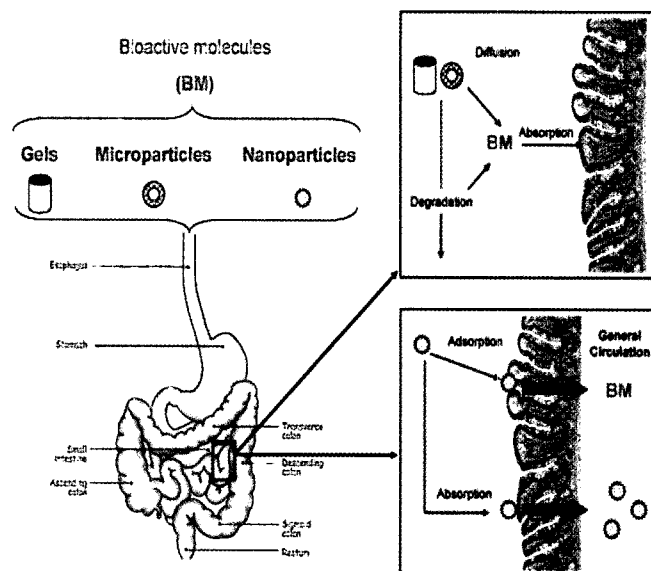


Fig. 4. Schematic representation of different absorption mechanisms of bioactive nanofood molecules. (Source: Chen, L. and Subirade, M. (2005) Chitosan/ β -lactoglobulin core-shell nanoparticles as nutraceutical carriers. *Biomaterials* 26, 6041-6953.)

abundant renewable sources, and acceptability as naturally occurring nutrient components degradable by digestive enzymes. As discussed in this paper, nanofood and their materials can be used to prepare a wide range of food materials and multicomponent materials in the form of hydrogel, micro- or nanoparticles, all of which can be tailored for specific applications in the development of innovative functional nanofood products. The ability to control the particle size of nanofood materials is of primary importance not only for determining nanofood product properties such as taste, aroma, texture, and appearance, but also for determining the release rates of the carried bioactive compounds and ultimately how much is absorbed into the body, and hence the overall efficacy of the compounds. In the case of hydrogel and nano- and micro-particles, nutraceutical compounds have to be released from the matrix to allow absorption by the intestinal wall, while nanoparticles may improve absorption of the nutraceutical either by adsorbing to the GI walls to prolong residence time or by direct uptake by the intestinal epithelium (Fig. 4).

In addition, owing to multiple functional groups in the primary sequences of polypeptides and the resulting diversity of chain folding structures, food proteins can be exploited to create different interactions with nutraceutical compounds and subsequently form three-dimensional networks to incorporate and protect these compounds in a matrix and deliver them to the site of action in the active form. It can be foreseen that, with improvements in manufacturing technologies, new strategies for stabilization of fragile nutraceuticals, and development of novel approaches to site-specific carrier targeting, nanofood-based materials will play an important

role in increasing the efficacy of functional nanofood over the next decade. However, at the present stage, greater fundamental understanding of nanofood-nanofood and nanofood-nutraceutical interactions at the molecular level and their impact on functional properties of nanofood is required to ensure design of ideal nutraceutical carriers for use in the nanofood industry.

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