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*Review Article*

# An Overview of Nanotechnology in Food Science: Preparative Methods, Practical Applications, and Safety

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As the researches to utilize nanotechnology in food science are advanced, applications of nanotechnology in various fields of the food industry have increased. Nanotechnology can be applied to the food industry for production, processing, storage, and quality control of foods. Nanomaterials, unlike conventional microscale materials, having novel characteristics can improve sensory quality of foods by imparting novel texture, color, and appearance. Nanotechnology has been used to design nanosensors for detection of harmful components in foods and a smart packaging system enabling to recognize food contamination very rapidly and sensitively. Nanoencapsulation is the most significant technology in food science, especially for bioactive compounds and flavors. Targeted delivery systems designed with nanoencapsulation can enhance bioavailability of bioactive compounds after oral administration. In addition, nanoencapsulation enables to control the release of flavors at the desired time and to protect the degradation of flavors during processing and storage. In this review, current applications of nanotechnology in food science including flavor control, enhancement of bioavailability of bioactive compounds, and detection of deleterious substances in foods are presented. Furthermore, this article overviews classification, preparative methods, and safety issues of nanomaterials for food science. This review will be of help to provide comprehensive information for newcomers utilizing nanotechnology to the food sector.

## 1. Introduction

Nanotechnology is defined as the creation, utilization, and manipulation of materials, devices, or systems at the nanometer scale [1]. Nanomaterials are usually defined as materials smaller than 100 nm and have unique properties when compared with their macroscale counterparts, due to the high surface to volume ratio and novel physicochemical properties such as color, solubility, and thermodynamics [2, 3]. These novel properties provide opportunities to improve the sensory qualities of food such as taste, texture, and color. In addition, nanomaterials can be used to improve protection mechanisms for food. Utilizing nanosensors and nanopackaging materials enables rapid, sensitive, and reliable detection of microbial contamination, harmful chemicals, and pesticides. Nanoencapsulation systems have the potential to improve food processing by enabling the delivery of bioactive compounds for enhancing bioavailability in foods [4]. In this review, the classification, methods of preparation, and safety issues of nanomaterials are described. The main focus of the review is on nanotechnology applications for foods and includes controlled release of flavors, targeted delivery of bioactive compounds for enhancing the bioavailability, and nanosensors for pathogens

and chemical detection in foods. The aim of this review is to describe the circumstances of nanotechnology utilized in the food sector and to present a comprehensive perspective to food scientists embarking on research about nanotechnology.

## 2. Classification of Nanocarriers

Nanocarriers can be widely classified as organic-based, inorganic-based, or a combination of both (Table 1) [5]. Organic nanocarriers are comprised of polymeric nanoparticles and lipid-based nanoparticles such as liposomes, nanoemulsions (e.g., micelles and reversed micelles), dendrimers, and carbon-based nanocarriers (e.g., fullerenes and carbon nanotubes). Inorganic nanocarriers are comprised of metallic nanostructures such as quantum dots (Figure 1).

*2.1. Polymeric Nanoparticles.* Polymeric nanoparticles are based on biocompatible and biodegradable polymers derived from natural and synthetic sources. Biodegradable polymers are typically composed of synthetic polymers such as poly(lactic acid), polyglycolic acid, poly(lactic-co-glycolic acid), poly($\varepsilon$-caprolactone), polymethyl methacrylate, and poly(amino acid). Biodegradable polymers may also consist of natural polymers including, but not limited to, agarose, sodium alginate, chitosan, collagen, and fibrin [6]. Polymers that can provide a controlled drug release of core materials are desirable and have given rise to the popularity of polymeric nanoparticles for anticancer treatment and vaccine delivery [7]. The chemical properties of polymeric nanoparticles and their flexibility has made them suitable for integration with biomaterials (e.g., genetic material and growth factors) and for targeted delivery to stimulate tissue regeneration [8].

*2.2. Liposomes.* Liposomes are concentric lipid-bilayered nanocarriers comprised of an aqueous core enclosed by surfactant that can be of either natural or synthetic phospholipids. Liposomes can be categorized based on their structure as multilamellar vesicles (MLVs), oligolamellar vesicles (OLVs), and unilamellar vesicles (ULVs). Based on the size of the ULVs, they are further divided into small unilamellar vesicles (SUVs) of 20 to 100 nm diameter, medium unilamellar vesicles (MUVs), large unilamellar vesicles (LUVs) of larger than 100 nm diameter, and giant unilamellar vesicles (GUVs) of larger than 1,000 nm diameter [9]. Liposome-based carrier systems such as immunoliposomes, virosomes, stealth liposomes, and archaeosomes contain lipid bilayers that are biocompatible and may improve the solubility and stability of core materials [10–13].

*2.3. Dendrimers.* Dendrimers are monodispersed macromolecular compounds composed of repetitively branched molecules around an inner core. Dendrimers can be structured from monomers by convergent or divergent polymerization methods. The desired size and shape of a dendrimer is dependent on the number of branching units on the repeating unit as seen when using different units, such as chitin, melamine, polyamidoamine, poly L-glutamic acid, polyethyleneimine, polyethylene glycol, and polypropyleneimine [14]. Core materials can be loaded either in the interior or conjugated to a large number of free surface groups to enhance targeted delivery [15].

*2.4. Carbon-Based Nanocarriers.* Carbon nanotubes are carbon-based tubular structures that are arranged in the shape of a graphene sheet that has been wound into a cylinder or capped at both ends to produce a buckyball shape [14]. There are two carbon-based configurations: single-walled nanotubes (SWNTs) and multiwalled nanotubes (MWNTs). Whereas SWNTs are composed of a single graphene cylinder, MWNTs are composed of more than two concentric cylindrical shells of graphene sheets around a central hollow core [16]. Depending on the functionalization, the nanotubes are further categorized as target-oriented, ligand-attached, solvent-dispersed, and surfactant-grafted. In addition to tubular types, fullerenes are also common carbon-based nanocarriers that represent geometric cage-like structures composed of hexagonal and pentagonal carbon faces [17].

*2.5. Hydrogel Nanoparticles.* Hydrogels are three-dimensional polymer networks that can absorb a large volume of water or biological fluid. Water-absorbing ability of the hydrogels is dependent on the presence of hydrophilic groups (e.g., -OH, -CONH-, -$CONH_2$-, and –$SO_3H$) [18]. The crosslinks in the polymer networks are provided by covalent bonds, hydrogen bonds, dipole-dipole interactions, van der Waals interactions, and physical entanglements [19]. These crosslinks can be categorized by physical entanglements or crystallites, and chemical tie-points and junctions [20]. In a drug delivery system, polymer materials such as alginate, chitosan, poly (vinyl alcohol), poly(ethylene oxide), poly(vinyl pyrrolidone), and poly-*N*-isopropylacrylamide are widely used to make cross-linked networks. These networks are affected by the electric field, light intensity, pH, and temperature [21, 22].

*2.6. Quantum Dots.* Quantum dots are nanocrystals of inorganic fluorescent semiconducting atoms and have a size range of 2–10 nm. The semiconducting material, cadmium selenide, consists of a core, and aqueous zinc sulfide shell that insulates the core to enhance optical properties. Quantum dots can be constructed to emit light from the ultraviolet to infrared wavelength. Emitted wavelengths are intense enough to be detected at the subcellular level [23]. In addition, quantum dots are a stable and inert delivery vessel as biomolecules can be conjugated to the outer aqueous shell [24].

*2.7. Nanoemulsions.* Nanoemulsions consist of droplets with a size range of 10–100 nm and can be categorized into two types based on the relative spatial organization of the oil and water phases. A micellar system comprised of oil

Table 1: Physicochemical properties and applications of various nanomaterials.

| Types | Size (nm) | Physicochemical properties | Applications |
|---|---|---|---|
| Carbon nanotubes | 0.5–3 (diameter) 20–1,000 (length) | Third allotropic crystalline form of carbon sheets either single layer (single-walled nanotube, SWNT) or multiple layer (multiwalled nanotube, MWNT). These crystals have remarkable strength and unique electrical properties (conducting, semiconducting, or insulating) | Functionalization enhanced solubility, penetration to cell cytoplasm and to nucleus, as Carrier for gene delivery, peptide delivery |
| Dendrimer | <10 | Highly branched, nearly monodispersed polymer system obtained from controlled polymerization; three main parts core, branch, and surface | Long circulatory, controlled delivery of bioactive compounds, targeted delivery of bioactive compounds to macrophages, liver targeting |
| Liposome | 50–100 | Phospholipid vesicles, biocompatible, versatile, good entrapment efficiency and different vesicle types depending on the structure multilamellar vesicles (MLV): >500 nm; oligolamellar vesicle (OLV): 100–500 nm; unilamellar vesicles, and unilamellar types depending on the size as small unilamellar vesicles (SUV): 20–100 nm; large unilamellar vesicles (LUV): >100 nm; giant unilamellar vesicles (GUV): >1,000 nm | Long circulatory, offer passive and active delivery of gene, protein, peptide, and various other components |
| Metallic nanoparticles | <100 | Gold and silver colloids, very small size resulting in high surface area available for functionalization, high stability | Drug and gene delivery, highly sensitive diagnostic assays, thermal ablation, and radiotherapy enhancement |
| Nanocrystals quantum dots | 2–9.5 | Semiconducting material synthesized with II-VI and III-V column element; size between 10 and 100 Å; bright fluorescence, narrow emission, broad UV excitation, and high photo stability | Long-term multiple color imaging of liver cell; DNA hybridization, immunoassay; receptor-mediated endocytosis; labeling of breast cancer marker HeR2 surface of cancer cells |
| Polymeric micelles | 10–100 | Block amphiphilic copolymer micelles, high drug entrapment, payload, and biostability | Long circulatory, target specific active and passive drug delivery, diagnostic value |
| Polymeric nanoparticles | 10–1,000 | Biodegradable, biocompatible, and offer complete drug protection | Excellent carrier for controlled and sustained delivery of drugs; Stealth and surface modified nanoparticles used for active and passive delivery of bioactive compounds |

droplets suspended within a water phase is referred to as an oil-in-water (O/W) nanoemulsion, whereas a reversed micellar system that is comprised of water droplets suspended in an oil phase is referred to as a water-in-oil (W/O) nanoemulsion [25]. O/W nanoemulsions are usually kinetically stable and slightly turbid to transparent. Due to the weak light scattering of particles in nanoemulsions, they are suitable for incorporation into optically transparent products such as fortified soft drinks and waters, whitening cosmetics, sauces, and soups [26–29].

## 3. Preparation Methods for Nanocarriers

There are several conventional and emerging methods for the preparation of nanocarriers. Typical methods based on emulsification technology are most commonly used but specific methods must be developed for each type of nanocarrier. In this section, the conventional and emerging methods for the preparation of nanocarriers are described (Table 2) [18].

### 3.1. Conventional Methods

*3.1.1. High-Pressure Homogenization.* High-pressure homogenization has been widely used for the preparation of lipid-based nanocarriers such as nanoemulsions and solid lipid nanoparticles. High shear stress produces high pressures (100–2,000 bar), resulting in disruption of particles into the nanometer range [30]. This method is divided into hot homogenization and cold homogenization. The former gives lower particle size because of the decreased viscosity of the phase at a higher temperature but may result in an increased degradation rate of the core material in the nanocarrier. The latter was developed to overcome the limitations of the hot homogenization, incurred by high temperatures, and involves the

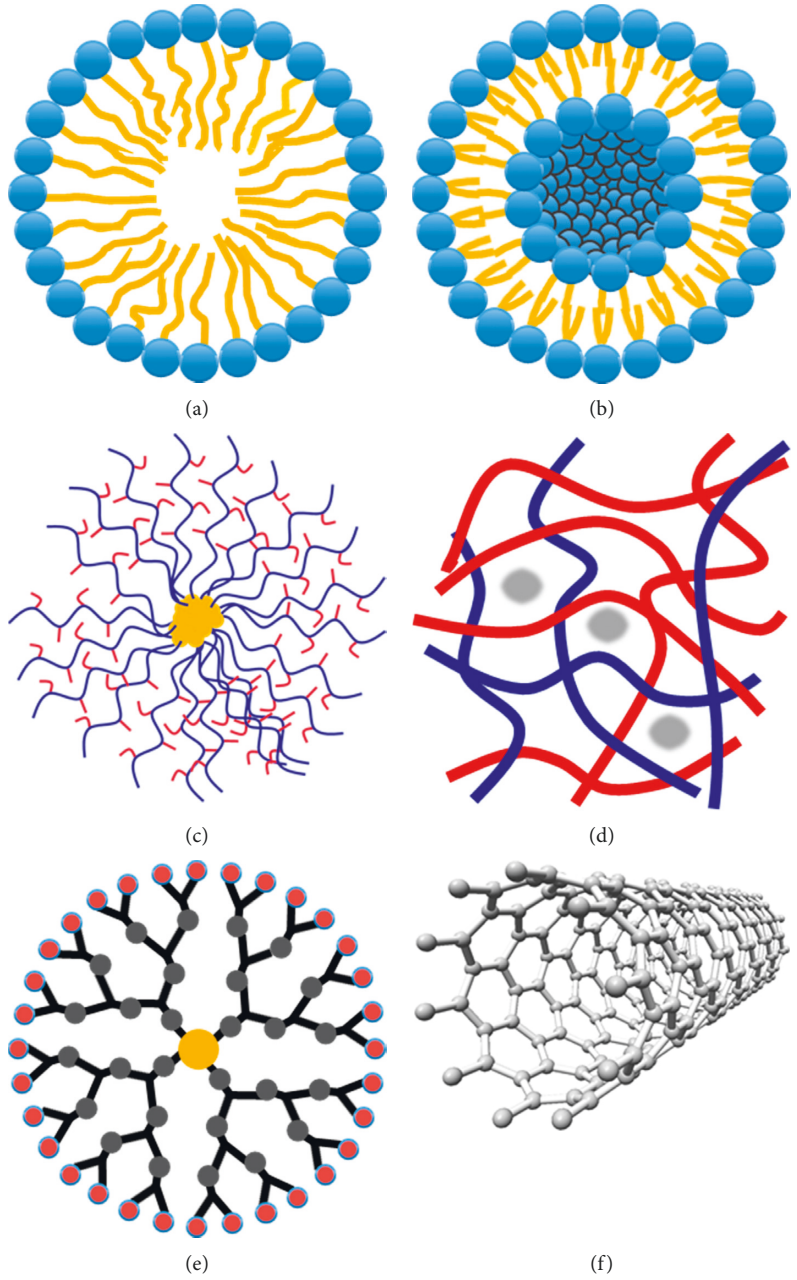


Figure 1: Schematic diagrams of 6 types of nanocarriers. (a) Micelle. (b) Liposome. (c) Polymeric nanoparticle. (d) Hydrogel nanoparticle. (e) Dendrimer. (f) Carbon nanotube.

solubilization or dispersion of core material above the melting point of nanocarriers (5–10°C) [31]. High-pressure homogenization has high encapsulation efficiency thereby enabling the controlled release of the core material.

*3.1.2. Solvent Emulsification-Diffusion Method.* Solvent emulsification-diffusion is the most commonly used method for the preparation of lipid-based and polymeric-based nanoparticles. The oil phase contains the polymer in an organic solvent whereas the aqueous phase contains a stabilizer in water. When mixed together, the water induces the diffusion of the organic solvent resulting in the formation of nanoparticles [31]. The solvent used for the preparation of nanoparticles must be removed. Moreover, emulsification methods for the production of more complex nanocarriers required a double emulsion [32]. The first step is to add a small amount of aqueous media to a larger volume of immiscible organic solvents to dissolve the phospholipid. The organic solution containing the water droplets is added to a large volume of aqueous media producing a water-in-oil-in-water (W/O/W) emulsion. A lipid monolayer forms around the organic droplets resulting in aqueous cores surrounded by two lipid monolayers that are separated by an organic layer. Unilamellar liposomes with high entrapment

Table 2: Conventional and emerging methods for preparation of nanocarriers.

| Preparation method | Advantages | Disadvantages |
|---|---|---|
| *Conventional methods* | | |
| High homogenization | Large-scale production, high encapsulation efficiency | Deactivation of core material in nanocarrier |
| Solvent injection (ethanol or ether) | Ability to control vesicle size | Dilution of nanocarrier, heterogeneous population, use of high temperature |
| Reverse phase evaporation | High encapsulation efficiency, economic | Organic solvent traces, not suitable for fragile molecules or food ingredients |
| Solvent-emulsification | High encapsulation efficiency | Multivesicular, unstable |
| Postformation processing | Reduced processing time, high encapsulation efficiency | Low lamellarity and heterogeneity |
| *Emerging methods* | | |
| Microfluidic channel method | Synthesis of monodisperse nanocarrier, high encapsulation efficiency | Fabrication could be complex and needs optimization |
| Supercritical fluid method | Control over particle formation, easily translated to large-scale production, environment-friendly | Elevated pressure and temperatures |
| Self-assembly method | Handy and controllable method for changing the shape of nanocarriers | Poorly understood experimental conditions |
| Spray drying | Environment-friendly process, high encapsulation efficiencies | Expense and time-required |
| Freeze drying of monophase solutions | Monodisperse nanocarrier that can be stored for a long time in a sealed container | Time-required |
| Membrane contactor method | Nanocarriers have homogeneous and small size, high encapsulation efficiency, simplicity for scale-up | Hydrophilic drug encapsulation needs optimization |

of the initial aqueous media can then be formed by the removal of the organic solvent [33, 34].

*3.1.3. Injection Methods.* The two injection methods for preparation of lipid-based nanocarriers utilize ether or ethanol. Diethyl ether and ether-methanol mixtures are widely used for dissolving the lipids [35]. The lipid-ether solution is injected into the aqueous media and nanocarrier vesicles are formed [36, 37]. LUVs are formed as the injection speed increases. An advantage of the ether injection method is the removal of the solvent from the product, allowing extended process-running time and producing a concentrated liposomal product with high entrapment efficiencies. However, this technique creates a heterogeneous population (70–200 nm) with a requirement for high temperatures to encapsulate the organic products [38].

The ethanol injection method dissolves the lipids in ethanol [39]. The high concentration of the core materials in the aqueous phase can be increased by multiple injections of the lipid solution. An advantage of this technique is the quick and simple formation of MLVs [40]. Disadvantages include producing a heterogeneous population (30–110 nm), low concentration of enabled liposomes, and a high level of difficulty when removing the ethanol. Ethanol removal poses a significant problem when using liposomes for biological cell culture or microorganism treatment, as all of ethanol the must be removed [41].

*3.1.4. Reverse Phase Evaporation Method.* The reverse phase evaporation method was first shown by Szoka and Papahadjopoulos and is based on the creation of reversed micelles [42]. Reversed micelles are in the aqueous phase with a central core surrounded by lipid and dispersed in an organic solvent [43]. Reversed micelles are produced by dissolving the lipids in an organic solvent, adding a small volume of aqueous phase, and sonicating the solution to produce inverted micelles. The organic solvent is removed using a rotary evaporator resulting in a viscous gel [44]. When sufficient solvent has been removed, the gel collapses, and an aqueous suspension of vesicles forms [45]. The disadvantage of the reverse phase evaporation method is that the compound to be encapsulated within the vesicles is in contact with an organic solvent. Consequently, this method is not suitable for fragile molecules or food ingredients despite the potential to achieve encapsulation efficiencies of up to 80% [44].

### 3.2. Emerging Technologies

*3.2.1. Microfluidic Channel Method.* The microfluidic channel method consists of two silicon wafers such as polydimethylsiloxane (PDMS), vertically attached together [46]. In this case the microchannel, the width of which is 200–1,000 $\mu$m, was carved on one side of the PDMS layer. Two inlet lines (outside inlet and central inlet) and one outlet were directly connected with the microchannel. In the case of liposome preparation, a lipid solution is injected into the central inlet while aqueous solutions are injected to the outside inlet, which intersects with the central position. Liposomes are formed due to the different shear forces that are generated at the liquid interfaces by the changing flow rate ratio. The process involves a stream of lipid dissolved in solvent passing between two aqueous streams in

a microfluidic channel. Mixing occurs at the liquid interfaces creating nanocarriers [47, 48]. An advantage of this technique is the ease of control concerning vesicle size and monodispersion although a continuous system is yet to be developed.

*3.2.2. Supercritical Fluid Methods.* Methods involving supercritical fluids for nanocarrier preparation are used in pharmaceutical research and industry to address limitations associated with conventional methods [32]. A supercritical fluid can be either a liquid or gas, such as water or carbon dioxide, under conditions that are above its thermodynamic critical point of temperature and pressure (e.g., carbon dioxide at 60°C and 250 bar). Supercritical fluid methods are separated into two categories: rapid expansion and antisolvent precipitation [31]. The advantages of these methods over conventional methods include a reduction of impact on the environment and improved design of particle morphology (size and shape). The disadvantage of this method is poor scalability for industrial manufacturing, which may result in variable particle characteristics [49].

*3.2.3. Self-Assembly Methods.* Self-assembly is the physical process where preexisting disordered components or molecules arrange themselves into regulated structures by physical or chemical reactions without external influences [50]. Protein folding and liposome assembly are examples of self-assembly. Self-assembly has the potential to be used in nanotechnology, where a desired structure could be encoded into the properties of the nanomaterials being used. Nevertheless, it has not been used to its full potential as yet because experimental conditions under which a set of components self-assemble remain poorly understood [31].

## 4. Applications in the Food Sector

*4.1. Flavor Control.* Flavors are considered important ingredients in any foods, playing a significant role in sensory quality and influencing the consumption of food. The increasing interest on the stability of flavors in different types of food is linked to the quality and acceptability of the food [51]. However, it is difficult to control and stabilize flavors, mainly during the storage and manufacturing processes [52]. To limit flavor degradation or loss during processing and storage, it is beneficial to encapsulate the flavor before use in food, improving chemical stability, and providing controlled release. Encapsulation with a protective carrier guard against interactions between flavors, reactions induced by light, and oxidation [53]. Popular carriers are biopolymers such as carbohydrates (e.g., starch, maltodextrins, and dextrose), gums (e.g., gum arabic, alginates, and carrageenan), proteins (e.g., whey proteins and gelatin), and chitosan [51]. When designing an encapsulation system, factors for consideration are the physicochemical properties of the flavor (solubility) and the carrier (viscosity). Especially, the carriers should not react with the flavors [54].

Nanoencapsulation packs substances into nanocarriers and provides final product functionality that includes controlled release of the core materials [55]. With a properly designed controlled release system such as sustained release and burst release, the flavors can be released at the desired time and at a desired rate [56]. This system has a slow or near zero release of flavors in solvated conditions but have a burst release due to changes in pH and/or ionic strength or temperature when a food product is in contact with saliva. Nanocarrier encapsulation provides sustained release of the flavor compounds maintaining the flavor quality during shelf-life storage. Sustained release can be achieved by encapsulating a compound in appropriate nanocarriers that maintain physical stability under the expected performing conditions and durations. Factors influencing the release mechanisms include the type of carrier to encapsulate the flavors, the method of preparation, and the environment where the flavors are released. On the release mechanism, processes of diffusion, degradation, melting, and osmosis may also be important [52]. Controlled release of flavor compounds can be manipulated by interactions between core materials and carrier materials.

*4.2. Enhancing the Bioavailability of Bioactive Compounds.* The bioavailability of bioactive compounds is the most important factor for consideration when producing functional foods. Bioavailability is defined as the amount of a bioactive compound that can enter the bloodstream [57]. When bioactive compounds are administrated orally, these compounds pass through the mouth, stomach, and intestines to access the bloodstream. Protection against the gastrointestinal tract (GIT) environment requires defense against digestive enzymes, pH, and temperature [33]. It is necessary to increase the stability of bioactive compounds and improve their absorption by epithelium cells, to increase bioavailability.

Several target delivery systems using nanocarriers have been developed to improve the bioavailability of various bioactive compounds. Bioactive compounds can be classified into lipophilic and hydrophilic types based on their solubility in water. Many of the bioactive compounds are highly lipophilic molecules, such as polyunsaturated lipids, oil-soluble vitamins, phytosterols, curcuminoids, carotenoids, and flavonoids. The lipophilic bioactive compounds have low bioavailability within the human GIT due to poor absorption in the gastrointestinal fluids [58]. These bioactive compounds are usually encapsulated to resist the high acidity and degradation by enzymes in the stomach and duodenum but also to enhance their low water-solubility, which interferes with applications in food such as beverages [59].

Nanocarriers provide an increased surface area and enhance solubility and bioavailability of the encapsulated bioactive compounds when compared to microsize carriers. Reducing the particle size improves the delivery efficiency, solubility, and biological activity of the compounds due to greater surface area per unit [60]. It was demonstrated that the bioavailability of $\beta$-carotene encapsulated within O/W

nanoemulsions increased with decreasing particle size [58]. These findings have been confirmed with Coenzyme $Q_{10}$ and lipophilic compounds when fed to animals [61]. It was concluded that a more rapid digestion of the lipid phase in emulsions occurred when the lipid droplet size decreased. More mixed micelles cause to solubilize the lipophilic bioactive compounds within the fluids of the small intestine [58]. Although carbohydrate, protein, and lipid-based nanocarriers have several advantages, the carbohydrate- and protein-based carriers currently have low potential for scale-up due to the requirement for complicated chemical or heat treatments in the process that cannot be adequately controlled. On the other hand, lipid-based nanocarriers, including nanoemulsions and nanoliposomes, solid lipid nanoparticles, biopolymer nanoparticles, and microgels, have a greater potential for industrial scale-up and have the advantage of higher encapsulation efficiency and low toxicity [1].

Many targeted delivery systems have been proposed but none can currently be considered as a universally applicable system for bioactive compounds because individual bioactive compounds have their own characteristic molecular structure necessitating different systems. It was demonstrated that each compound could have differences in molecular weight, polarity, and solubility, resulting in the need for different encapsulation approaches to meet the specific physicochemical and molecular requirements for a specific bioactive compound [59]. When targeted delivery systems are designed, an important requirement is encapsulation efficiency of core materials into carriers. The efficiency is related to the type of molecule to be encapsulated and the specific products that serve as carriers [62]. Whilst high encapsulation efficiency is important, it is essential to choose a system that can be easily incorporated without interfering with the texture and taste of the food. Food products have various physicochemical properties and sensory characteristics, such as appearance, texture, flavor, and mouthfeel. Some food products are optically clear low-viscosity liquids (such as fortified waters), whereas others are optically opaque semisolids or solids (such as yogurts and spreads) [58]. Delivery systems for a bioactive compound must be incorporated into the final food product without adverse effect on its quality.

*4.3. Detection of Deleterious Substances in Foods.* Nanosensors are an important area in food industry. These devices may be able to detect and quantify low concentrations of pathogens, organic compounds, and other chemicals. Furthermore, these devices have the potential to exhibit high sensitivity, fast response, and recovery and integrate addressable arrays on a large scale [63].

An example of a nanosensor application is organophosphate for pesticide detection in fruit and water [64]. High interface sensitivity caused by the loading of more enzyme/antibody, low detection limits, and excellent selectivity are some of the advantages of nanosensors. An example of applying semiconductors to the use of quantum dots in the detection of the pesticide 2,4-dichlorophenoxyacetic acid was studied [65]. Quantum dots are semiconductor fluorescent nanoparticles, which can be used to monitor pesticide with high sensitivity [66]. Another example of a nanosensor is an invention by Kraft Foods. They developed a nanosensor to be incorporated within food packaging consisting of an array of nanosensors that are extremely sensitive to gases produced by food as it spoils. As the food spoils and these gases are detected, the sensor strip changes color providing a clear optical signal of food freshness [66].

Nanosensors have also been used for pathogen and mycotoxin detection in foods. Conventional control of these microorganisms is complicated, but the nanosensor can rapidly detect toxins and pathogens in foods, during processing, and in storage. The nanosensor can be used for smart packaging where the sensor fluoresces in different colors when the sensor contacts with different food pathogens. Different devices have been developed to detect numerous toxins, pathogens, and chemicals in food packaging using nanowires and antibodies [58].

In the food market, nanoelectromechanical systems (NEMS) are already in use to analyze deleterious substances. NEMS could be used in quality control devices for foods because they consist of advanced transducers for specific detection of chemical and biochemical signals [67]. The use of nanosensors has several advantages for food technologies, such as portable instrumentation with quick responses and low costs. Nanocantilevers are another innovative class of nanosensors. The detection is based on the principle to detect biological-binding interactions through physical and/or electromechanical signals (e.g., antigen and antibody, enzyme and substrate or cofactor, and receptor and ligand) [68]. These nanosensors consist of tiny pieces of silicon-based materials that have the capability of recognizing proteins and detecting pathogenic bacteria and viruses [69].

## 5. Safety Issues in Food Nanotechnology

A recent innovation in nanotechnology has fostered a number of nano-based scientific and industrial areas with the market for nanomaterial-containing products experiencing steady growth. Despite its various advantages, the rapid proliferation of nanotechnology in food technology has also raised public safety and environmental, ethical, policy, and regulatory issues. Nanomaterials may exhibit substantially different physicochemical and biological properties compared to their conventional form, and these unknown properties may create unpredictable hazards.

The potential hazard of direct contact of nanomaterials with humans through oral intake is still a concern, even though the nanoencapsulation technology of bioactive compounds has been very extensively studied in the food industry [70]. The fate of nanocarriers in GIT varies greatly depending on their susceptibility to hydrolysis by digestive enzymes and the conditions of GIT [71]. Nevertheless, free nanocarriers typically cross intestinal/cellular barriers, which could lead to an increase in the bioaccumulation of foreign materials in human blood, cells, and tissues.

The high usage of organic solvents and emulsifiers for the preparation of nanocarriers can lead to risks due to their

toxicity [25]. The organic solvents must be removed by an evaporation process but can lead to unexpected residual solvents remaining in the final product, causing safety implications if their concentration is unknown. Solvents and emulsifiers have been classified as toxic, with safe usage levels documented by organizations including the World Health Organization (WHO), the Food and Drug Administration (FDA), and the European Food Safety Authority (EFSA) [25].

In fact, the available information on the potential safety risks that may arise from the nanotechnology is sparse. The safety of nanomaterials and associated hazards remain uninvestigated and require further risk assessment. The direct and indirect effects of nanomaterials to human health must be explored and include the biological fate of nanomaterials after digestion, their behavior within GIT, and their possible interactions with biological systems. Moreover, it is of great importance to develop regulatory controls to protect the public from potential adverse effects of nanotechnology [72].

Modern food legislation, with the help of several world organizations, regulates many issues related to consumer health, many of which may be applied to nanotechnology and nanomaterials used in foods. Despite the current lack of specific regulation and risk management for nanotechnology, it is evident that there have been significant advances in the application and regulation of novel nanotechnology in the food industry. By keeping modern food regulations, any new specific nanotechnology regulation, information transparency and a willingness to provide the public with information in mind, the safety of nanomaterials in the food industry can be assured.

## 6. Conclusions

Advances in nanotechnology have brought benefits for the food industry, with many applications yet to be realized. Nanotechnology has already demonstrated its applicability in the areas of food production, processing, packaging, and safety. Although nanotechnology in foods has progressed year upon year, further research is necessary to maximize the number of uses within the food industry. In particular, the safety concerns regarding the consumption of nanomaterials in foods must be addressed before the products are released to the market. Therefore, it is necessary to standardize test procedures to determine the impact of nanomaterials. Furthermore, regulations must be introduced that can ease consumer worry and improve consumer acceptability. The uptake of nanotechnology will cause rapid development of the food industry with nanotechnology-based foods becoming more readily available to the consumer.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Authors' Contributions

Hyunjong Yu and Jun-Young Park contributed equally to this work.

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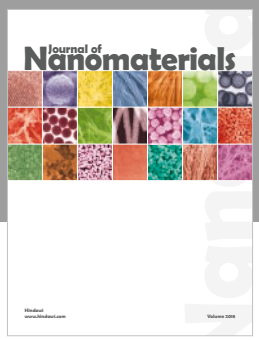

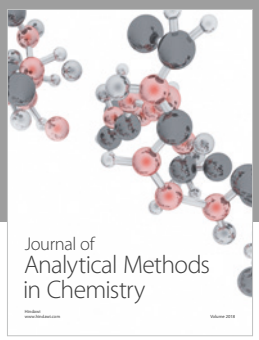

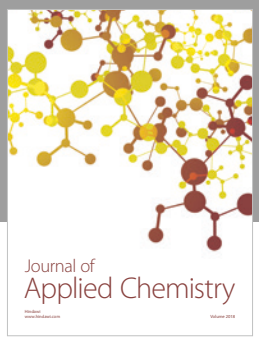

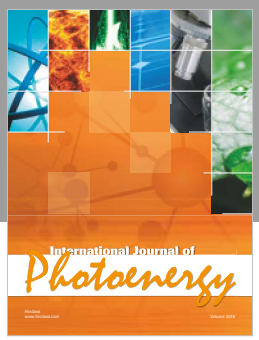

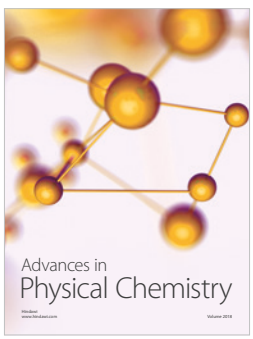

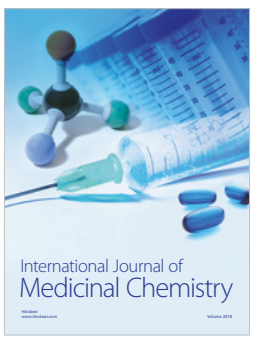

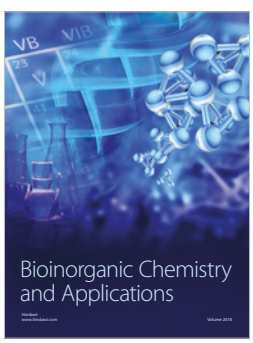

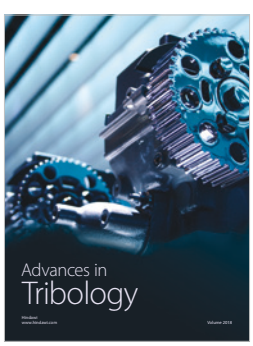

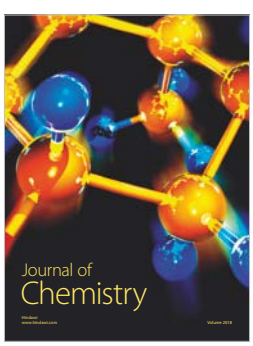

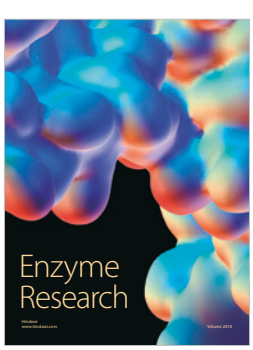

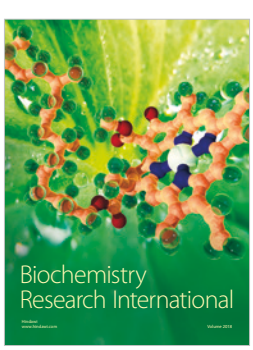


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