

# Nanotechnology Applications in Functional Foods; Opportunities and Challenges

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**ABSTRACT:** Increasing knowledge on the link between diet and human health has generated a lot of interest in the development of functional foods. However, several challenges, including discovering of beneficial compounds, establishing optimal intake levels, and developing adequate food delivering matrix and product formulations, need to be addressed. A number of new processes and materials derived from nanotechnology have the potential to provide new solutions in many of these fronts. Nanotechnology is concerned with the manipulation of materials at the atomic and molecular scales to create structures that are less than 100 nm in size in one dimension. By carefully choosing the molecular components, it seems possible to design particles with different surface properties. Several food-based nanodelivery vehicles, such as protein-polysaccharide coacervates, multiple emulsions, liposomes and cochleates have been developed on a laboratory scale, but there have been very limited applications in real food systems. There are also public concerns about potential negative effects of nanotechnology-based delivery systems on human health. This paper provides an overview of the new opportunities and challenges for nanotechnology-based systems in future functional food development.

**Keywords:** functional foods, nanotechnology, delivery systems, nanoencapsulation, bioactive compounds

## FUNCTIONAL FOODS AND NANOTECHNOLOGY

Since the end of the 20th century, there has been a growing realization of the pivotal link between diet and human health. This has led to the development of a new category of foods, the so-called functional foods. Functional food is simply a convenient way to describe foods, or their components, that may provide health benefits beyond nutrition. In other words, functional foods contain a variety of components, nutrients and non-nutrients that affect a range of body functions that are relevant to a state of well-being and health and/or reduce the risk of a disease (1-6).

From a practical viewpoint, a functional food can be a natural, whole food that contains sufficient quantities of beneficial components. Many, if not most, fruits, vegetables, grains, and fish contain several natural components that deliver benefits beyond basic nutrition, such as lycopene in tomatoes, omega-3 fatty acids in fish, and soluble fibre in oats. The functional components can be enhanced through special growing conditions, or through breeding techniques, e.g.  $\beta$ -carotene-rich rice, vitamin-enriched broccoli, and soybeans. Meat, poultry, fish, and

eggs can have their composition altered by the animal's diet, e.g. increased level of conjugated linoleic acid or omega-3 in meat and milk products. The delivery of truly unique health benefits will probably require genetic engineering, which is not yet accepted by consumers.

Other foods may be specially formulated with specific components to provide health benefits. Examples are probiotic bacteria added to yoghurts, plant-sterol-enriched margarines, flour with added folic acid, and omega-3-enriched bread. A food from which a component has been removed so that the food has fewer adverse effects on health (e.g. reduction in saturated fatty acids) can also be considered to be a functional food. Moreover, a food can be regarded as functional if the nature of one or more components has been modified through processing to improve health (e.g. the hydrolysis of protein by enzymes, suppression of the food matrix through heating/shearing to release bioactive compounds).

The functional foods segment of the food industry is estimated to be worth about 168 billion dollars and is growing at about 9% per annum (6,7). The key drivers that have given rise to this growth include a greater availability of scientific information regarding the link between diet and health, an aging population with great-

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er prevalence of age-related diseases, particularly in Western countries, and an increasing rate of metabolic disorders (heart disease, obesity, diabetes, and arthritis). To meet future demand for functional foods, the food industry must address several critical challenges, including discovering the potential bioactivity of beneficial compounds, establishing optimal intake levels, and developing adequate food delivery matrices and product formulations. The development of functional foods also faces many regulatory challenges (1,2).

There is a large body of scientific evidence showing that eating foods with functional benefits on a regular basis as part of a varied diet can help to reduce the risk of, or manage, a number of health concerns, including cancer, cardiovascular disease, and gut health (1). Table 1 shows some examples of functional foods, their components and their potential health benefits for human health.

Food components with health benefits are often referred to as 'bioactive compounds' and these compounds typically occur in small quantities in certain foods. Many bioactive compounds have been intensively studied to evaluate their effects on human health, in particular their protective effects against hypertension, cardiovascular disease and cancer (1,6). For example, lycopene in tomatoes and other fruits is thought to protect against prostate and other cancers. Omega-3 fatty acids from fish have cardioprotective effects and are thought to protect against immune response disorders (e.g. rheuma-

toid arthritis, diabetes, and inflammatory bowel disease) and mental disorders.

The intake of sufficient quantities of many of these compounds by consuming large amounts of a variety of fruits, vegetables, whole grains, legumes, oils, and nuts that are rich in bioactive compounds is not always practical. Consequently, there is great interest within the food industry in delivering required quantities of bioactive compounds to the consumer by 'fortifying' everyday foods (such as milk, bread, and beverages) with bioactive compounds, isolated from natural food sources. However, many technological problems occur when food products are fortified with bioactive compounds, due mainly to the many reactions of these compounds with other food components during processing, storage, and transport. In some cases, the bioactive compound can be poorly soluble in aqueous solution. It may be sensitive to oxygen, light, temperature, and shear, which may lead to adverse changes in colour, flavour, and odour. In other cases, the bioactive compound may be bound tightly within the food matrix so that it is not readily released in the limited period during which it is within the gastrointestinal tract.

Table 1 and 2 provide a list of several useful bioactive compounds and the problems associated with their incorporation into foods. For example, lipophilic bioactive compounds, such as omega-3 fatty acids, carotenoids, polyphenols, and phytosterols, differ widely in their molecular and physicochemical properties.

**Table 1.** Examples of bioactive compounds in foods and their potential health benefits (based on information presented in 1, 3, 5, and 6)

Bioactive components	Source	Potential health benefits
Lutein	Green vegetables	Contributes to maintenance of healthy vision
Insoluble fibre	Wheat or oat bran	May reduce risk of colon cancer
Lactobacillus	Yoghurt or other fermented dairy products	May improve gastrointestinal health
Soy protein	Soy-based products	May reduce risk of cardiovascular diseases
Omega-3 fatty acids	Salmon, tuna, and fish/marine oils	May reduce risk of cardiovascular diseases and improve brain health, visual functions
Lycopene	Tomato or red vegetables	May reduce risk of prostate cancer
Phytosterols	All plants	May reduce risk of cardiovascular diseases, cholesterol reduction effects

**Table 2.** Bioactive compounds for which delivery systems would improve their incorporation into foods (based on information presented in 1, 9, and 10)

Bioactive components	Issues surrounding use
Carotenoids (e.g. lycopene)	Insoluble in water, susceptible to light, oxygen, and auto-oxidation; solid at food storage and body temperature
Omega-3 fatty acids	Insoluble in water, highly susceptible to oxidation, affect flavour and taste of foods
Phytosterols	Hydrophobic in nature, very high melting point, form insoluble crystals
Flavonoids (e.g. catechins)	Strong bitter taste, low solubility
Minerals (e.g. iron)	React with other food components, catalyst for oxidation of oils, cause protein aggregation, affect taste, and discolor food

It is often advantageous to deliver these compounds in an aqueous medium because this increases their palatability, acceptability and bioactivity. As these compounds are not readily dispersible in water and are generally susceptible to oxidation, some kind of delivery system is required when they are to be incorporated into a beverage or a high moisture food. The incorporation of bioactive compounds into foods to address sensory and stability problems without compromising health benefits remains a major research challenge.

Nanoscience and nanotechnology have the potential to provide new solutions in the development of functional foods, in particular the inclusion of bioactive compounds without affecting the sensory perception of the consumer and improving the uptake of certain components. Scientifically, nanoscience is defined as the study of phenomena and the manipulation of materials at the atomic, molecular, and macromolecular scales, where the properties differ from those at a larger scale. Nanotechnology is defined as the design, production, and application of structures, devices, and systems through control of the size and shape of the material at the nanometre scale. These terms are usually applied to structures less than 100 nm in size in one dimension.

Recently, there has been considerable interest in developing high-performance delivery vehicles for the encapsulation and protection of biologically active substances of food origin, using nanotechnology approaches. Many nutrients, bioactive ingredients and phytochemicals can be loaded into biocompatible and biodegradable nanoparticles, which will improve their aqueous solubility, stability, bioavailability, and circulation time in the body. Compared with micrometre-sized systems produced by traditional microencapsulation techniques, nanometre-sized delivery systems provide more surface area and have the potential to improve solubility, enhance bioavailability, improve controlled release, and enable greater precision targeting of entrapped compounds. By carefully choosing the molecular components, it seems to be possible to design nanoparticles with different surface properties and to deliver active compounds directly to appropriate sites. However, much of this work is at a laboratory scale, with some requiring fundamental research to fully define the relevant parameters controlling the system. In many respects, food researchers are adapting many of the delivery systems developed by the pharmaceutical industry, where nanotechnology-enabled drug delivery and diagnostic platforms have been developed to overcome problems associated with protection and selective delivery.

Some of the emerging nano-encapsulation technologies that may be suitable for functional foods are discussed in the following section. The traditional microencapsulation technologies, including spray drying or spray cooling,

extrusion, fluidized-bed coating, and inclusion complexation, can also be used to incorporate health-promoting compounds into foods, but the particle/capsule sizes tend to be very large (of the order of several microns). These systems are not considered in this review.

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## NANO-ENCAPSULATION SYSTEMS FOR BIOACTIVE COMPOUNDS

There are several kinds of encapsulation systems that can be assembled from food-grade components. Encapsulation systems in which particle diameters (at least in one dimension) are below 100 nm can be classified as nano-encapsulation systems; these systems are of great interest as they not only provide stability to the entrapped bioactive compounds but also have the potential to improve the absorption and bioavailability of the entrapped material (8,9).

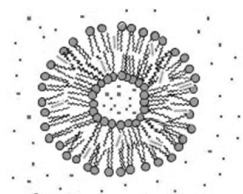
These nano-encapsulation systems must serve as a means of delivering and protecting the bioactive compound in a physical form that can be easily incorporated into foods or beverages. The system must be compatible with the food matrix and it must not adversely affect the appearance, taste, flavour, texture, and shelf life of the product. A further consideration is that the materials used in the encapsulation system must be food grade, generally recognized as safe or listed by the appropriate regulatory authority. A number of nano-encapsulation systems have been developed, based on both natural and synthetic materials (Table 3).

The most promising nanostructured systems are discussed in the following sections, and include liposomes, nanoemulsions, microemulsions, solid lipid nanoparticles (SLNs), and polymeric nanoparticles. The dispersibility, stability and bioavailability of many bioactive compounds can be improved by encapsulation into these nanocarrier particles (10). However, there is still a major gap in the regulatory framework, and most countries are still relying on existing legislation to regulate nanomaterials. Improving the actual legislation framework is a crucial step to prevent consumers' misinformation regarding nanotechnology applied to foods. While legislation is still being adapted, other actions may be taken to improve consumers' confidence in foods integrating nanotechnology based ingredients, such as the guarantee of use of food-grade materials for nanosystems production. Another important aspect is the cost: scaling-up of nanoencapsulation systems is still very expensive.

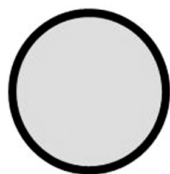
Liposomes are spherical structures, with diameters ranging from 20 nm to several microns, formed through the self-assembly of amphiphilic molecules, usually phospholipids. They consist of one or more phospholipid bilayers enclosing an aqueous core (Fig. 1A). The nano-

**Table 3.** Nano-structured systems for delivery of nutrients (based on information presented in 9, 10, 11, 19, 24, and 39)

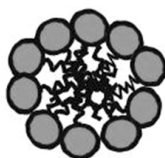
Delivery systems	Descriptions	Potential applications
Nano-emulsions	Stable dispersion, droplet size on order of 100 nm, uses different lipids and emulsifiers	Delivery and stabilization of lipophilic compounds
Solid lipid nanoparticles	Emulsified systems made with crystalline or semi-crystalline lipids, stabilized by an emulsifier coating	Delivery and stabilization of hydrophobic materials
Liposomes	Vesicles formed with phospholipid bi-layer with aqueous interior. Single layer of multi-layers	Delivery of both hydrophilic and hydrophobic compounds
Microemulsions	Stable mixtures of water, oil and surfactants. Size range 5~100 nm	Solubilisation and delivery of hydrophobic and hydrophilic compounds
Casein micelles	Self-assembled nanostructures in milk size range 20~300 nm	Delivery of minerals, proteins and vitamins
Protein nanoparticles	Hydrogels and nanoparticles formed by controlled aggregation of proteins	Delivery of various hydrophilic compounds, provide nanoscale structure to food to affect texture and mouthfeel
Protein fibrils	Some proteins can form fibrils and nanotubes under certain processing conditions	Delivery of various hydrophilic compounds, affect texture of foods
Protein-polysaccharide nanoconjugates	Covalent conjugation or electrostatic complexation between proteins and polysaccharides	Delivery of both hydrophobic and hydrophilic compounds



A. Liposomes



B. Nanoemulsions



C. Microemulsions



D. Solid-lipid nanoparticles



E. Biopolymeric nanoparticles

**Fig. 1.** Schematic presentation of various types of nano-encapsulation systems.

metric version of a liposome is usually referred to as a nanoliposome and has similar structural, physical and thermodynamic properties to those of a liposome. Because of the smaller size of nanoliposomes, they have a larger interfacial surface area for contact with biological tissues, possibly providing greater bioavailability of encapsulated compounds (11,12). During the formation process, hydrophobic bioactive can be incorporated in the lipid bilayers and the release of the entrapped material can be through membrane disruption caused by changes in pH or temperature (13). Release of the entrapped material can be either a gradual process, resulting from diffusion through the membranes, or almost instantaneous, following membrane disruption caused by changes in pH or temperature. Several studies have shown that liposomes can be used to encapsulate vitamins (14), antioxidants (15), proteins, peptides (16), minerals (17), and fatty acids (18). Various reviews and book chapters on the applications of liposomes in pharmaceutical and food products have been published in recent years (11,12).

Despite many potential applications for liposomes in the development of functional foods, the high cost of the phospholipids, combined with problems finding a large-scale, continuous production method suitable for use in the food industry, has limited the use of liposomes in

food systems. Moreover, further information is needed to determine the bioavailability and efficacy of liposomes and the encapsulated material once they reach the intestinal environment.

### Nanoemulsions

A nanoemulsion is defined as an intimate dispersion of at least one immiscible liquid and/or liquid crystal in another in the form of discrete droplets with a mean diameter generally ranging from 20 to 200 nm (19,20) (Fig. 1B). Because of the nanometre-scale size range of the droplets, nanoemulsions are optically transparent or translucent, but are thermodynamically unstable systems. There are basically two types of nano-emulsion: oil-in-water (O/W) type and water-in-oil type. Nanoemulsions are only metastable, i.e. they are non-equilibrium systems with a tendency to separate into the constituent phases over a period of time. Generally, compared with macroemulsions, nano-emulsions may possess a higher kinetic stability against creaming, flocculation, and/or coalescence, due mainly to the characteristic narrow droplet size distribution, low viscosity, and Brownian motion between the droplets dominating over their low gravitational separation force (19-22). Although there is potential interest for application of nanoemulsions in personal and health care products (19,22), there has been very limited prog-

ress in the area of the application of nano-emulsions in the food sector. The main limitations to developing food nanoemulsions are the high cost of production and finding suitable food-grade surfactants; most of the surfactants used for making nanoemulsions in other industrial applications are not food grade.

### Microemulsions

Microemulsions are thermodynamically stable mixtures of water, oil and one or more amphiphilic molecules, which assemble spontaneously into nanometer-scale droplets (Fig. 1C). Suitable food grade surfactants include ethoxylated mono- and diacylglycerides and phospholipids (23). Ethanol may be required as a co-surfactant to solubilize long chain triglycerides (24). O/W microemulsions are an efficient vehicle for incorporating lipophilic compounds into aqueous systems, e.g. lycopene and lutein (25,26). As a result, microemulsions have found numerous applications over a wide range of areas, including pharmaceuticals, cosmetics and as models for biological membranes. However, the application of microemulsions in foods is limited by the type of surfactants that are used to facilitate their formation. Many surfactants are not permissible in foods and many more may be added at only very low levels. Moreover, the solubilisation of the long-chain triglycerides that are important for food applications is more difficult to achieve than the solubilisation of short- or medium-chain triglycerides. Short-chain alcohols are often utilised as co-surfactants, but are not suitable for use in foods. In addition, many microemulsion systems cannot be diluted, i.e. the microemulsion system breaks down at increased water concentration. This restricts the application of some microemulsions in food systems (23).

Few studies have reported food-grade microemulsions that use medium-chain triglycerides or essential oils as the oil phase. Flanagan et al. (24) used food-grade ethoxylated mono- and diglycerides (EMD), food-grade phospholipids and non-food-grade polyoxyethylene oleyl ether (POE), for microemulsion formation using soybean oil. They showed that it is possible to formulate microemulsions at low EMD and POE surfactant concentrations, and suggest that these microemulsion systems may potentially be used for the encapsulation of oil-soluble bioactives, e.g.  $\alpha$ -tocopherol, in food systems.

### SLNs

SLNs with diameter 50~1,000 nm are made from lipids that solidify at room temperature to form a crystalline or amorphous undercooled matrix in which the bioactive compound is incorporated (Fig. 1D). The particle is stabilized by a surfactant layer, which typically consists of a mixture of surfactants (27). To prepare SLNs, the bioactive compound is first solubilized in melted lipid, form-

ing a 'melt', and nanoparticles are prepared from the melt in a number of different ways (27-29). The most common approach involves dispersion of the melt in a hot aqueous solution of surfactant followed by homogenization at temperatures above the melting point of the lipid phase. The mixture is then cooled so that some or all of the lipids are crystallized. Another approach involves cooling the melt to low temperatures and then grinding to microparticles. These particles are dispersed in cold surfactant solution and homogenized, which produces cavitation forces that are sufficient to break microparticles into nanoparticles. SLNs can be manufactured from nano-emulsions or microemulsions to yield particles that are below 100~200 nm and with different properties. It is possible to create a variety of different internal matrix structures by controlling the crystallization of the lipids: a homogeneous matrix, a core-shell with the outer shell enriched with bioactive compound or a core-shell with the inner core enriched with bioactive (27-29).

SLNs have been used for the delivery of drugs, but their use in foods has been very limited. They have the potential to provide greater stability to labile hydrophobic compounds by trapping them in a structured solid matrix, and to provide controlled release of these compounds by designing systems with different melting characteristics. SLNs have been used to deliver and protect fat-soluble vitamins (A, D, and K) (30,31). A major drawback of SLNs is the possible loss of the bioactivity of heat-labile compounds during the heating step (to melt the lipid) of their preparation. The impact on the *in vivo* digestibility of the crystalline lipids and the consequent release of bioactive compounds also need to be investigated.

### Protein nanoparticles

The gel-forming properties of proteins are commonly exploited in developing nanoparticles for the encapsulation and delivery of bioactive molecules. The formation of protein gels involves the assembly of protein molecules, triggered by acidification, shearing, addition of ions, heat treatments, and high-pressure treatments. The gel structure serves as the matrix for the entrapment of the active molecules. By controlling the assembly of protein molecules during the gelation process, hydrogels, microparticles, and nanoparticles suitable can be produced. Various kinds of microparticles based on whey proteins, caseins, soy proteins, zein, gelatin, and wheat gliadin have been developed (32-36) for the encapsulation and delivery of a variety of bioactive compounds, including minerals, vitamins, omega-3 fatty acids, antioxidants, and probiotic bacteria. Decreasing the gel matrix size to a nanometre scale remains a real technical challenge. A monodisperse dispersion of 40 nm whey protein nanospheres was obtained by Chen et al. (32) by heating whey

proteins at a relatively low protein concentration and ionic strength and a temperature around 55°C. The potential of these nanospheres as carriers of nutraceutical agents was studied *in vitro*. Heat-induced nanogel formation was used for preparing bovine serum albumin (BSA) nanospheres containing both surface-functionalized magnetic nanoparticles and a photo-sensitizable agent, silicon (IV) phthalocyanine, for photodynamic cancer therapy (37).

The heat treatment required to produce these protein nanoparticles limits their application to formulations that do not contain heat-sensitive bioactive molecules. This problem could be overcome to some extent by cold-induced gelation of some proteins (whey proteins and soy proteins), which can be achieved by adding salts to a preheated protein dispersion. This method may be more suitable for entrapping heat-sensitive bioactive compounds; however, it is usually not possible to achieve nanometre-scale particles using this method.

Under some conditions, proteins can self-assemble into non-random, elongated structures called 'fibrils' (38-40). The mechanism of self-assembly varies and appears to be specific for each protein. For example,  $\beta$ -lactoglobulin has been shown to form long, thin and semi-flexible aggregates (called fibrils) when heated at low pH and low ionic strength. The heat-induced conversion of  $\beta$ -lactoglobulin monomers into fibrils involves protein hydrolysis, 'activation', nucleation, polymerization and termination steps (41,42). Partial hydrolysis of a whey protein,  $\alpha$ -lactalbumin, by a protease from *Bacillus licheniformis* has been shown to produce peptides that self-assemble into nanometre-sized tubular structures under certain conditions (43). These micrometre-long hollow tubes, with a diameter of only 20 nm, have potential applications in the delivery of bioactive compounds.

It is also possible to assemble casein proteins into casein-micelle-like particles *in vitro* under appropriate pH, ionic strength and calcium concentrations. Hydrophobic compounds, such as vitamin D<sub>2</sub>, can be incorporated into casein particles, formed by the re-assembly of caseins (44). These re-assembled casein particles can provide partial protection against UV-light-induced degradation of the vitamin D<sub>2</sub> entrapped within them. Casein micelles have been suggested for delivering curcumin, a natural spice with potential cancer-therapeutic attributes (45). Clearly, further understanding of the self-assembly properties of caseins would allow us to create novel nanometre-scale structures suitable for the delivery of bioactive compounds.

#### **Protein-polysaccharide composite systems**

Biopolymer composite particles formed from proteins and/or polysaccharides are widely used for encapsulating, protecting and delivering bioactive compounds. At

pH values below their isoelectric points, proteins carry positive charges and can interact with polysaccharides bearing carboxylic, phosphate, or sulphate groups. This inter-biopolymer complexation of positively charged proteins and anionic polysaccharides can lead to the formation of soluble and insoluble complexes (46). The characteristics of the complexes formed depend primarily on the types and concentrations of the biopolymers used, as well as on solution pH and ionic strength. The complex formation of proteins, e.g. gelatin,  $\beta$ -lactoglobulin, BSA, egg albumin, and soy protein, and several polysaccharides has been extensively studied (47,48).

Electrostatic complexes formed by  $\beta$ -lactoglobulin and pectin have been characterized by a number of researchers (49-51). The nature of the complexes formed depended on the linear charge density and hydrophobicity of the pectin molecules, as well as on the pH and ionic strength of the solution (52,53) Zimet et al. (54) produced electrostatic complexes, consisting of  $\beta$ -lactoglobulin and pectin, that entrapped docosahexaenoic acid (DHA) molecules. These systems showed very good colloidal stability and had a mean particle size of about 100 nm and were shown to effectively confer protection to DHA against its oxidation.

Nanoparticle complexes can be formed in mixtures of gum arabic/chitosan and sodium caseinate, and the particle characteristics can be tailored by manipulating the ratio of caseinate to gum arabic/chitosan (55,56). On the mixing of gum arabic and sodium caseinate, soluble and stable complexes can be formed over a wide pH range (pH 4 to pH 5.4); the complexes are in stable dispersions with particle size between 100 and 200 nm (55). The mechanism of the formation of these nanoparticles involves self-association of caseins and the electrostatic interaction between the aggregated particles of casein and gum arabic molecules. Similar to the sodium caseinate-gum arabic nanoparticles, the caseinate-chitosan complexes that formed were stable and soluble in the pH range 4.8 ~ 6.0. Between pH 4.8 and pH 6.0, the particles formed by the complexation of chitosan and caseinate had sizes between 250 and 350 nm, but, above pH 6.0, the nanoparticles associated to form larger particles (56). Such protein-carbohydrate nanoparticle complexes may be suitable vehicles for the encapsulation of bioactive compounds.

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## **CONCLUSION**

Inspired by nanotechnology, the functional food industry will see major advances in the development of new delivery systems for nutraceuticals and bioactive compounds. This will provide great potential for improving the effectiveness and efficiency of bioactive compounds

to improve human health. Already, many food materials have been exploited to create delivery systems to incorporate and protect these compounds in a food matrix from harsh food-processing and storage conditions. In the future, improvements in manufacturing technologies will create true nanodelivery systems (with particle sizes less than 100 nm); these materials will play an important role in increasing the efficacy of bioactive compounds in functional foods. These nanodelivery systems will increasingly focus on improving the bioavailability or absorption of bioactive materials and will target delivery to specific parts of the gastrointestinal tract. In fact, a number of food-related nanoproducts are already being marketed. Examples include: nanoparticles of carotenoids that can be dispersed in water, providing improved bioavailability; nano-based mineral supplements, such as nano-iron and nano-calcium; nanometre-sized micellar systems that are claimed to provide delivery systems for vitamins, minerals, and phytochemicals.

The important issues to consider over the next decade are the possible negative effects of nanometre-scale particles on human health. For example, enhanced levels of absorption of certain compounds may lead to bioaccumulation, reduced excretion and possible toxic effects. New acceptable daily intakes may need to be established for these kinds of compounds in the nano-form. The human gastrointestinal tract is generally well equipped to deal with various food and other particles, but greater understanding of the digestion and metabolism of nano-forms of the materials and their penetration through biological barriers will be required to ensure the design of safe nanocarriers for use in the food industry.

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## AUTHOR DISCLOSURE STATEMENT

The authors declare no conflict of interest.

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