J. Mat. NanoSci. 2015, 2(1), 8-14 Review Article

Journal of
Materials NanoScience

Integrated Science

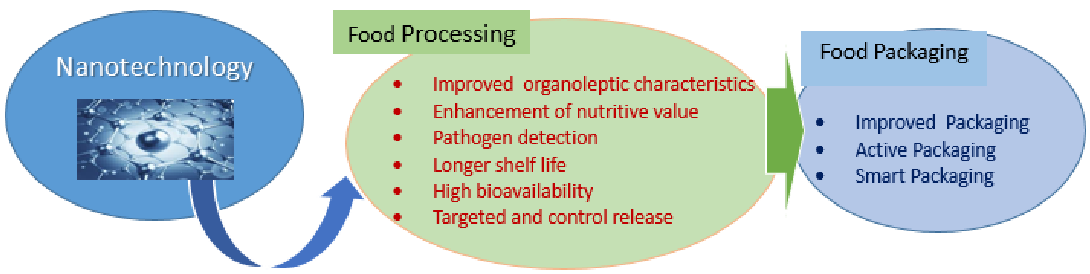
Significance of nanotechnology advances in food processing and packaging: consequences on human health

Indu Nashier Gahlawat, Manisha Wadhwa nee Dabas, Poonam Lakra*

Aditi Mahavidyalaya, University of Delhi, Bawana, Delhi. India.

Submitted on: 12-Feb-2015 Accepted and Published on: 4-Jun-2015

ABSTRACT



Nanotechnology has revolutionized many scientific and industrial fields and has also made a good beginning in the food science and technology. Recent research has revealed enormous applications of nanomaterials for food processing and packaging. Nanomaterials brings a remarkable difference not only in terms of food quality but also in various health aspects. In food processing, it improves the sensory characteristics like taste, texture, and appearance, extends shelf life, enhances nutritional bioavailability of nutrients, and removes chemicals and pathogens from food. Nano food packaging technology extends food life due to high barrier packaging material and improves food safety. The application of nanosensors allows consumers to identify whether food is contaminated or spoiled. Controlled and continuous release of preservatives help to prolong the food's life in the package. The intelligent packaging nanomaterial can slow down product deterioration and can tell about product safety and quality. As research in nanotechnology continue to expand, its applicability to the food industry will increase further. The use of nanomaterials also raises a serious concern about the toxicity of nanoparticles in food. This necessitates more studies to establish their impact on health.

Keywords: nanotechnology, nanomaterials, processing, package

INTRODUCTION

Recently, nanotechnology has gained importance in several fields of the food sector.[1,2] It is a technology that deals in nanometer scale to create and use materials with unique and novel properties. The technical revolution initiated by nanotechnology has a wide range of applications in the food industry. Nanotechnology offers several opportunities to develop and apply structures, materials, or systems with novel properties in various fields like agriculture, food, materials[3] and medicine.[4–6] It is observed that these materials have properties different from their macroscale counterparts due to the high surface to volume ratio. They exhibit many novel physicochemical properties like color, strength, diffusivity, toxicity, optical, thermodynamic behaviour.[7]

The food market demands technologies necessary to maintain market leadership in the food industry to produce fresh, healthy, convenient, and appealing food products. Extending the product shelf life, freshness and the nutritional quality of food are the major targets while designing the materials for food packaging. In this context, the nanoscience and nanotechnology based scientific advancements have the possible potential to revolutionize the food industry.[1,2]

The demand for nanoparticle-based materials has been on the rise in the food industry, as many of them possess essential

Corresponding Author: Dr. Poonam Lakra
Aditi Mahavidyalaya, University of Delhi, Bawana, Delhi. India.
Tel: xx
Email: poonam03lakra@gmail.com

Cite as: *J. Mat. NanoSci., 2015, 2(1), 8-14.*

 ISSN 2394-0867 http://pubs.iscience.in/jmns

elements, and are also reported to be nontoxic,[8] and these materials have been observed to be stable at high temperature and pressure.[9] Nanotechnology covers a broad range of food improvement from food manufacturing and processing to packaging. Nanomaterials, along with the improvement of food quality and safety, also has health benefits.

In food processing, the nanomaterials can be used as food additives, carriers of nutrients, antimicrobial agents, fillers for improving the physical strength and durability of the packaging material, etc. Food nanosensors can be used to achieve better food quality and as a safety check.[10] In this review, the role of nanotechnology in food processing and packaging along with the safety aspects associated with this technology have been discussed.

NANOTECHNOLOGY AND FOOD PROCESSING

Food processing involves the conversion of raw materials into marketable products having a long shelf life. Nano Technology finds varied use in food processing. It is associated with improvement in many functional properties like taste, texture, consistency, and bioavailability of food products.[11] The nanomaterial helps to provide the right color and flavor to improve the product appeal. The shelf life of meat, fruits, vegetables, bakery, and confectionery products can be extended by using edible nano-coating as they act as gas and moisture barriers and thus help to bring down the food wastage due to microbial infestation.[12] Some innovative uses of this technology include removing any component from the food ingredient to make it suitable for a particular group of consumers, like substituting lactose in the milk with other sugar to make it ideal for lactose intolerant patients. Production of healthier processed foods with low fat, sugar, and salt is also feasible. Nanocarriers are being used as food additives in food products without changing their basic morphology (Figure 1).

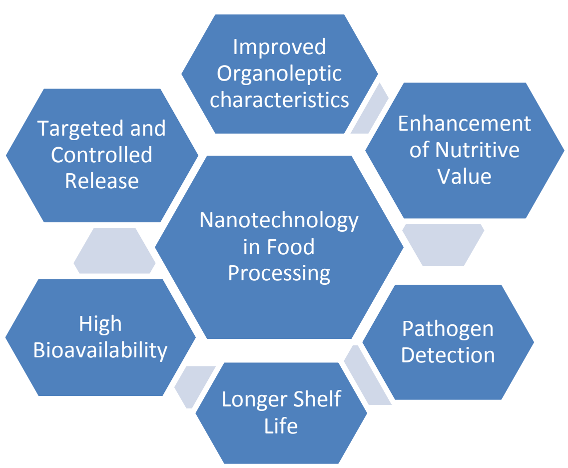


Figure 1. Role of nanotechnology in Food Processing

The role of nanotechnology in food processing can be discussed under the following categories:

Improve Organoleptic Characteristics of foods:

Nanotechnology has made advancements to improve the sensory qualities of foods like taste, texture, and appearance. Encapsulation, a process in which one material is used to deliver another material inside the human body, has been improved using nanotechnology.[13] Nano encapsulated food products and supplements are helpful to mask the bad taste. Nanocapsules can be used to incorporate vitamins or specific fatty acids. These nanocapsules bypass the taste buds, open on reaching the stomach, thus avoiding the unpleasant taste. This technique successfully improves the release and retention of the flavor of unstable and highly reactive pigments like anthocyanins.[14] Nanomaterials like SiO2 are most commonly used as carriers of fragrances or flavors in food products.[15] Rutin is a widely used dietary flavonoid with pharmacological activities, but it has restricted use in the food industry due to low solubility. The ferritin nanocages encapsulation increased the solubility and stability of rutin trapped inside ferritin compared to rutin in free form. Nanoemulsions can be used to deliver lipid-soluble bioactive compounds as they are formed easily with natural food ingredients. These may be designed to improve qualities like water-dispersion and bioavailability.[16]

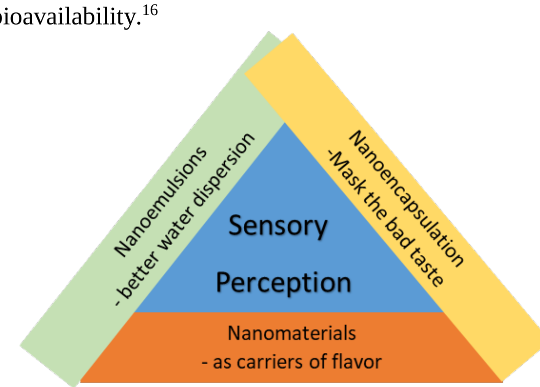


Figure 2. Nanotechnology used for organoleptic characteristics

Enhancement of nutritional value:

Nanotechnology offers viable solutions to improve the nutrition, health, and wellbeing of masses by increasing the availability of nutrients with various food vehicles having different physicochemical properties. Several nano delivery vehicles like association colloids,[17] lipid-based nanocarriers, nanoemulsions,[18] biopolymeric nanoparticles,[19] and nanofibers[20] are developed. The stomach acidic environment denatures many bioactive substances like lipids, proteins, carbohydrates, and especially vitamins. Encapsulation helps these bioactive substances overcome such adverse conditions and facilitate their ready assimilation in food products. This property is available only in encapsulation as in non-capsulated form, there is poor assimilation due to low water-solubility of these substances. To improve the availability of medicines, vitamins, or other essential micronutrients in daily foods, nanoparticles-based, tiny edible capsules are being manufactured.[21] Moreover, gastrointestinal permeability can be improved by choosing suitable formulation surfactants. This can increase both the absorption and bioavailability of nutrients. For example, soy protein based nanoemulsions has the ability to enhance the stability, bio accessibility and permeability of green tea catechins. Due to surface-modified nano delivery systems,[22,23] their interactions with biologic milieu and biodistribution could be better controlled. With the chemical grafting of hydrophilic molecules, it is possible to modify the nano delivery systems. Poly (ethylene glycol) is the most commonly used hydrophilic molecule. In this way, molecular transformation can be changed for maximum bioavailability and absorption. Several nutritional supplements containing nano ingredients (e.g., vitamins, antioxidants, etc.) are currently available. All of these products claimed to have enhanced absorption and bioavailability of components in the body.

Provide a table here for the examples of nanomaterials used for specific methods towards increase in nutritional value (as discussed above).

Longer Shelf life:

Bioactive compounds in foods often get degraded soon, leading to their inactivation due to the unfavorable environmental conditions. Nanoencapsulation of these bioactive compounds helps to extend their shelf-life by delaying the degradation processes till the product reaches the target site. The edible nano-coatings on several food materials help provide a barrier that prevents moisture from entering and inhibits gas exchange factors for the deterioration of the product. For example, the shelf life of tomato is extended by the bionanoencapsulated quercetin (biodegradable poly-D,L-lactide). This approach can extend the shelf life of other fruits and vegetables. Besides, it provides colors, flavors, antioxidants, enzymes, and anti-browning agents and helps extend the shelf-life of packaged foods, even after being opened.[24] Encapsulating the functional components slows chemical degradation processes by altering the properties of the interfacial layer around them. For example, curcumin, a very active and less stable bioactive compound of turmeric, was reported to be stable during pasteurization and at various ionic strengths upon encapsulation. Also, nanoencapsulation of probiotics is an efficient way to deliver them to the gastrointestinal tract efficiently.

Furthermore, an edible coating is the most common way to prevent browning in fresh-cut fruits.[25] Browning of fresh-cut fruits during storage is due to the conversion of phenolic compounds into colored pigments in the presence of oxygen.[26] These undesirable changes can be prevented by applications of nanomaterials as anti-browning agents. Nano-ZnO-coated active packaging has been used to improve shelf-life properties of freshly cut "Fuji" apples.[27] It was reported that the activities of polyphenol oxidase and pyrogallol peroxidase decreased significantly in cut fruits stored in nano-ZnO packaging.

Nanoencapsulation	• Extends shelf life of bioactive compounds. • For example helps to deliver probiotics efficiently to gastrointestinal tract.
Edible nanocoating	• Prevents moisture loss and gaseous exchange and thus extends shelf life • Serves as anti-browning agents for cut fruits

Figure 3. Preservation of food materials by nanotechnology

Pathogen detection:

Nanomaterials are used for the construction of biosensors having high sensitivity along with novel attributes. These nanosensors are used to detect pathogens in processing plants or in food material and alert the consumers and distributors about food safety status.[28] The nanosensor works as an indicator that respond to changes in the environment, such as humidity or temperature during storage, microbial contamination, or product degradation.[29] Thousands of nanoparticles on a platform have been designed to fluorescence in specific colors when they contact food pathogens. Several nanostructures like nanofilms, rods, particles, and fibers have been considered for their possible use in biosensors.[30] When specific protein molecules are immobilized on sensor chips in these sensors, they emit signals to detect target molecules.[31] For example, a dimethylsiloxane microfluidic immunosensor has been constructed by integration of specific antibody with immobilization on an alumina nanoporous membrane and evaluated for rapid detection of foodborne pathogens like Escherichia coli.[32] It was reported that nanotechnology is also useful in the detection of pesticides,[33] pathogens, and toxins[34] in the food quality chain. Further, an electronic tongue or nose possessing an array of nanosensors are used to monitor the food condition. It gives signals according to aroma or gases released by food items.[35,36]

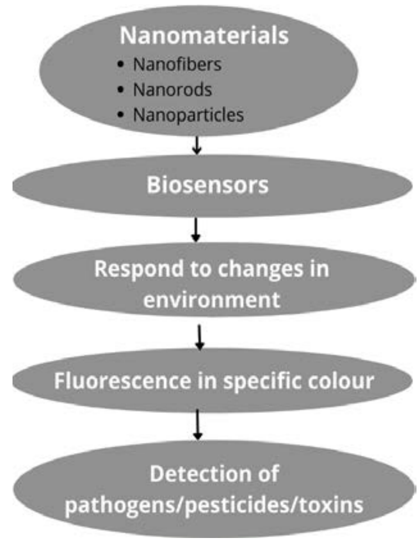


Figure 4 Pathogen detection by nanosensors

Food Additives:

Food additives are the substances added to the food to improve their functional properties like antioxidants, emulsifiers, antimicrobials, colorants, etc. Because of changing perception and safety issues, these food additives are being replaced by nanoencapsulated additives. Their use can affect the nutritional value and bioavailability of health-promoting nutrients.

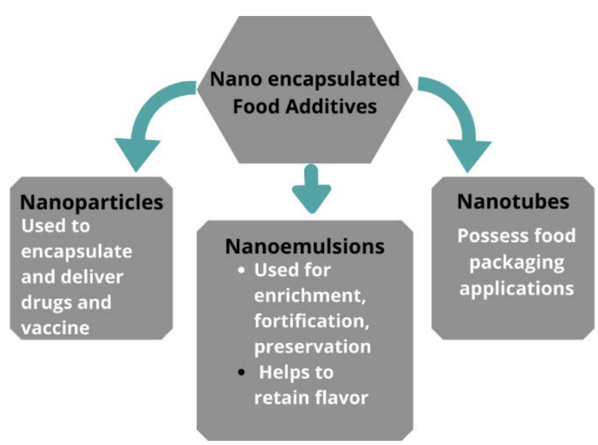


Figure 5 Nanomaterials as food additives.

Nanotechnology has introduced value-added properties in new foods. Additives are rarely utilized in their pure form; they are generally used as coatings or incorporated as nanoscale formulations. Many nanoscale matrics have been designed for encapsulation systems like nanoemulsions, nanoparticles, and nanofibers.

Nanoemulsions:

Nanoemulsions are the most commonly used nanostructure in the enrichment, fortification, and preservation of food matrix. Broadly, nanoemulsions are nontoxic when formulated with oil and are in the category of Generally Recognized As Safe (GRAS) for human consumption by the United States, Food and Drug Administration. Nanoemulsions are preferred in comparison to conventional emulsions as a large exposed surface facilitates easy digestion, thus better absorption. Another difference between them is that when a nanoemulsion is added to a food item, it does not change its appearance. Nanoemulsions are used to manufacture food products like salad dressing, flavored oils, sweeteners, and other processed foods. They help release different flavors with the help of stimulations such as heat, pH, ultrasonic waves, and so forth.[37] They efficiently retain the flavors and prevent the loss by oxidation and enzymatic reactions. These in the form of proteins such as egg, milk, or vegetable protein and carbohydrates such as starch, pectin, carrageenan, and guar gum provide better texture and lead to uniformity of the food products.[38] The nanoemulsions are made by dispersing the liquid phase in a continuous aqueous phase. A lipophilic component is required for the creation of nanoemulsion. Its placement within the nanoemulsion is dependent on the molecular and physicochemical properties like solubility, melting point hydrophobicity, and surface activity.[39] Nanoemulsions possess antimicrobial activity and are used against Gram-positive organisms instead of Gram negative-organisms[40] as a result they are used for decontamination of the food packaging articles. Microbial growth could be restricted by using nanoemulsions developed by utilizing non-ionic surfactants, soybean oil, and tributyl phosphate. Nanoemulsions have proved beneficial in delivering phytochemicals like polyphenols and carotenoids as the smaller size of lipids led to their higher bioavailability.[41–45]

Nanoparticles:

Food-grade biopolymers, such as polysaccharides or proteins, can be utilized to produce nanosized particles. A single biopolymer breaks into smaller nanoparticles with aggregative or segregative interactions. These nanoparticles can be further utilized to encapsulate functional ingredients. Most common nanoparticles such as polylactic acid (PLA) are commonly used to encapsulate and deliver drugs and vaccines, but it has certain limitations. It used to be quickly removed from the bloodstream and may remain isolated in the liver and kidneys. Thus, PLA needs to be associated with a compound like polyethylene glycol to successfully deliver the active components to other parts of the body.[46]

Nanofiber:

The use of nanotubes is mainly applied for non-food applications. Few food grade materials like Sea Cucumber/Gelatin Nanofiber have been made with fibers that can be used for packing.[47] Carbon nanotubes are generally used as low-resistance conductors (like use in sensor for presence of specific contaminants and microbes) and their role in the food industry have mainly been explored for the food packaging applications.[48]

Nanotechnology and Food Packaging

Every year about one-third of the total food produced worldwide get wasted due to spoilage. Food contamination and spoilage have a huge impact on human health. It also has economic implications and raised medical care expenses. Due to globalization, food packaging requires longer shelf life, a food safety monitoring system, and quality at par with international standards. To address these current needs, nanotechnology might potentially help out with new food and beverage packaging technologies. Nanotechnology has been used to develop innovative packaging materials over the last years, which had an important impact on the food market. Nanotechnology application in food packaging can be segregated into three main categories.[49]

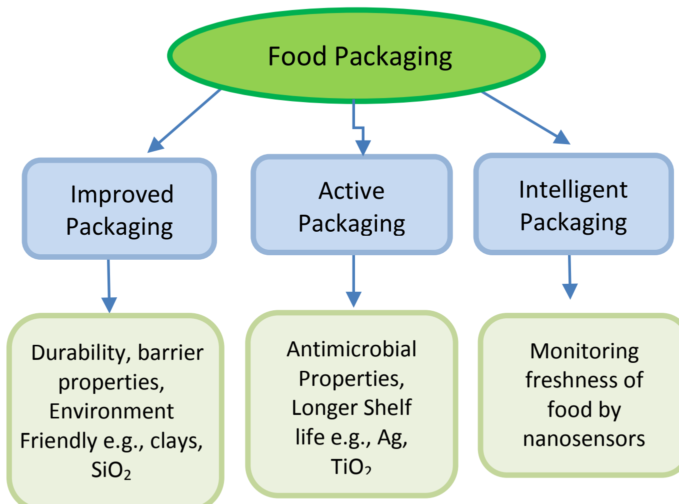


Figure 6. Role of nanotechnology in Food Packaging

Improved packaging: Nanotechnology-based food packaging presents certain advantages over conventional packing materials in terms of properties like temperature resistance, more durability, flameproof, barrier to microbial damage, recycling, and easy process-ability due to lower viscosity. It helps to deliver active materials into the biological systems along with minimum costs with fewer environmental issues. They are widely used in food packaging applications of products like processed meat products, cereals, cheese, confectionery items, boil-in-the-bag foods. Along with this, it helps in extrusion-coating applications for products like fruit juices, dairy products, beer and carbonated drinks.[50]

Active packaging: Inactive packaging are deliberately included in or on the packaging material or on the package space to improve the package system's performance. Active packaging is a designed packaging system with components that would release antimicrobial agents or absorb oxygen and water vapor from the food environment. Usage of active compounds like antimicrobial agents, preservatives, oxygen, and water vapor absorbers, acts in more effective way for improving the shelf life and quality of food product.[51] Various metals and metal oxides derived nanomaterials have been used in active packaging applications.[52] Nanomaterials like nano copper oxide, silver nanoparticles, and carbon nanotubes can provide antimicrobial properties. Nowadays, the use of silver nanoparticles in food packaging as antibacterial agents is increasing. Silver nanoparticles are the most commonly used nanoparticles due to their well-known antimicrobial potential against multiple pathogenic strains.[53] Also, silver nanoparticles inhibit various fungi and viruses. Silver inhibits bacterial metabolism by associating with its DNA, proteins, and enzymes; thus, bacteriostatic effects have been achieved by using silver nanoparticles. Silver nanoparticles also disrupt the cytoplasmic membranes.[54]

Intelligent packaging: It helps to sense biochemical or microbial changes occurring in the food. It can detect specific pathogen growing in the food by sensing gases from the food spoiling. Some smart packaging has been designed to use as a detecting device for food safety. Such a system uses different communication methods such as nanosensors, oxygen sensors, nanoscale, freshness indicators, etc.[29,55] The nanosensors in food packaging systems helped to detect the changes that occur during spoilage, various pathogens, and chemical contaminants, thus giving the exact status of food products freshness.[56] Usually, nanosensors can be applied as coatings to food packaging to detect the package's integrity by checking leaks. This applies to foodstuffs packed in a vacuum or inert atmosphere.[57] Gas sensors are used to detect the gas in the package. Nanoparticles, due to the presence of the unique chemical and electro-optical properties, respond to environmental changes (e.g., temperature, humidity, levels of oxygen), product degradation, or microbial contamination. Therefore, such technology would be beneficial to consumers, industry stakeholders, and food regulators.

SAFETY ISSUES

Although there is an enormous range of food products available for the consumer made by the application of nanotechnology, the serious question raised is about the safety of these products. The GRAS list of universally accepted additives needs to be re-examined when used at the nanoscale level. There are safety issues regarding the use of nanotechnology in its various food applications.

In packaging, the un-intended transfer of harmful packaging constituents may raise the safety concerns of consumers. The extent of the migration of nanoparticle(s) to the food matrix depends mainly on the chemical and physical properties of the food and packaging polymer. Some other controlling factors are the concentration, particle size, pH reading, molecular weight, solubility, temperature, polymer structure and viscosity, contact time, and food composition. The solubility of nanoparticles in an aqueous solution is dependent on temperature and inversely proportional to the food pH, which increases the inflow of metal into the food matrix.

Nanoparticles are likely to enter the body through inhalation, ingestion, or crossing the skin barrier. Besides the route of entry of nanoparticles into the body, nanoparticles' toxicity also depended upon the host susceptibility.[58] It is essential to understand the interface between nanoparticles, cells and tissues of the organism. On entering the human body, these nanoparticles come in contact with biomolecules like protein, sugar, and lipids present in body fluids such as lymph, blood, interstitial fluid. The pH and ionic composition of the gastrointestinal fluids affects the surface potential and electrostatic interactions among nanoparticles, which further influence their aggregation state and interactions with other components. Gastrointestinal fluids possess surface-active components, such as proteins, bile salts, phospholipids, and free fatty acids (FFAs). These components may adsorb to nanoparticle surfaces and modify their interfacial properties and, ultimately, their biological fate. It has been reported that the interfacial properties of inorganic nanoparticles are modified significantly when they enter the gastrointestinal tract (GIT), which affects cellular, and tissue response to the nanoparticles.[59] Gastrointestinal fluids contain digestive enzymes that may change the properties of nanoparticles. For example, nanoparticles having starch, proteins, or lipids may be acted upon by enzymes like amylase, protease, or lipase respectively.[60]

Consequently, these nanoparticles' properties may be very different when compared with those of the ingested nanoparticles. Gastrointestinal tract (GIT) bacteria may produce products that affect some properties of ingested nanoparticles. On the other hand, ingested nanoparticles may influence the properties of gastrointestinal tract (GIT) bacteria. To be precise, many types of inorganic nanoparticles possess antimicrobial properties that may alter the composition of different bacterial species in the colon, thus leading to adverse health effects. Even after cellular uptake, inorganic nanoparticles may interact with blood proteins, which can further change their biological fat.[61] It is known that active or passive transport mechanisms absorb these nanoparticles. After being metabolized, they are either transferred out from the cells or accumulate within the cells. This depends on nanoparticle properties such as composition, dimensions, morphology, and aggregation state. The excessive accumulation of nanoparticles in the specific tissues may lead to long-term problems if the level reaches above a certain accumulation threshold. This is especially important for inorganic nanoparticles that are generally not digested or metabolized in gastrointestinal tract (GIT). Studies on titanium and silver nanoparticles have reported that insoluble substances are deposited in the organs.[62,63] The liver and spleen are the main organs responsible for the transportation of nanoparticles from the intestine to the blood circulation.

Few reports have been pointed towards the carcinogenic nature of nanoparticles. It might be possible that material is being considered as GRAS (generally regarded as safe) substance. More research is required to examine its nano counterparts' risk as the physiochemical properties differ in nano states than macrostates. ZnO nanoparticles are reported to have genotoxicity in human epidermal cells, whereas the bulk ZnO is nontoxic, which proves the role of particle size.[64] Earlier, in a study it was reported that the smaller nanoparticles are more toxic than, the larger ones.[65] High surface area enhances the interaction with the biological molecules, thus leading to adverse responses. Some reports prove inhalation of significantly high doses (10 mg/m3) of nano-TiO2 has been linked with the incidence of lung tumors.[66,67]

Nanoparticles also produce toxicity in cells through several mechanisms, depending on their composition and structure. There is a strong possibility that nanoparticles in the body can result in increased oxidative stress that, in turn, can generate free radicals, leading to DNA mutation, cancer, and possible fatality. It is reported that the toxicity of inorganic nanoparticles is due to their ability to generate singlet oxygen, superoxide, and hydroxyl radicals.[68] These further cause damage of the cell membranes and other cell organelles by reacting with macromolecules like lipids, proteins, or nucleic acids.[69] Due to this effect, many biochemical functions essential to maintain cell viability, such as ATP production, may be adversely affected. Several reports have been shown the ability of inorganic nanoparticles to produce cytotoxicity, including silicon dioxide nanoparticles, zinc oxide nanoparticles[70,71] and silver nanoparticles. Scientific evidence has indicated that free engineered nanoparticles can cross cellular barriers that may eventually lead to increased production of oxyradicals and ultimately oxidative damage to the cell.[72] Thus a number of possible health ailments are likely possible from the consumption of food and drinks containing nanosized ingredients and additives. Besides this, their entrance through skin penetration is a matter of great concern, especially for workers who come in direct contact of such nanoparticles.[73] Overall data available suggested that more research is needed before nanoparticles may be tagged as non-toxic or safe.

Conclusions

There are many benefits of nanotechnology, and they are expected to grow more. This rapidly developing technology impacts every aspect of the food system, from production to easy processing, active packaging, easy transportation, longer shelf life, and higher bioavailability. The range of nanomaterials' commercial applications in the food industry is expanding due to their unique and novel properties. With these advancements, human exposure to nanomaterials are also increasing. Hence, the health impact of human beings in the food industry is a primary public concern. Acceptance of food products containing nanomaterials should depend on their safety standards. A uniform international regulatory framework for nanotechnology in food processing and packaging is essentially needed. Nanomaterials should be synthesized or applied in such a way that it does not cause any risk to the health of consumers or to the environment. More research studies are required to investigate the hazards of nanomaterials, considering the nano state as some of chemical substances are safer when used in the form of large particles.

References and notes

1. N. Sozer, J.L. Kokini. Nanotechnology and its applications in the food sector. *Trends Biotechnol.* **2009**, 27 (2), 82–89.
2. R.K. Sastry, S. Anshul, N.H. Rao. Nanotechnology in food processing sector-An assessment of emerging trends. *J. Food Sci. Technol.* **2013**, 50 (5), 831–841.
3. A. Pal, B.S. Chhikara, A. Govindaraj, S. Bhattacharya, C.N.R. Rao. Synthesis and properties of novel nanocomposites made of single-walled carbon nanotubes and low molecular mass organogels and their thermo-responsive behavior triggered by near IR radiation. *J. Mater. Chem.* **2008**, 18 (22), 2593–2600.
4. R. Singh, H.S. Nalwa. Medical applications of nanoparticles in biological imaging, cell labeling, antimicrobial agents, and anticancer nanodrugs. *J. Biomed. Nanotechnol.* **2011**, 7 (4), 489–503.
5. S.K. Misra, P. Moitra, B.S. Chhikara, P. Kondaiah, S. Bhattacharya. Loading of single-walled carbon nanotubes in cationic cholesterol suspensions significantly improves gene transfection efficiency in serum. *J. Mater. Chem.* **2012**, 22 (16), 7985–7998.
6. B.S. Chhikara, S.K. Misra, S. Bhattacharya. CNT loading into cationic cholesterol suspensions show improved DNA binding and serum stability and ability to internalize into cancer cells. *Nanotechnology* **2012**, 23 (6), 065101.
7. H.S. Nalwa. Encyclopedia of Nanoscience and Nanotechnology. 10-Volume Set; American Scientific Publishers, **2004**.
8. M. Roselli, A. Finamore, I. Garaguso, M.S. Britti, E. Mengheri. Zinc Oxide Protects Cultured Enterocytes from the Damage Induced by Escherichia coli. *J. Nutr.* **2003**, 133 (12), 4077–4082.
9. J. Sawai. Quantitative evaluation of antibacterial activities of metallic oxide powders (ZnO, MgO and CaO) by conductimetric assay. *J. Microbiol. Methods* **2003**, 54 (2), 177–182.
10. P.N. Ezhilarasi, P. Karthik, N. Chhanwal, C. Anandharamakrishnan. Nanoencapsulation Techniques for Food Bioactive Components: A Review. *Food Bioprocess Technol.* **2013**, 6 (3), 628–647.
11. K.W. Powers, S.C. Brown, V.B. Krishna, et al. Research strategies for safety evaluation of nanomaterials. Part VI. characterization of nanoscale particles for toxicological evaluation. *Toxicol. Sci.* **2006**, 90 (2), 296–303.
12. H.M.C. Azeredo, L.H.C. Mattoso, D. Wood, et al. Nanocomposite edible films from mango puree reinforced with cellulose nanofibers. *J. Food Sci.* **2009**, 74 (5).
13. T. Zhang, C. Lv, L. Chen, et al. Encapsulation of anthocyanin molecules within a ferritin nanocage increases their stability and cell uptake efficiency. *Food Res. Int.* **2014**, 62, 183–192.
14. K. Nakagawa. Nano- and Microencapsulation of Flavor in Food Systems. In *Nano- and Microencapsulation for Foods*; **2014**; Vol. 9781118292, pp 249–271.
15. S. Dekkers, P. Krystek, R.J.B. Peters, et al. Presence and risks of nanosilica in food products. *Nanotoxicology* **2011**, 5 (3), 393–405.
16. B. Hu, Q.R. Huang. Biopolymer based nano-delivery systems for enhancing bioavailability of nutraceuticals. *Chinese J. Polym. Sci. (English Ed.* **2013**, 31 (9), 1190–1203.
17. M.J. Sáiz-Abajo, C. González-Ferrero, A. Moreno-Ruiz, A. Romo-Hualde, C.J. González-Navarro. Thermal protection of β-carotene in re-assembled casein micelles during different processing technologies applied in food industry. *Food Chem.* **2013**, 138 (2–3), 1581–1587.
18. M. Fathi, M.R. Mozafari, M. Mohebbi. Nanoencapsulation of food ingredients using lipid based delivery systems. *Trends Food Sci. Technol.* **2012**, 23 (1), 13–27.
19. T.G. Mason, J.N. Wilking, K. Meleson, C.B. Chang, S.M. Graves. Nanoemulsions: formation, structure, and physical properties. *J. Phys. Condens. Matter* **2007**, 19 (7), 079001.
20. S. Wongsasulak, M. Patapeejumruswong, J. Weiss, P. Supaphol, T. Yoovidhya. Electrospinning of food-grade nanofibers from cellulose acetate and egg albumen blends. *J. Food Eng.* **2010**, 98 (3), 370–376.
21. O.M. Koo, I. Rubinstein, H. Onyuksel. Role of nanotechnology in targeted drug delivery and imaging: a concise review. *Nanomedicine Nanotechnology, Biol. Med.* **2005**, 1 (3), 193–212.
22. A. Nasrolahi Shirazi, R. Tiwari, B.S. Chhikara, D. Mandal, K. Parang. Design and biological evaluation of cell-penetrating peptide-doxorubicin conjugates as prodrugs. *Mol. Pharm.* **2013**, 10 (2), 488–499.
23. H.K. Agarwal, B.S. Chhikara, M. Quiterio, G.F. Doncel, K. Parang. Synthesis and anti-HIV activities of glutamate and peptide conjugates of nucleoside reverse transcriptase inhibitors. *J Med Chem* **2012**, 55 (6), 2672–2687.
24. J. Weiss, P. Takhistov, D.J. McClements. Functional materials in food nanotechnology. *J. Food Sci.* **2006**, 71 (9).
25. H. Luo, Y. Bao, J. Jiang, et al. Edible coatings to incorporate active ingredients to fresh-cut fruits: a review. *Eur. food Res. Technol.* **2012**, 235 (6), 438–447.
26. A.M. Mayer. Polyphenol oxidases in plants and fungi: Going places? A review. *Phytochemistry* **2006**, 67 (21), 2318–2331.
27. X. Li, W. Li, Y. Jiang, et al. Effect of nano-ZnO-coated active packaging on quality of fresh-cut "Fuji" apple. *Int. J. Food Sci. Technol.* **2011**, 46 (9), 1947–1955.
28. B.P. Helmke, A.R. Minerick. Designing a nano-interface in a microfluidic chip to probe living cells: Challenges and perspectives. *Proc. Natl. Acad. Sci. U. S. A.* **2006**, 103 (17), 6419–6424.

29. H. Bouwmeester, S. Dekkers, M.Y. Noordam, et al. Review of health safety aspects of nanotechnologies in food production. *Regul. Toxicol. Pharmacol.* **2009**, 53 (1), 52–62.
30. C. Jianrong, M. Yuqing, H. Nongyue, W. Xiaohua, L. Sijiao. Nanotechnology and biosensors. *Biotechnol. Adv.* **2004**, 22 (7), 505–518.
31. A. Subramanian, J. Irudayaraj, T. Ryan. A mixed self-assembled monolayer-based surface plasmon immunosensor for detection of E. coli O157:H7. *Biosens. Bioelectron.* **2006**, 21 (7), 998–1006.
32. F. Tan, P.H.M. Leung, Z. Bin Liu, et al. A PDMS microfluidic impedance immunosensor for E. coli O157:H7 and Staphylococcus aureus detection via antibody-immobilized nanoporous membrane. *Sensors Actuators, B Chem.* **2011**, 159 (1), 328–335.
33. S. Liu, L. Yuan, X. Yue, Z. Zheng, Z. Tang. Recent Advances in Nanosensors for Organophosphate Pesticide Detection. *Adv. Powder Technol.* **2008**, 19 (5), 419–441.
34. I. Palchetti, M. Mascini. Electroanalytical biosensors and their potential for food pathogen and toxin detection. *Anal. Bioanal. Chem.* **2008**, 391 (2), 455–471.
35. M. García, M. Aleixandre, J. Gutiérrez, M.C. Horrillo. Electronic nose for wine discrimination. *Sensors Actuators, B Chem.* **2006**, 113 (2), 911–916.
36. M.S. Thakur, K. V Ragavan. Biosensors in food processing. *J. Food Sci. Technol.* **2013**, 50 (4), 625–641.
37. M.N.V. Ravi Kumar. A review of chitin and chitosan applications. *React. Funct. Polym.* **2000**, 46 (1), 1–27.
38. S.A. Hogan, B.F. McNamee, E. Dolores O'Riordan, M. O'Sullivan. Microencapsulating properties of sodium caseinate. *J. Agric. Food Chem.* **2001**, 49 (4), 1934–1938.
39. S. Sinha Ray, M. Okamoto. Polymer/layered silicate nanocomposites: A review from preparation to processing. *Prog. Polym. Sci.* **2003**, 28 (11), 1539–1641.
40. Y. Wang, Q. Zhang, C.L. Zhang, P. Li. Characterisation and cooperative antimicrobial properties of chitosan/nano-ZnO composite nanofibrous membranes. *Food Chem.* **2012**, 132 (1), 419–427.
41. Peter HM Hoet, Irene Brüske-Hohlfeld, Oleg V Salata. Nanoparticles – known and unknown health risks. *J. Nanobiotechnology* **2004**, 2 (12), 1ff.
42. B.S. Chhikara, K. Parang. Development of cytarabine prodrugs and delivery systems for leukemia treatment. *Expert Opin. Drug Deliv.* **2010**, 7 (12), 1399–1414.
43. B.S. Chhikara, D. Mandal, K. Parang. Synthesis and evaluation of fatty acyl ester derivatives of cytarabine as anti-leukemia agents. *Eur. J. Med. Chem.* **2010**, 45 (10), 4601–4608.
44. B.S. Chhikara, N. St. Jean, D. Mandal, A. Kumar, K. Parang. Fatty acyl amide derivatives of doxorubicin: Synthesis and in vitro anticancer activities. *Eur. J. Med. Chem.* **2011**, 46 (6), 2037–2042.
45. B.S. Chhikara, D. Mandal, K. Parang. Synthesis, anticancer activities, and cellular uptake studies of lipophilic derivatives of doxorubicin succinate. *J. Med. Chem.* **2012**, 55 (4), 1500–1510.
46. T.M. Taylor, P.M. Davidson, B.D. Bruce, J. Weiss. Liposomal nanocapsules in food science and agriculture. *Crit. Rev. Food Sci. Nutr.* **2005**, 45 (7–8), 587–605.
47. W. Hong, Q.S. Li, J. Jiao, et al. Research on the Preparation of Food-grade Sea Cucumber/Gelatin Nanofiber Membrane with Electrospinning Method. In *Advanced Materials Research*; Trans Tech Publ, **2012**; Vol. 427, pp 139–142.
48. P. Wang, X. Hu, Q. Cheng, et al. Electrochemical detection of amaranth in food based on the enhancement effect of carbon nanotube film. *J. Agric. Food Chem.* **2010**, 58 (23), 12112–12116.
49. T. V. Duncan. Applications of nanotechnology in food packaging and food safety: Barrier materials, antimicrobials and sensors. *J. Colloid Interface Sci.* **2011**, 363 (1), 1–24.
50. G.W. Padua. Nanocomposites in food packaging. *Food Eng. Ingredients* **2010**, 35 (4), 35–37.
51. S. Ranjan, N. Dasgupta, A.R. Chakraborty, et al. Nanoscience and nanotechnologies in food industries: Opportunities and research trends. *J. Nanoparticle Res.* **2014**, 16 (6).
52. D.N. Bikiaris, K.S. Triantafyllidis. HDPE/Cu-nanofiber nanocomposites with enhanced antibacterial and oxygen barrier properties appropriate for food packaging applications. *Mater. Lett.* **2013**, 93, 1–4.
53. R. Kumar, H. Münstedt. Silver ion release from antimicrobial polyamide/silver composites. *Biomaterials* **2005**, 26 (14), 2081–2088.
54. J.R. Morones, E. Jose Luis, C. Alejandra, et al. The bactericidal effect of silver nanoparticles. *Nanotechnology* **2005**, No. 10, 2346.
55. J.P. Kerry, M.N. O'Grady, S.A. Hogan. Past, current and potential utilisation of active and intelligent packaging systems for meat and muscle-based products: A review. *Meat Sci.* **2006**, 74 (1), 113–130.
56. F. Liao, C. Chen, V. Subramanian. Organic TFTs as gas sensors for electronic nose applications. *Sensors Actuators, B Chem.* **2005**, 107 (2), 849–855.
57. N.P. Mahalik, A.N. Nambiar. Trends in food packaging and manufacturing systems and technology. *Trends Food Sci. Technol.* **2010**, 21 (3), 117–128.
58. V. Sharma, R.K. Shukla, N. Saxena, et al. DNA damaging potential of zinc oxide nanoparticles in human epidermal cells. *Toxicol. Lett.* **2009**, 185 (3), 211–218.
59. M. Mahmoudi, F.B. Bombelli, I. Lynch, et al. Protein− nanoparticle interactions: opportunities and challenges. *Chem. Rev.* **2011**, 111 (9), 5610–5637.
60. K. Giri, K. Shameer, M.T. Zimmermann, et al. Understanding protein-nanoparticle interaction: A new gateway to disease therapeutics. *Bioconjug. Chem.* **2014**, 25 (6), 1078–1090.
61. P. Aggarwal, J.B. Hall, C.B. McLeland, M.A. Dobrovolskaia, S.E. McNeil. Nanoparticle interaction with plasma proteins as it relates to particle biodistribution, biocompatibility and therapeutic efficacy. *Adv. Drug Deliv. Rev.* **2009**, 61 (6), 428–437.
62. J.C. Carrero-Sánchez, A.L. Elías, R. Mancilla, et al. Biocompatibility and toxicological studies of carbon nanotubes doped with nitrogen. *Nano Lett.* **2006**, 6 (8), 1609–1616.
63. C. Johansson. Bio-nanocomposites for food packaging applications. *Nanocomposites with Biodegrad. Polym. Synth. Prop. Futur. Perspect.* **2011**, 9780199581.
64. A.L. Sharma, R. Singhal, A. Kumar, et al. Immobilization of glucose oxidase onto electrochemically prepared poly(aniline-co-fluoroaniline) films. *J. Appl. Polym. Sci.* **2004**, 91 (6), 3999–4006.
65. B.D. Chithrani, A.A. Ghazani, W.C.W. Chan. Determining the size and shape dependence of gold nanoparticle uptake into mammalian cells. *Nano Lett.* **2006**, 6 (4), 662–668.
66. A.P. Walczak, R. Fokkink, R. Peters, et al. Behaviour of silver nanoparticles and silver ions in an in vitro human gastrointestinal digestion model. *Nanotoxicology* **2013**, 7 (7), 1198–1210.
67. H. Shi, R. Magaye, V. Castranova, J. Zhao. Titanium dioxide nanoparticles: A review of current toxicological data. *Part. Fibre Toxicol.* **2013**, 10 (1).
68. H. Wu, J.J. Yin, W.G. Wamer, M. Zeng, Y.M. Lo. Reactive oxygen species-related activities of nano-iron metal and nano-iron oxides. *J. Food Drug Anal.* **2014**, 22 (1), 86–94.
69. V.K. Sharma, K.M. Siskova, R. Zboril, J.L. Gardea-Torresdey. Organic-coated silver nanoparticles in biological and environmental conditions: Fate, stability and toxicity. *Adv. Colloid Interface Sci.* **2014**, 204, 15–34.
70. Y. Wang, L. Yuan, C. Yao, et al. A combined toxicity study of zinc oxide nanoparticles and vitamin C in food additives. *Nanoscale* **2014**, 6 (24), 15333–15342.
71. M. Esmaeillou, M. Moharamnejad, R. Hsankhani, A.A. Tehrani, H. Maadi. Toxicity of ZnO nanoparticles in healthy adult mice. *Environ. Toxicol. Pharmacol.* **2013**, 35 (1), 67–71.
72. E. Oberdörster. Manufactured nanomaterials (fullerenes, C60) induce oxidative stress in the brain of juvenile largemouth bass. *Environ. Health Perspect.* **2004**, 112 (10), 1058–1062.
73. Ahmed M. Youssef. Polymer Nanocomposites as a New Trend for Packaging Applications. *Polym. Plast. Technol. Eng.* **2013**, 52, 635–660.