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Nanobiotechnology applications in food sector and future innovations

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Yogita Lugani[1], *Balwinder Singh Sooch*[1], *Poonam Singh*[2], *Sachin Kumar*[3]
[1]Enzyme Biotechnology Laboratory, Department of Biotechnology, Punjabi University, Patiala, Punjab, India; [2]Organic Building Materials, CSIR-Central Building Research Institute, Roorkee, Uttarakhand, India; [3]Biochemical Conversion Division, Sardar Swaran Singh National Institute of Bio-Energy, Kapurthala, Punjab, India

8.1 Introduction

The concept of nanotechnology was given by Nobel laureate Richard P. Feynman in 1959 during his famous lecture "There's Plenty of Room at the Bottom" (Feynman, 1960) where he demonstrated the concept of manipulation of matter at molecular and atomic level, i.e., nanoscale. Nanotechnology is one of the emerging and rapidly growing fields which has shown tremendous revolutionary developments in different fields of science including physics, chemistry, biology, and engineering, and its meaning varies with each field. The widely used definition of nanotechnology is synthesis of nanoscale materials (with size less than 100 nm) possessing new functions and properties (physical, chemical, electrical, optical, and magnetic) by understanding, controlling, and restricting of matter at nanometer level (NSTC, 2007). The nanomaterials used in different sectors for applications are metallic nanoparticles, carbon nanotubes, quantum dots, nanowires, nanoceramics, dendrimers, liposomes, and fullerenes, and these materials can be synthesized by top-down or bottom-up approaches (Lugani et al., 2018a).

Nanotechnology is gaining interest for research by many government and private organizations for research due to their myriad applications in different sectors such as food, cosmetics, energy, paints and coatings, textiles and clothing, medicines and drugs, and defense and security (Bryksa and Yada, 2012; Lugani et al., 2018a,b). Nanotechnology has been revolutionized in food sector for food processing, packaging, storage, and development of innovative products due to inimitable properties of such small particles like controlled release of nutraceuticals and food supplements, antimicrobial characteristics, enhancement of shelf life of food, and improvement of taste, flavor, texture, consistency and stability of food products, and mechanical and heat resistant properties due to unique properties of nanoparticles (Berekaa, 2015), as given in Box 8.1.

Development of nanosensors for the detection of contaminants and foodborne pathogens from foods is another advancement of nanotechnology in food sector, and many electrical companies are focusing toward developing electrically conducting materials

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Box 8.1 Unique properties of nanoparticles

- Improve nutritional value and texture of food products.
- Improve food consistency and prevent lump formation.
- Improve physical performance of food.
- Fortification of minerals and vitamins in foods.
- Enhance product shelf life.
- Reduce fat and sugar content.
- Provide controlled release at target site.
- Increase gas permeability, water resistance, and flame resistance.
- Nano-biosensors can detect foodborne pathogens.
- Able to bind and remove food contaminants.
- Help in innovative, lighter, stronger, and active packaging.

for manufacturing sensors (Wesley et al., 2014). The global market of nanotechnology is enhancing tremendously in food sector due to commercial applications of nanomaterials in food products. Further, advanced techniques like microfluidics, microelectromechanical systems, and DNA microarrays help in realization of use of nanotechnology for food applications for rapid sampling of biological and chemical contaminants, bioseparation of proteins, smart delivery of nutrients, and nanoencapsulation of nutraceuticals (Ravichandran, 2010). There are many industries in USA, UK, Germany, Switzerland, and Netherlands where nanoencapsulated food additives have been commercialized (Food Encapsulation Market, 2018–2024). However, nanoparticles have shown hazardous effects on environment and human health, which are the major concerns for their industrial use. Table 8.1 shows the benefits and risks of nanoparticles in food sector. The greater toxicity of nanomaterials compared to larger particles is due to their bioavailability and greater chemical reactivity, but it is unclear whether nanomaterials can accumulate in the food chain, and what levels of these materials can harm the environment and human health (Bumbudsanpharoke and Ko, 2015). Hence, it has been recommended to conduct *in-vivo and in-vitro* toxicity studies with nanomaterials before recommending for public use.

This book chapter provides a comprehensive overview on approaches used for synthesis of nanoparticles, innovations of nanotechnology in food sector, and global market of agribusiness. Further, a brief outlook has been given to safety aspects of nanoproducts with special emphasis to toxicity and health concerns with their use.

8.2 Types of nanoparticles

Nanoparticles are broadly classified into two categories i.e., organic and inorganic based on their composition (Moghtaderi and Abargouei, 2018). There are three types of organic nanoparticles i.e., carbohydrate-based, protein-based, and lipid-based nanoparticles (fat crystals, micelles, oil droplets, and vesicles) which are highly used in

Table 8.1 Benefits and risks of nanoparticles in food sector.

Benefits	Risks
• Keep foods fresh for long duration. • Remove foul smell and provide antimicrobial effects. • Help in dispersion and bioavailability of nutrients in foods, and retention of volatile ingredients. • Temperature, pH, and moisture triggered controlled release. • Nanosilver materials provide natural and powerful antibiotic, antioxidant, and antibacterial properties. • Nanocomposite materials improve mechanical and rheological properties of foodstuffs. • Synthesis, and applications in food sector are under standards of FDA (Food and Drug Administration), USA. • Able to bind and remove food contaminants. • Provide better absorption, better stability, and targeted delivery of nutraceuticals. • Use for agrochemicals delivery,	• Excess use results in environmental poisoning. • Promote allergic pulmonary inflammation. • Accumulation in different tissues and organs like skin, liver, lung, kidney, spleen, brain, vascular, and reproductive tissue. • Altered absorption profile and metabolism in body. • Abnormal cellular morphology, cell shrinkage, and chromosomal damage. • Induce oxidative stress, and alter cell signal transduction pathways, which may result in carcinogenesis. • Occurrence of autoimmune diseases such as rheumatoid arthritis, scleroderma, and systemic lupus erythematosus. • Enhanced antigen-specific immune reactions and hypersensitivity responses.

commercial food products (Shin et al., 2015). Inorganic nanoparticles mainly consist of metals, and metal oxides such as silver, titanium dioxide (TiO_2), zinc dioxide, silicon dioxide, and iron oxide (He and Hwang, 2016). Organic nanoparticles are claimed to be less toxic than inorganic ones due to their easy digestion within gastrointestinal tract (Clements and Xiao, 2017). Nanostructure materials are classified into zero dimensional (nanoparticles, nanoclusters, quantum dots, and fullerenes), one-dimensional (nanorods and nanotubes), two-dimensional (thin films), and three-dimensional (dendrimers and nanocomposites) based on structural elements (Pathakoti et al., 2017). Metallic nanoparticles are used in biosensors, drug delivery, and in treatment of cancer, and among these, silver and gold nanoparticles are of prime importance for medical use (Nikalje, 2015). The metallic nanoparticles which are used in food sector are silver, titanium, zinc, and silica (Martirosyan and Schneider, 2014). Quantum dots are inorganic semiconductor fluorescent nanoparticles which consist of CdSe core, and they are functionalized by coating with different polymers. They are used in food industry for detection of pathogenic bacteria and proteins (Bonilla et al., 2016).

Different types of nanomaterials used in food management are liposomes, micelles, dendrimers, nanospheres, nanocapsules, nanofilms, and nanoconjugates (Predhan et al., 2015). Liposomes are types of nanocapsules which are small in size (50−200 nm), biocompatible, versatile with good entrapment efficiency, and they are used for specific and controlled delivery of additives, antimicrobials, enzymes, nutrients, and vitamins (Godwin et al., 2009; Nikalje, 2015). Dendrimers are hyper branched, tree like structures with size less than 10 nm, and they are used for controlled long circulatory delivery of bioactive materials (Nikalje, 2015). Carbon nanotubes are small macromolecules and possess unique physical properties, size, and shape. Nanocapsule is defined as nanovascular system with a core-shell structure consisting of polymer membrane or coating and the target drug or food formulation is added within the cavity (Sekhon, 2010). Nanocapsules provide several benefits in food sector like consecutive release of multiple active ingredients, change in flavor character, ease of handling, enhanced bioavailability, efficacy and stability, long-lasting organoleptic perception, moisture and pH triggered controlled release, protection against oxidation, retention of volatile ingredients, antibacterial properties, and improved taste making (Chaudhry et al., 2008). Nanofilms are nanoscale materials used in sunglasses, cameras, and computer displays due to water repellent, antimicrobial, antifog, ultraviolet (UV) and infrared-resistant, self-cleaning, antireflective, electrical conductive and scratch-resistant properties (Bhattacharyya et al., 2009). The antibacterial action mechanism of nanoparticles is shown in Fig. 8.1.

Carbon nanodots are nanomaterials of size below 10 nm, having strong fluorescence. They are obtained through electrophoresis. According to Nuclear Magnetic Resonance (NMR) study, C-nanodots are derived from candle soot which is sp^2 hybridized with no saturated sp^3 carbon atoms. C-nanodots are good electron donor and electron acceptors too. They can be used as nanoprobes for sensitive ion detection, bioimaging as they have high PL quantum yield and photostability (Li et al., 2012). Fullerenes are cage-like molecules constituents, the third form of pure carbon. C60, the archetype, is the roundest molecule that can possibly exist. Other than C60, C20, C70, and C82 also exist, which are mainly used in catalysis and fullerene containing polymers. High fullerene containing living polymers are synthesized using norbornene derivative of fullerene (Nimibofa et al., 2018).

Nanoclusters composed of small number of atoms can be of single or multiple elements. Due to different electric structure and unusual physical and chemical properties, nanoclusters developed as new branch of fluorophores. They can be used in sensors and bioimaging because of attractive characteristics like ultrasmall in size, good dispensability, and good biocompatibility (Zhang and Wang, 2014). One of the noticeable aspects of properties of nanoclusters is superatom structure, ascribed to which nanoclusters exhibit similar properties to those of atoms of periodic table (Liu and Astruc, 2018).

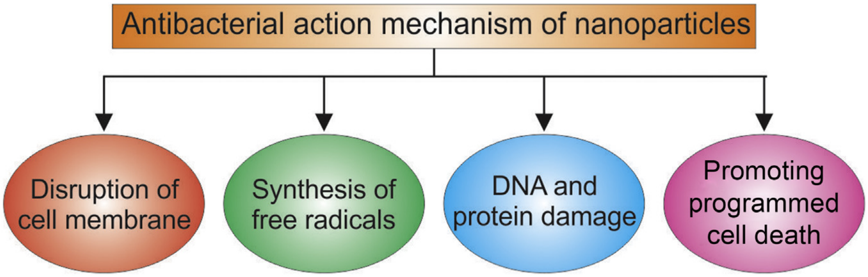

Figure 8.1 Mechanism of antibacterial action of nanoparticles.

8.3 Nanoparticle synthesis approaches

There are two common methods for preparation of nanomaterials i.e., top-down (size reduction from bulk material) and bottom-up (synthesis of materials from atomic level). In top-down approach, physico-mechanical methods such as crushing, electroplating, laser-ablation, lithography, milling, and grinding are used for production of nanomaterials from bulk materials (Abobatta, 2018). Basically, nanolithography is a method of fabrication, which is used to print the desired shape and structure on any light sensitive material of minimum one dimension i.e., size range of 1−100 nm. But, this process is comparatively expensive. To synthesize metal nanoparticles, laser ablation is proved to be a reliable method, which involves production by various solvents with the help of laser beam that condenses a plasma plume to fabricate nanoparticles. Thermal decomposition is another chemical method which is one of the top-down processes and produces particles endothermally by breaking chemical bonds. But, the synthesis of secondary products is the main challenge with this process. For milling and postannealing of particles, mechanical milling is believed to be the most popular method (Ealias and Saravanakumar 2017).

In bottom-up approach, there is production of uniformly distributed complex nanomaterials by self-assembly of small molecules. Different techniques like chemical vapor deposition, laser pyrolysis, liquid phase techniques, molecular self-assembly, and sol−gel processing are used for the synthesis of nanostructures using this approach. The ratio of chemical concentration and selected capping material are the main determinant for estimating the shape and size of nanostructure (Abobatta, 2018). Sol−gel is a wet chemical method, and it is commonly used because of its versatility as wide variety of nanoparticles can be synthesized. Chemical solution used in this method acts as precursor for the integrated system. The synthesis of nanoparticles can also be carried out by spinning disc reactor. Reactor is equipped with rotating disc inside with temperature controller and filled with nitrogen gas to avoid any chemical reaction due to the presence of oxygen.

Chemical vapor deposition is another method, which is basically the deposition of gaseous reactant on substrate in thin film form. Reaction is occurred by combination of substrate and combined gaseous molecules at ambient temperature followed by deposition. For industrial scale production of nanoparticles, pyrolysis is the best process. It proceeds by burning of a precursor in flame at high pressure (Ealias and Saravanakumar 2017).

8.4 Nanobiotechnology in food sector

Nanobiotechnology is an innovative technology gaining momentum in food sector which results in improvement of food quality and safety along with development of novel food products having thermal stability, better solubility, and oral availability (Semo et al., 2007). Various applications of nanomaterials and their impact in food sector are summarized in Table 8.2. This is one of the emerging technologies to meet global food demand and enhance incomes in developing countries (Roco, 2002). There are many positive effects of nanomaterials in agriculture in different forms like nanofertilizer (Abobatta, 2019), nanopesticide (Corradini et al., 2010), nanosensors (Das et al., 2009), postharvest

Table 8.2 Applications of nanomaterials in food sector.

Food application	Nanomaterial	Positive effect	Reference
Food preservation and packaging	Nanosilicates	Reduce food spoilage and rancidity by acting as gas, and moisture barrier in films.	Neethirajan and Jayas (2007)
	Zinc oxide nanosensor	Reduces change in color, and flavor of foods by blocking ultraviolet light.	Neethirajan and Jayas (2007)
	Nanosilver	Maintain healthy conditions on food surface with reducing microbial growth.	Travan et al. (2009)
	Nanocomposites	Lighter, stronger, and fire resistance packaging with better thermal properties and less permeability to gases.	Llorens et al. (2012)
	Nanolaminates	Enhance quality and shelf life of coated foods by incorporating active functional agents like antioxidants, antibrowning agents, antimicrobials, colors, enzymes, flavors into films.	Wesley et al. (2014)
	Chitosan nanoparticles	Possess broad spectrum antibacterial, antiviral, and antifungal activity.	Beyth et al. (2015)
Food contact material (crockery and cooking equipment)	Silver nanoparticles	Enhance antibacterial properties.	Miller and Senjen (2008)
Nutritional supplement	Silicamineral hydride complex	Act as antioxidant, and enhance potency and bioavailability.	Miller and Senjen (2008)
	Lipid nanoparticles	Improve bioavailability and retention of active biochemicals result in providing high-loading capacity and improved stability.	Gong et al. (2012)
	Selenium nanoparticles	Promote human health with additional antimicrobial and anticancer properties.	Skalickova et al. (2017)

Table 8.2 Applications of nanomaterials in food sector.—cont'd

Food application	Nanomaterial	Positive effect	Reference
Nutritional drink	Iron nanoparticles	Improve toddler health by increasing bioavailability and reactivity.	Miller and Senjen (2008)
Pathogen detection	Specified protein on silica chip	Detects specific foodborne pathogens by luminescence.	Homer et al. (2006)
	Luciferase nanosensor	Emission of light or fluorescence by attachment of dye with *Salmonella* and *Campylobacter*.	Fu et al. (2008)
	Carbon nanotubes and silicon nanowire transistor	Detection of cholera and staphylococcal enterotoxin B toxin.	Mousavi and Rezaei (2011)
	Immunogold nanoparticles	Detection of *Cronobacter sakazakii*.	Aly et al. (2018)
Testing of food quality	Nanobarcodes	Detection of quality of agricultural products.	Coles and Frewer (2013)
	Nano-smart dust	Detection of environmental pollution.	Coles and Frewer (2013)
	Gold and silver nanoparticles	Detection of food contaminants like melamine and malathion.	Paul et al. (2017)

technology (Meetoo, 2011), biosensors for aquaculture (Kumar et al., 2013), waste management (Bharathi et al., 2016), plant growth regulators (Choy et al., 2007), and agricultural engineering aspects (Melendi et al., 2008) due to improved targeted activity (Lu et al., 2002) and controlled release (Raliya et al., 2015) with safe and relaxed transport. It has been reported that nanotechnology is an emerging technology in animal husbandry in under developed countries (Eguchi et al., 2013).

8.4.1 Nanotechnology for food security

The UN millennium goal can be achieved by applications of nanotechnologies in agriculture and food sectors to ensure food security and safety (Sabourin and Ayande, 2015). Different crop management techniques have been improved significantly using nanotechnology-based agrochemicals. Nanotechnology helps in increasing the efficacy of pesticides, herbicides, and fertilizers through controlled release, and under environment friendly manner. In a previous study, chitosan and sodium alginate was used for encapsulation of imidacloprid which resulted in enhancement of its efficacy in soil applications (Guan et al., 2010). Nanomaterials are used in processing of meat products, its storage, and marketing (Gallocchio et al., 2015). Nano-feed, produced by nanosized additives and nanoclay, is used to provide better feed to animals by removing pathogens and toxins from processed foods for improving resistance against diseases, encouraging activation of animal's own self-healing forces, improving bone growth and phosphate utilization, and reducing mortality rate (Sekhon, 2014). Nanotechnology promises to improve feeding effectiveness and nutrition of animals and plant pathogen detection, reduce animal losses due to diseases, targeted genetic engineering, enhances conservation and management of crops, fisheries, and animal production (Singh, 2016a; Pramanik and Pramanik, 2016). This technology can be used to improve crop yield by developing healthy seeds and improving the effectiveness of fertilizers and pesticides (Teng et al., 2011; Seabra et al., 2013). It is also used for soil and water cleaning, remediation, and genetic engineering and molecular-based crop breeding to enhance the crop production (Parisi et al., 2015; Wani and Kothari, 2018). Nanocarriers are used for controlled release of plant growth regulators, herbicides, and pesticides. In a recent study, treatment of mustard plant (*Brassica juncea*) with atrazine (using poly epsilon-caprolactone as carrier) nanocapsules showed improved herbicidal activity, decreased photosynthetic rates and stomatal conductance, increased oxidative stresses, weight loss, and growth reduction (Oliveira et al., 2015). Nanoparticle-mediated DNA or gene transfer in plants has been used for developing insect resistant plant varieties by some researchers (Khot et al., 2012; Sekhon, 2014).

8.4.2 Nanotechnology for food preservation and storage

Nanotechnology is observed to be efficient for extending shelf life of food products with minimum loss of nutrients. Efficient and improved techniques such as nanosensors, nanocomposites, and nanoparticle in packaging are available for food preservation and storage. These techniques help in providing better food stability, bioavailability, preservation of color, etc. This technology has the potential to enhance storage period of fruits and vegetables (Parisi et al., 2015; Wani and Kothari, 2018). Different forms of nanosystems such as nanobarcodes, nanosensors, nanocapsules, nanocomposites, nanofibers, nanoparticles, and nanotubes have been used in food processing, packaging, and preservation as shown in Fig. 8.2 (Duncan, 2011; Bajpai et al., 2018). Nanocomposites are made of nanoparticles and polymers, and they are used in food sector for enhancing the shelf life of food products, keeping the products fresh, devoid of microbial action, and providing gas barrier to minimize the leakage of carbon dioxide from carbonated beverages (Pandey et al., 2013; Hamad et al., 2018). Guard IN Fresh is a nanocomposite-based commercialized product used for ripening of fruits and vegetables by scavenging ethylene gas (Gupta and Moulik, 2008). Nano-Ceram PAC is an ecofriendly nanocomposite-based coating material which helps in rapid absorption of unpleasant components of food, results in avoiding foul odor, and repulsive taste (Bordes et al., 2009).

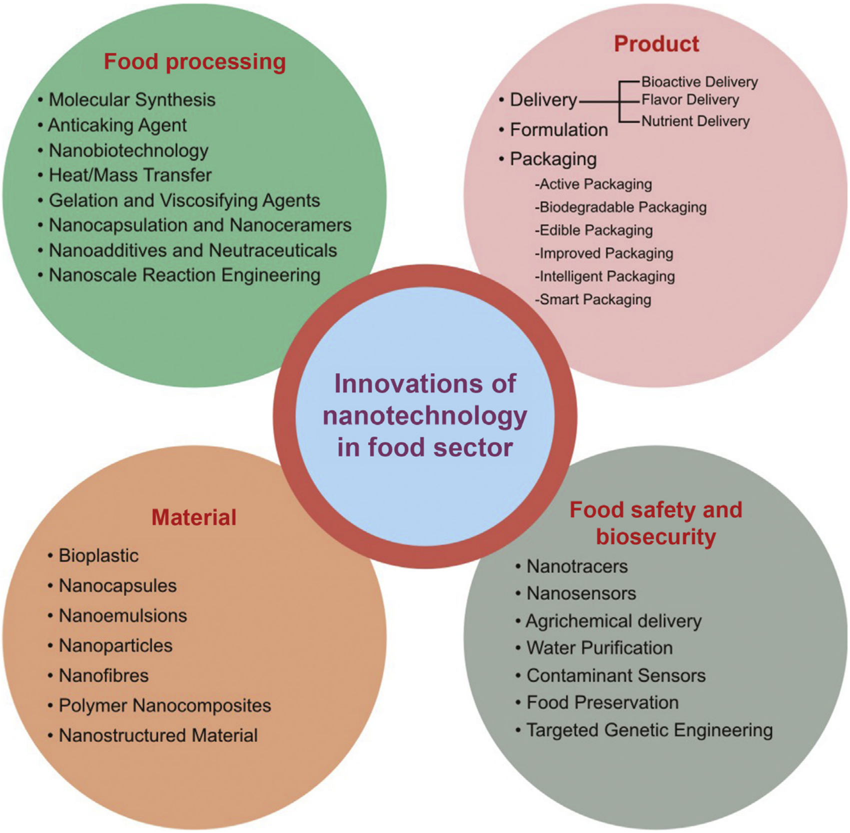

Figure 8.2 Different forms of nanosystems used in different food applications.

8.4.3 Nanotechnology in food packaging

Nanotechnology has provided better packaging options for food products by enhancing shelf life, better traceability of food products, and above all safety. One of the future advancement of this technology is use of polymer composites which provide active, flexible, and intelligent packaging (Aigbogun et al., 2017). Biologically synthesized silver and gold nanoparticles from *Fusarium* sp., *Pseudomonas struzeri, P. aeruginosa*, and *Penicillium* sp. are used for antimicrobial packaging (Sadowski et al., 2008; Khalilabad et al., 2013). Metallic nanoparticles like silicate nanoparticles, titanium oxide, and zinc oxide (ZnO) are used to remove chemicals and pathogens from foods, by reducing the flow of oxygen in the packaging containers, leakage of moisture, and keeping the food fresh for longer time (Nam et al., 2003; Horner et al. 2006). Nanoparticles such as ZnO, silver nanoparticles, inorganic nanoceramics (Arshak et al., 2007), silicon dioxide (Coma, 2008), TiO_2 (Acosta, 2009), and polymeric nanoparticles (Bouwmeester et al., 2009) are used in food packaging and preservation. It has also been reported that use of active coating by incorporating cinnamon oil and solid wax using nanotechnology provide protection to different foods such as bakery, cheese, and sliced meat against spoilage (Rodriguez et al., 2008). Active packaging films also results in selective control of oxygen transmission and aroma affecting enzymes, and hence avoid unnecessary oxidation of fats and oils, rancidity, off-odor, and flavor problems in packed foods (Rivett and Speer, 2009). Nanosilver, montmorillonites, and silver zeolite nanoparticles were used for producing chitosan-based edible nanoparticle films (Rhim et al., 2006). The use of nanoclay in plastic bottles stiffen the packaging and keep the beer fresher by minimizing loss of carbon dioxide from products, enhancing product shelf life and reducing gas permeability (Zhao et al., 2008). The incorporation of ZnO nanoparticles into plastic packaging provide antibacterial protection, improve strength and stability of plastic films, and reduce the chances of food contamination (Neethirajan and Jayas, 2011). One of the widely used nanomaterial for food packaging is nanoclay due to its low cost, corrosion resistance, thermal, mechanical, and barrier properties (He et al., 2019). A significant improvement in interlaminar fracture toughness and enhanced glass transition temperature by 6°C was observed with 3% nanoclay loaded woven carbon fiber/compatibilized polypropylene nanocomposites (Gabr et al., 2015). The nanoclay materials which have been listed under GRAS (Generally Regarded As safe) status and in effective Food Contact Substances (FCS) by U.S. FDA are montmorillonite and bentonite (He et al., 2019). The organic chemicals based edible coatings used for food packaging of perishable products are lemon grass essential oil (Trujillo et al., 2015), pectin from apples (Gorrasi and Bugatti, 2016), and quinoa protein/chitosan (Robledo et al., 2018).

8.4.4 Nanomaterials as antimicrobials

The conventional techniques used for controlling the microbial growth in food are thermal processing and chemical preservation. Recently, there is increased demand of natural food products for better health by consumers. Nanotechnology provides better alternate materials for providing antimicrobial activity with minimum toxic and undesirable side effects compared to physical and chemical methods. Moreover, this technology is one of the powerful tools to improve the shelf life of agri-food chain through technological advancement. The antimicrobial properties of nanoparticles result by inhibition of microbial growth on nonsterilized foods, and prevention of post-contamination of pasteurized foods. Silver nanoparticles are quite stable with broader spectrum of antimicrobial activity, and these nanoparticles are reported to be safe for biological system when incorporated within standard limits approved by Food and Drug Association (Zhao et al., 2008). The other nanoparticles which have been reported for antimicrobial activity are copper and copper oxide, chitosan, cadmium, magnesium oxide, selenium, single-walled carbon nanotubes, and telluride (Arshak et al., 2007). The antimicrobial activity of silver-coated nanocomposites, ZnO, and pediocin incorporated nanoparticles in nanocomposite films, and PEG (polyethylene glycol) coated with garlic oil composite has already been published (Moraru et al., 2003). Nanoparticles of ZnO possess antibacterial and antifungal activity against *Aspergillus niger, A. flavus, A. fumigatus* (Rajiv et al., 2013), *Fusarium graminearum* (Dimkpa et al., 2013), *F. culmorum*, and *F. oxysporum* (Rajiv et al., 2013). In a recent study, the antibacterial properties of *Lactobacillus plantarum* were enhanced through the induction of mild stress by pullulan nanoparticles (Hong et al., 2019). In another study, green synthesized gum stabilized nanoparticles loaded with flavonoids showed antimicrobial activity against infections caused by brain eating amoebae and multidrug resistant bacteria (Anwar et al., 2019).

8.4.5 Nanotechnology in nutraceuticals production and their delivery

Nanomaterials are used in food processing methods for incorporation of nutraceuticals like vitamin and mineral fortification, nanoencapsulation of flavors, and gelation and viscosifying agent and their delivery to the target site (Huang et al., 2010; Bajpai et al., 2018). β-carotenes, lycopene, and phytosterols like nutraceuticals are incorporated into foods in nanoformulations for effective delivery (Mozafari et al., 2006). The controlled delivery of nutraceuticals, antimicrobials, enzymes, food additives, etc., has been achieved using lipid-based nanoemulsions like archaesomes, nanoliposomes, and nanocochleates (Mozafari et al., 2008). Nanoemulsions are also used in food processing in the form of proteins (milk, egg, and vegetable proteins), carbohydrates (alginate, pectin, carrageenan, dammar gum, guar gum, sucrose-acetate isobutyrate, and xanthan) for improving the texture and uniformity of ice creams, reducing creaming and sedimentation, dispersion and availability of food nutrients, and production of food products like sweeteners, salad dressing, beverages, and other processed foods (Oberdorster et al., 2007; Kang et al., 2007; Fernandez et al., 2008). Nanotechnology is used for delivery of nutraceuticals and bioactive compounds available in functional foods like β-glucan from oats, β -carotene from carrots, conjugated linoleic acid from cheese, isoflavones from soyabean, omega-3-fatty acid from salmon oil, lycopene from tomato (Chen et al., 2006). The nanosized micelles produced by milk protein, casein, is used as vehicle for delivery of sensitive health-promoting ingredients including vitamin D2 (Semo et al., 2007). Fig. 8.3 represents the processing of raw materials for their introduction in foodstuffs.

There are several benefits of nanoencapsulation system such as enhanced stability and integrity, change in flavor, enhanced bioavailability, easy handling of food products, pH- and moisture-triggered controlled release, long-lasting organoleptic perception, retention of volatile ingredients, taste making, protection against rancidity and oxidation, and consecutive delivery of multiple active ingredients (Shefer, 2008). Nanoencapsulation

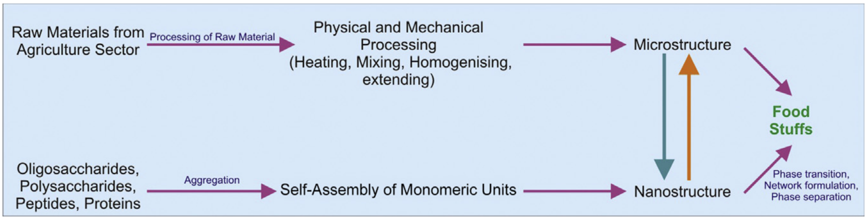

Figure 8.3 Preparation of nanoparticles for their applications in foodstuffs.

with calcium alginate is observed to improve the viability of probiotic microorganisms such as *Bifidobacterium* sp., *Lactobacillus casei, Lb. acidophilus*, and *Lb. rhamnosus* in freeze-dried yogurt (Duncan, 2011). George Weston Foods, Australia, has integrated nanocapsules into bread to avoid unpleasant taste, and odor from tuna fish oil, and hence provides controlled release of beneficial probiotic microorganisms to promote gut health (Neethirajan and Jayas, 2007). Encapsulation of curcumin into hydrophobically modified starch showed improvement in its anticancerous property (Yu and Huang, 2010). Polylysine nanoparticles are smaller than phytoglycogenoctenyl succinate nanoparticles and used as antioxidant in foods to prevent unnecessary oxidation of oils (Scheffler et al., 2010). The nanocoating alginate/lysozyme nanolaminate is used to preserve the quality of fresh foods during storage (Medeiros et al., 2014), chitosan/nanosilica coatings (Shi et al., 2013), chitosan film with nano-SiO_2 (Yu et al., 2012), and gelatin-based edible coatings containing cellulose nanocrystals (Fakhouri et al., 2014). Nanomaterials provide promising approach for improving the bioavailability of nutraceutical compounds due to their subcellular size (Singh et al., 2017). Carotenoid nanoparticles showed improved bioavailability of carotenoids and nano-based mineral supplements (nano-iron and nano-calcium). Nanometer-sized micellar systems are also available for delivery of minerals, phytochemicals, and vitamins (Singh, 2016b). The most frequently used nano-formulations for food supplements are micelles, nanoemulsions, nanocapsules, nanosponges, nanogels, nanofibers, nanoliposomes, core—shell nanoparticles, solid lipid nanoparticles, layered double hydroxides, mesoporous silica nanoparticles, and cyclodextrin complexes (Jampilek et al., 2019).

8.4.6 Nanosensors in food sector

Nanosensors are electronic devices which possess a sensing part and an electronic data processing part. The sensing part is used for the detection of gases (hydrogen, ammonia, sulfur dioxide, hydrogen sulfide, and nitrogen oxides), heat, light, foodborne pathogens, humidity, and chemicals, and electronic data processing part produces electrical signals (Rubio et al., 2006; Kang et al., 2007). Zhao et al. (2004) has developed 60 nm fluorescent biosensor for *in-situ* pathogen quantification by using Ab-conjugated silica in ground beef. Similarly, many fluorescent dye biosensors and magnetic nanoparticles—based biosensors have been developed for the detection of *Salmonella* (Fu et al., 2008), *Campylobacter* (Stutzenberger et al., 2007) and *Escherichia coli* (Cheng et al., 2009) in food samples. In a recent study, luminescence oxygen biosensor is reported to be relatively cheap and more compatible for smart food packaging (Kelly, 2017). A fluorescent nanobarcode detection system has been developed for detection of several foodborne pathogens such as *E.coli*, anthrax, tularemia bacteria, Ebola, and severe acute respiratory syndrome (SARS) virus by different color codes in a computer scanner (Li et al., 2005). A Dip-pen nanolithography technique has been developed by NanoInk, Skokie, for detection of food products and pharmaceutical pills. This detective tool is currently used by Barcode, a registered US company, for traceability to ensure wholeness (Zhang et al., 2009). Reflective interferometry was used previously for the detection of *E. coli* contamination in packaged foods (Wanekaya et al., 2006). In a previous study, metal-based nanosensors (palladium, platinum, and gold) were used in food packaging for detection of change in food color and gases produced by spoilage (Kang et al., 2007).

Similarly, single-walled carbon nanotubes and DNA were used for detection of presence of pesticides on the surface of fruits and vegetables, and monitoring of soil conditions required for growth of crops (Sozer and Kokini, 2009). Several immunosensors have been developed for detection of toxins such as cerium oxide immunosensor for ochratoxin A, and chitosan-based nanocomposites, silicon nanowire transistors, and carbon nanotubes for Cholera toxin and Staphylococcal enterotoxin B (Rai et al., 2012). Nano-smart dust is observed to be useful in food packaging for detection of any kind of environmental pollution. Biomimetic sensors and smart biosensors were used for detection of presence of mycotoxins, bacteria, viruses, and other pathogens (Coles and Frewer, 2013). In a recent study, the use of nanomaterial-based sensors have been reported for sustainable management of agricultural soil, detection, and protection against pathogens, for food quality and safety, for improvement of crop practices, food quality, and packaging methods (Kim et al., 2018).

8.5 Other applications of nanotechnology

There are tremendous applications of nanotechnology in different sectors like food and agriculture, paper and pulp, paints and coatings, textiles and clothing, defense and security, medicines and drugs, bioengineering, optical engineering, medicine, cosmetics, electronics, energy, space exploration, and transportation (Mihindukulasuriya and Lim, 2014). Liposomes, TiO_2, ZnO, dendrimers, nanoemulsions, and nanocrystals are used in sunscreen, moisturizers, makeup, and hair care products. The use of ionic or metallic silver has been reported in different sectors such as sunscreen lotions, steel coatings, wastewater treatment, and textile fabrics (Duran et al., 2007). In modern cosmetic world, nanosized components are reserving their place in products like moisturizer, hair products, and makeup products. The main interest is liposome-based antiaging topical formulation. Nanoparticles such as TiO_2 and ZnO are used as UV fillers. The main reason behind the use of nanoparticles in cosmetic industry is to improve the penetration capacity of certain ingredients like vitamins, unsaturated fatty acids, and antioxidants along with the stability of these ingredients. Due to certain properties shown by nanoparticles, they increase the efficiency and tolerance of UV filters on skin (Mu and Sprando, 2010).

Hydrogen economy is gaining huge attention and so is the implementation of nanotechnology in storage of hydrogen and advances in the use of nanomaterials for solar hydrogen nanostructure of semiconducting metal oxides as TiO_2, ZnO, and Fe_2O_3 are stable than common solar cell materials and cheaper too that make the commercial viability (Krol et al., 2008). Along with disciplines of biology, chemistry, engineering, or medicine nowadays, nanotechnology is expanding its uses and wide interest in interdisciplinary research like cancer nanotechnology. Issues in dealing with cancer nanotechnology are cancer detection, diagnosis and treatment which are quite different from conventional therapeutics like nanosystems can diagnose the problem as well can carry therapeutic payload. Alongside multiple cells can be targeted with high affinity. Nanosystems are designed to accommodate multiple drug molecules for cancer treatment like toxicity in normal cell can be monitored (Misra et al., 2010).

The field of drug delivery is improved by enhancing the treatment methods like artificial implant and organ transplants with the help of nanotechnology and the advances in the reproduction and repair of damaged tissues methods. Nanotechnology makes the process of construction quicker, safer, and cheaper. With the use of nanoparticles, mechanical properties of composites can be improved, and it provides better blocking of light and heat penetration. Addition of relevant nanoparticles enhances self-healing ability to provide insulation. These paints can be used for coating purpose to prevent from salt water attack because of its hydrophobic properties. For the treatment of surface water and to remove heavy metals, pathogens, and organic contaminants, nanotechnology is the leading remediation. Nanoparticles can also be used to clean oil spills as well as for the treatment of sludge and industrial wastewater produced (Ealias and Saravanakumar, 2017). As per studies, nanoparticles and nanoclusters show appreciable applications for catalysis purpose. In the case of gold, nanoclusters are proved to be more reactive than that of nanoparticles because of well-defined size and structural properties shown by them (Safari and Zamegar, 2014; Nasiruddin et al., 2018).

8.6 Global status of nanotechnology in food sector

The companies which are making advancements in the field of nanotechnology all around the world include Adnano Technologies, Dabur Pharma, Meda Biotech, Nano-Bio Chemicals, NanoShel, NanoXpert Technologies, Sisco Research Laboratories, Quantum Corporations, and Velbionanotech (http://www.foresight.org/policy/brief1.html). The major players of nanoencapsulated food additives in the world are Advances BioNutrition Corporation, ABCO Laboratories, Inc., Aveka Group, Aveka Inc., Balchem Corporation, Coating Place Inc., Encapsys LLC, LycoRed Ltd., Maxx Performance Inc., Sensient Technologies Corporation, Cargill Inc. (USA), Royal DSM N.V, FrieslandCampina Kievit (The Netherlands), Firmenich SA (Switzerland), Symrise AG (Germany), and Taste Tech Ltd. (UK) (Food Encapsulation Market, 2018−2024). Nanoencapsulation with canola active oil has been used by Shemen in Haifa, Israel, for several commercialized food products (Bikker and Kruif, 2006). Nanoencapsulation is also used by other companies for different food products such as Fortified Fruit Juice by High Vive, NanoResveratrol by Life Enhancement, Spray for Life Vitamin Supplements by Health Plus International, Daily Boost by Jamba Juice Hawaii, Color Emulsion by Wild Flavors, Nanoceuticals Slim Shake Chocolate by RBC Life Sciences Inc., and Nanotea by Qinhuangdao Taiji Ring Nano-Products Co. Ltd (Cobb and Macoubrie, 2004; Donaldson and Seaton, 2007). A sponsorship program has been launched in 2007 by Working Party on manufactured nanomaterials of the Organization for Economic Cooperation for

Development for the testing of manufactured nanomaterials (OECD, 2007). The share of nanotechnology in global food and beverage industry is multitrillion dollars (Cushen et al., 2012), and the worldwide economic impact of nanotechnology is targeted to three trillion dollars by 2020 (Roco et al., 2011). Second Regulatory Review on nanomaterials by EU (European Union) recommended the compulsory labeling of nanoingredients in food products and this policy was applicable from December 2014 (EU, 2012a). EU MEMO (2012) has made regulations for nanomaterials in environmental legislations such as water, waste, and air (EU, 2012b). Taiwan FDA guidelines (2017) consider nanomaterials as new food contact substances and enforce safety assessment of food packaging nanomaterials with premarket approval (https://www.fda.gov.tw/TC/newsContent). In USA, the R&D agencies which are actively indulged in nanobiotechnology research especially in food sector are Agriculture and Food Research Initiative (AFRI), Center of Nanoscale Science and Technology (CNST), National Nanotechnology Initiative (NNI), National Institute of Health (NIH), National Institute of Food and Agriculture (NIFA), and US Department of Agriculture (USDA). NNI is announced to provide nearly $1.4 billion in 2019 for basic research, early-stage applied research, and technology transfer efforts in the field of nanotechnology (http://www.nano.gov/about-nni/what/funding). The funding bodies of Europe in the field of nanotechnology are Austrian Nano Initiatives (ANI), Biotechnology and Biological Sciences Research Council (BBSRC), European Commission (EC), Engineering and Physical Sciences Research Council (EPSRC), Medical Research Council (MRC), and Regional Developmental Agencies (RDA) (http://atip.org/index.php/atip-publications-2/atip-reports/2008-1/6214-atip08-007-nanosciencenano-funding-in-europe-an-overview). The funding bodies in India which provide funds for innovations in the area of nanotechnology are Council of Scientific and Industrial Research (CSIR), Defense Research Development and Organization (DRDO), Department of Atomic Energy (DAE), Department of Biotechnology (DBT), Department of Science and Technology (DST), Indian Council of Medical Research (ICMR), and Ministry of New and Renewable Energy (MNRE) (McClements and Rao, 2011).

8.7 Safety issues of nanoproducts in food

Nanomaterials can cause harmful effects on environment and human health due to their participation in different chemical reactions resulting by their unique physical and chemical properties. The enhanced concern on safety issues of nanomaterials by private and government sectors are due to their extensive use in food products as color additives or flavoring agents. Nanomaterials have been disposed of by many manufacturing industries, and these nanomaterials can accumulate in soil and water which results in disruption and alteration of microbiota of that region. Nanoparticles are observed to accumulate on the surface of marine bodies, which lead to toxic effects on phytoplanktons that in turn affect the pelagic species. The benthic species also get affected when surface nanoparticles accumulate at the bottom of marine bodies. The inhibition of plant growth by aluminum nanoparticles has also been reported (Morones et al., 2005). It has been pointed in an editorial note entitled "Nanofood for Thought" that benefits of nanotechnology can reap in food industry if issues related to their safety are addressed honestly and companies are more open about what they are doing (Nature Nanotechnology, 2010). Several previous studies have revealed the toxicity effects of nanomaterials used in food ingredients and packaging. For the evaluation of risk assessment of nanomaterials, it is essential to quantify various factors like biological molecules, commensal microbes, osmotic concentration, physical factors, chemical forces, osmotic concentration, absorption, distribution, metabolism, and excretion (He et al., 2015). The toxicity effects of nanomaterials on human organs directly depends on their physicochemical characteristics such as their concentration in food, amount of that food consumed, bioavailability, and biodistribution (He et al., 2015; He and Hwang, 2016; Wani and Kothari, 2018).

Absorption, distribution, metabolism, and excretion of nanoemulsions change with change in size, and it is one of the major complications for ingestion of nanofoods (Chawengkijwanich and Hayata, 2008). Nanoparticles behave similar to asbestos (Hett, 2004), and these particles may settle in brain or trigger immune response (Scrinis, 2008). The small sized nanoparticles possess large surface area, and hence, they can easily pass through biological barriers and accumulate in tissues like central nervous system (Borm and Kreyling, 2004). Chemical composition of nanoparticles is very crucial to estimate the toxicity level of semiconductor nanoparticles and carbon nanotubes. Different cytotoxic effects have been reported with different levels of titanium oxide crystallinity (Stolle et al., 2009), and iron ions may accelerate cellular oxidative stress (Murray et al., 2009). Toxicological effects of absorbed nanoparticles in human system are influenced by their surface chemistry, charge, roughness, and hydrophobicity (Kirchner et al., 2005). Positively charged nanoparticles are found to be more toxic than negatively charged and neutral nanoparticles, and hydrophilic polymer i.e., PEG decreases the toxic effect of nanomaterials (Sukhanova et al., 2018). Solubility is another important parameter affecting the toxicity of nanoparticles, and soluble titanium oxide nanoparticles are reported as more toxic than insoluble ones (Oberdorster, 2001).

Similarly, the carcinogenic effects of soluble nickel compounds have already been published (Salnikow and Kasprzak, 2005). There are different effects of digestible organic nanoparticles (carbohydrates, proteins, lipids, and surfactants), and nondigestible inorganic nanoparticles (metals and minerals) on the body (Chen and Evans, 2005). One of the major factors affecting the toxicity of nanoemulsion is bioavailability of components within biological system. The low bioavailability of component within nanoemulsion but its high absorption rate may result in bioaccumulation of component within living system. Consumption of large amount of nanoemulsions may show adverse toxic effects in human system due to chemical nature of solvents and surfactants (Cushen et al., 2012). Silver nanoparticles have been reported to show adverse effects on human lung fibroblast by increasing reactive oxygen species, damaging DNA and mitochondria, chromosomal aberrations, and decreasing ATP content. Hence, cytotoxic, genotoxic, and carcinogenic effects of silver nanoparticles have been detected on biological system (Kim et al., 2007).

Carbon nanotubes, which are commonly used in food packaging, showed toxic effects on human skin and lungs (Mills and Hazafy, 2009). The gradual accumulation of TiO_2

nanomaterials in the body has been reported by Jovanovic (2015) after consuming chewing gum containing TiO_2 nanomaterials. In a similar study, SiO_2 nanoparticles have been found to accumulate in the gut epithelium after consuming food containing E551 (Athinarayanan et al., 2014). Nanomaterials promote the allergic pulmonary inflammation by increasing the production of reactive oxygen species (Syed et al., 2013), and by inducing nanoparticle-specific immune response (Hirai et al., 2014). Increased gene expression of interleukins (IL-4, IL-10, IL-13) and allergy-associated Th2 cytokines were observed when exposed with small sized (22 nm) carbon black nanoparticles (Lefebvre et al., 2014). Different metallic nanoparticles such as ZnO (Fukui et al., 2012), Ag (McShan et al., 2014), and CuO (Karlsson et al., 2013) can show adverse effects into food stimulants by enhancing intracellular reactive oxygen species, which may result in lipid peroxidation and DNA damage (Fukui et al., 2012). The toxic effects of nanoparticle components have also been approved by Great Britain, which recommends the toxicity assessment of nanomaterials by scientific institutions before their approval for use in food products (Krishnan et al., 2018). However, traditional methods such as 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) or casein AM (CAM) are not useful to evaluate the toxicity of various nanostructures like quantum dots, fullerene, and single-walled carbon nanotubes (SWCNT). Moreover, there are limited toxicological studies on nanomaterials used for edible coatings and food packaging, and hence, future *in-vivo, in-vitro*, and *in-silico* evaluations are needed to establish standard protocols for risk assessment and control the safety issues associated with use of nanomaterials in food sector.

8.7.1 Global concerns about safety issues of nanoproducts

The regulatory bodies that govern use and applications of nanosystems in food in different regions are Consumer Product Safety Commission (CPSC), National Institute for Occupational Safety and Health (NIOSH), Occupational Safety and Health Administration (OSHA), US Patent and Trademark Office (USPTO), USDA, Environmental Protection Agency (EPA), European Food and Safety Authority (EFSA), and Food and Drug Administration (FDA) (Qi et al., 2004). Food industries involved in food processing, packaging, and its preservation need to follow these regulations. Size of nanoparticle is another concern for consumer, and regulations on particle size have met by European Parliament and Council Legislation (Carvajal et al., 2010). The food industries have to strictly adopt precautionary principle to avoid incorporation of engineered nanomaterials in the food (Rhim and Ng, 2007). Other regulations approved by EC states that engineered nanomaterials should be free from mycotoxins, heavy metals (Scampicchio et al., 2008), prevent change in inherent, and organoleptic properties of food (Silva et al., 2012) should not promote deterioration of food and harmful health effects, and nanocomponent should be assessed as food additive before its use as packaging material (Sondi and Sondi, 2004).

The emerging applications of nanotechnology in agriculture, food processing, packaging, preservation, water treatment, and safety concerns with use of nanomaterials have been discussed in the conference entitled "Nanotechnologies in the Food and Agriculture Sectors: Potential Food Safety Implications" held by Food and Agriculture Organization of the United Nations (FAO) and World Health Organization

(WHO) in 2009. Experts from 13 countries (Australia/New Zealand, Brazil, Canada, China, European Union, Indonesia, Japan, Malaysia, Mexico, The Republic of Korea, South Africa, Switzerland, and United States) around the world have attended this meeting and shared the safety concerns of nanomaterials on human health, and recommended early consideration of their safety (FAO/WHO, 2010, 2013). In 2012, FAO and WHO have released an article entitled "State of the art on the initiatives relevant to risk assessment and risk management of nanotechnologies in the food and agriculture sectors", and this article includes the applications of nanomaterials in food packaging, recent activities in risk assessment, and management of nanomaterials at national and international levels, and current status of nanosafety management in the participatory countries (FAO/WHO, 2012). Requirement of one-time reporting and record keeping for control of have been proposed by nanoscale materials EPA, US, in 2015 under Toxic Substances Control Act, Section 8(a) (EPA, 2015). The use of selenium nanoparticles in multilayer films for food packaging was observed to be safe by European Food Safety Authority (EFSA) Panel on Food Contact Materials, Enzymes, Flavorings, and Processing Aids (Bergeson and Hutton, 2018).

The regulatory norms are still not strictly followed in many developing countries, where no specific regulatory framework is followed. However, it is utmost essential to set strict regulatory guidelines of nanoparticles at global level for safe use of nanomaterials in food products.

8.8 Conclusions and future recommendations

It has been concluded that nanobiotechnology is one of the emerging field of nanotechnology in food sector due to its potential applications. Food shortage is one of the major challenges which is expected to be faced by the world in the near future due to expanding population growth, pressure on environment, and efficiency on production system. The major challenge of food sector is development of better food manufacturing, preservation, and storage techniques to provide healthier and nutritious food for human welfare. Hence, nanobiotechnology is an alternate opportunity to overcome global problem and help in providing authenticated, nutritious, safe, secure, shelf-stable, high-quality, fortified, and therapeutic food products to future generations. It is widely accepted that nanofoods will be available largely to consumers worldwide in coming years. Nanotechnology can offer reduced chemical inputs, improved plant growth, use of nanofertilizers and nano-pesticides, and improved crop yield, and productivity for sustainable future. This technology is considered as one of the six "Key Enabling Technology" by EC to support greener farming and growth in food sector. Therefore, nanotechnology can be integrated with agriculture to reduce poverty, food security, agriculture growth, management of environment sources, and securing social outcomes. Moreover, many innovative hybrid technologies can be developed by integrating nanotechnology with pharmaceuticals, biotechnology, molecular biology, and computational technology.

Nanoparticles have great potential to enhance the bioavailability of nutraceuticals, and bioactive compounds, their controlled release with fine-tuning of bioavailability, pharmacokinetics, and bioefficacy. The major concerns for food scientists and regulatory bodies are consumers' benefit and safety of food products. Hence, it is essential to invest financial resources, sufficient time, and technological means to achieve commercialization of nanoproducts in the market. There are many regulatory agencies like European Food Safety and FDA, which stress upon the importance of nanoparticle characteristics like particle size, and surface properties, and association of nanomaterials with intestinal absorption along with hazardous analysis of tiny molecules. The industries should strictly follow the regulatory guidelines given by regulatory bodies like FDA and WHO to evaluate the safety of food, food packaging, storage, and use of food supplements. There is limited information about safety after oral administration of nanomaterials, their absorption, distribution, metabolism, and excretion. It is also required to develop novel and standardized tests for testing the toxic hazardous effects of nanomaterials on environment and human health, tissue distribution, and risks associated with their exposure. In addition, it is essential to set strict regulatory guidelines of nanoparticles at global level for safe use of nanomaterials in food products. The use of instrumentation and computational science can help researchers and scientists to gain unprecedented information about toxicological effect of nanomaterials on human cell lines. Hence, technological, scientific, and social considerations are required to enhance the applications of nanotechnology in different sectors in the coming years. Further, some focus is required to engineer nanomaterials with modern and advanced technologies to make this technology more efficient in food industry in coming years.

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