Application of nanotechnology in food, nutraceuticals and pharmaceuticals

SaiRuthwik Putheti

Dulaney High school, 255 East Padonia Road, Timonium
Maryland-21093, email:rrutwik@gmail.com

Abstract

Nanotechnology is an enabling technology that has revolutionized many related disciplines such as food, pharmaceutical, cosmetics and nutraceuticals. Driven by increasing consumer demand for healthy food products and need for better drug delivery systems, researchers have been applying tools and knowledge in nanotechnology to address the specific relevant issues. Nanotechnology holds great promise to provide benefits for improving the understanding and designing better products. This paper addresses the general applications of nanotechnology to food, nutraceutical and pharmaceuticals sectors.

Introduction

The word "nano" comes from the Greek for "dwarf". A nanometer is a thousandth of a thousandth of a thousandth of a meter (10^{-9} m). One nanometer is about 60,000 times smaller than a human hair in diameter or the size of a virus, a typical sheet of paper is about 100,000 nm thick, a red blood cell is about 2,000 to 5,000 nm in size, and the diameter of DNA is in the range of 2.5 nm. Therefore, nanotechnology deals with matter that ranges from one-half the diameter of DNA up to 1/20 the size of a red blood cell. Nanoparticles are generally accepted as those with a particle size below 100 nanometers where unique phenomena enable novel applications and benefits. Nanomaterials exhibit properties that are different from materials of the same chemical composition, but with much larger particles.

Within the past few decades, the evolution of a number of new science disciplines and technologies such as biotechnology, information technology and nanotechnology has revolutionized R&D in a number of fields including food, nutraceutical and pharmaceutical sectors. Most notable among these is nanotechnology, which is a broad interdisciplinary area of research, development and industrial activity that involves the manufacture, processing, and application of materials that have one or more dimensions of the order of 100 nanometers (nm) or less. Nanotechnology is an enabling technology that is being used as a means to understand how physicochemical characteristics of nano-sized substances can change the structure, texture and quality.

Many of the current nanotechnology applications in the food sector appear to have emerged from related sectors, such as pharmaceutical, cosmetics and nutraceuticals. The boundaries between food, medicine and cosmetics, are already obscure, and the advent of nanomaterials, which can interact with biological entities at a near-molecular level, is likely to further blur these boundaries.

Nanotechnology in recent years has developed into a wide-ranging, multibillion-dollar global industry. The global market impact of nanotechnology is widely expected to reach 1 trillion US$ by 2015, with around 2 million workers [1]. It is also clear from a number of reports, reviews, patent applications, and company products that applications of nanotechnology have also started to make an impact on different aspects of the food, nutraceutical and pharmaceutical industries [2].

Nanotechnology in food sector

The applications of nanotechnology in the food sector are only new emergent, but they are predicted to grow rapidly in the coming years. Applications in this area already span development of improved tastes, color, flavor, texture, and consistency of foodstuffs, increased absorption and bioavailability of nutrients and health supplements, new food packaging materials with improved mechanical, barrier and antimicrobial properties, and nano-sensors for traceability and monitoring the condition of food during transport and storage.

The novel properties of nanomaterials offer many new opportunities for the food industry [3]. Different types of functional nanostructures can be used as building blocks to create novel structures and introduce new functionalities into foods. These include: nanoliposomes, nanoemulsions, nanoparticles and nanofibers. Engineered nanomaterials (ENMs) used in food applications include inorganic compounds, organic substances and surface functionalized materials [4].

Inorganic nanomaterials for application in food, food additives, food packaging or storage include (ENMs) of transition metals, such as silver and iron; alkaline earth metals, such as calcium and magnesium; and non-metals, such as selenium and silicates. Other ENMs that can potentially be used in food applications include titanium dioxide. Food packaging is the major area of application of metal (oxide) ENMs. Nanosilver is finding a growing use in a number of consumer products, including food and health food, water, and food contact surfaces and packaging materials. Amorphous nanosilica is known to be used in food contact surfaces and food packaging applications.

Surface functionalized nanomaterials add certain types of functionality to the matrix, such as antimicrobial activity or a preservative action through absorption of oxygen. For food packaging materials, functionalized ENMs are used to bind with the polymer matrix to offer mechanical strength or a barrier against movement of gases, volatile components (such as flavors) or moisture. Compared to inert nanomaterials, they are more likely to react with different food components, or become bound to food matrices, and hence may not be available for migration from packaging materials, or translocation to other organs outside the GI tract. The nanoclay mineral is mainly montmorillonite (also termed as bentonite), which is natural clay obtained from volcanic ash/rocks. Nanoclay has a natural nanoscaled layer structure and is organically modified to bind to polymer matrices. The use of functionalized nanoclays in food packaging can help to develop materials with enhanced gas-barrier properties.

Organic nanomaterials (many of them naturally-occurring substances) are used (or have been developed for use) in food/ feed products for their increased uptake and absorption, and improved bioavailability of vitamins, antioxidants in the body, compared to conventional bulk equivalents. A wide range of materials are available in this category, for example food additives (eg, benzoic acid, citric acid, ascorbic acid) and supplements (eg, vitamins A and E, isoflavones, beta-carotene, lutein, omega-3 fatty acids, and coenzyme-Q10). An example of an organic nanomaterial is the tomato carotenoid lycopene. A synthetic nanosized form of lycopene has been produced and found as equivalent sources of lycopene compared to natural lycopene [5].

The food industry is also looking out for new technologies to improve the nutritional value, shelf-life, and traceability of their food products. They are also aiming to develop improved tastes, reduce the amount of salt, sugar, fat and preservatives, address food-related illnesses (e.g. obesity and diabetes), develop targeted nutrition for different lifestyles and aging population, and maintain sustainability of food production, processing, and food safety. A number of new processes and materials derived from nanotechnology can provide answers to many of these needs, as they offer the ability to control and manipulate properties of substances close to molecular level. For example, in terms of increasing the absorption of nano-sized nutrients and supplements and therefore enhancing the nutritional value of food, development of new tastes and sensations, and creamier textures through nanostructuring of food ingredients with less (or no additional) fat. It is therefore not surprising that one of the fastest moving sectors to embrace new technologies, such as nanotechnology, to realize the potential benefits is the food industry.

Nanotechnology in nutraceuticals

One important application of nanotechnology in food and nutrition is to design and development of novel functional food ingredients (that is, nutraceuticals) with improved water solubility, thermal stability, oral bioavailability, sensory attributes, and physiological performance. Driven by increasing consumer demand for novel food products, as well as increased fortification with healthy food ingredients, the nutraceutical market has increased significantly. Nutraceuticals, which are food supplements with health benefits, are commonly used as part of the daily diet. Because of their low solubility, many nutraceuticals are poorly absorbed by human body, thus one of the most important and interesting applications for encapsulation of nutraceuticals is to enhance the bioavailability of nutraceuticals by changing the pharmacokinetics (PK) and biodistribution (BD). In recent years, extensive research has been carried out to study the health promotion properties of different nutraceuticals and to devise novel encapsulation materials and methods, trying to incorporate functional ingredients into foods [6]. To enhance nutritional quality and stability of the nutraceuticals, one option is to encapsulate the functional ingredients using food-grade or “generally recognized as safe” (GRAS) materials that can exhibit controlled-release behavior. Materials that can fulfill these requirements include polysaccharides of plant (for example, pectin, starch, gum Arabic, carrageenan, and so on) or microbial (that is, Xanthan gum, dextran) origin, food proteins (for example, soy proteins, casein, gelatin, oat proteins, whey proteins, and so on), emulsifiers, such as lecithin, Tweens, Spans, sugar esters, monoglycerides, and so on. Encapsulation and controlled-release of active food ingredients are important applications in food and nutrition that can be attained with nanotechnological approaches.

Administration of active pharmaceutical or nutraceutical ingredients into the human body requires the use of an appropriate vehicle for bringing an effective amount of the active component intact to the desired site in the body. The desired site varies and it may be the blood stream, organs, and cells, and so on. Majority of pharmaceutical or nutraceutical are either poorly soluble or lipophilic compounds. It is known that the delivery of these active ingredients is significantly influenced by their physicochemical properties, such as water solubility, partition coefficient, lipophilicity, and crystallinity, and so on. Active components that poorly dissolve in oil or water pose a problem as to the route for their administration, transport, and reaching their targets, resulting in a poor oral bioavailability. To overcome instability, poor water solubility, and to enhance the bioavailability of active components, one option to entrap the compound of interest into a nanoemulsion. Nanoemulsions are a class of extremely small droplet emulsions that appear to be transparent or translucent with a bluish coloration. They contain continuous phase, dispersed phase and emulsion stabilizer, the emulsifier or called the surfactant. They are usually in the range 50 to 200 nm but much smaller than the range (from 1 to 100 μm) for conventional emulsions [7]. Since an emulsifier molecule size is typically 2 nm long, a micelle, that is, a surfactant molecule aggregate in water is typically 5 nm or more in diameter. When oil phase molecules enter the micellar core, the aggregates get swollen, sometimes to a large extent, to produce a spherical object whose size can reach 100 nm or more. Compared with conventional methods, such as co-solvent addition, micronizing/milling, spray drying, and salt formation, the use of lipid based delivery systems, such as micro/nanoemulsions and micelles, offers many advantages: (i) high kinetic or thermodynamic stability, which provides significantly better stability over unstable dispersions, such as conventional emulsions and suspensions; (ii) either hydrophilic or lipophilic active component can be incorporated into the same nanoemulsions; and (iii) because of the small droplet sizes, active component can be transported through the cell membranes much more easily, resulting in an increased phytochemical concentration in plasma and bioavailability.

Bioavailability is defined as a measurement of the extent of a therapeutically active component that reaches the systemic circulation and is available at the site of action. It is one of the key pharmacokinetic properties of a nutraceutical or drug. Phytochemicals with health benefits, such as plant polyphenols (that is, curcumin, resveratrol, epigallocatechin gallate, and so on) and carotenoids (that is, lycopene, β-carotene, lutein, zeaxanthin, and so on), have received much attention from the scientific community, consumers, and food manufacturers because they can be used to lower blood pressure, reduce cancer risk factors, regulate digestive tract system, strengthen immune systems, regulate growth, regulate sugar concentration in blood, lower cholesterol levels, and serve as antioxidant agents [8].

Nanotechnology in pharmaceuticals

Pharmaceutical nanotechnology has provided more fine-tuned diagnosis and focused treatment of disease at a molecular level. Pharmaceutical nanotechnology is most innovative and highly specialized field, which will revolutionize the pharmaceutical industry in near future. Pharmaceutical nanotechnology presents revolutionary opportunities to fight against many diseases. It helps in detecting the antigen

associated with diseases such as cancer, diabetes mellitus, neurodegenerative diseases, as well as detecting the microorganisms and viruses associated with infections.
Size reduction is a fundamental unit operation having important applications in pharmacy. It helps in improving solubility and bioavailability, reducing toxicity, enhancing release and providing better formulation opportunities for drugs. In most of the cases, size reduction is limited to micron size range, for example, various pharmaceutical dosage forms like powder, emulsion, suspension etc. Drugs in the nanometer size range enhance performance in a variety of dosage forms. Major advantages of nanosizing include (i) increased surface area, (ii) enhanced solubility, (iii) increased rate of dissolution, (iv) increased oral bioavailability, (v) more rapid onset of therapeutic action, (vi) less amount of dose required, (vii) decreased fed/fasted variability, and (viii) decreased patient-to-patient variability.

Novel drug delivery comprises of a number of features of nanotechnology, which make it a suitable tool to address major issues. The scope of pharmaceutical nanotechnology is very wide from smart material for tissue engineering to intelligent tools for delivery of drugs and diagnostics, and more recently, artificial RBC etc. Current applications of nanotechnology in pharmacy are development of nanomedicine, tissue engineering, nanorobots, advance diagnostic, as carrier of diagnostic and therapeutic modalities and as biosensor, biomarker, image enhancement device, implant technology, bioactive surfaces etc. A large number of nanosystems, which have been investigated in pharmacy todate, are liposomes, dendrimers, metallic nanoparticles, polymeric nanoparticles, carbon nanotubes, quantum dots, nanofibres etc.

Miniaturization is often beneficial in pharmaceutical technology. Although it has increased complexicity yet it imparts large number of benefits in drug delivery and diagnostic. Miniaturization is helpful in overcoming various physiological, biochemical and pharmaceutical barriers. Pharmaceutical nanotechnology provides wide array of systems or device of nanosize, which offer numerous benefits [9]. Some major advantages are (i) improved bioavailability, (ii) reduced toxicity, (iii) sustained and controlled release, (iv) ability to target, (v) do not occlude blood capillaries and traverse easily to most physiological biobarrier and provide effective delivery to brain and intracellular compartment, (vi) protects fragile drugs/proteins from harsh biological environment, (vii) faster, safer and more accurate disease diagnosis, (viii) more accurate, less invasive surgery, (ix) inexpensive, and (x) large-scale production is feasible. However some shortcomings in pharmaceutical applications of nanotechnology are (i) high aggregation in biological system due to high surface energy, (ii) poor solubility and poor biocompatibility in case of carbon nanotubes, (iii) quickly scavenged by RES system of body resulting in low biological half life, (iv) poor target and site specificity, (v) high immunogenicity or foreignness, (vi) undefined and unpredictable safety issue, and (vii) acute and chronic toxicity.
Inspite of the above shortcomings, there are various pharmaceutical and biomedical areas where pharmaceutical nanosystems have achieved remarkable breakthrough and realized their market applications.

Pharmaceutical nanotechnology has provided fine-tuned diagnosis and focused treatment of disease. However some ethical, scientific, social and regulatory issues posing various challenges in practical realization of pharmaceutical nanotechnology.

Some major health risk associated with such devices includes cytotoxicity, translocation to undesired cells, acute and chronic toxicity; some unknown, unpredictable and undefined safety issues, environmental impacts of nanomaterials and non-biocompatibility. Some ethical issues are altered gene expression, ultimate fate and altered or permanent anomaly in cell behavior/ response on short/long term exposure. There are no specific FDA directives to regulate pharmaceutical nanotechnology based products and related issues. Altogether these challenges cause urgent need to regulate these nanotechnology based products and delivery devices. The characterization, safety and environment impact are three main elements that need to be regulated. The lack of adequate and conclusive research on the health risks of nano-based substances demand the need for a dialogue on regulatory adequacy, inadequacy, or possible alternatives.

Some FDA approved nanotechnology based products, which have entered the market are liposome, nanoparticles, monoclonal antibody based product, polymer drug conjugate, polymer–protein conjugate and some polymeric drugs. Well-tuned, coordinated and sincere effort of government, industries, academia and researchers over guidelines for regulation must be drawn in order to utilize the benefit of nano-based technology without hampering its development.

Conclusion

During the past decade, many efforts have been devoted to the design and development of improved food, nutraceutical and pharmaceutical products and significant progresses have been achieved. Nanotechnology has the potential to improve foods, making them tastier, healthier, and more nutritious, to generate new food products, new food packaging, and storage. However, many of the applications are currently at an elementary stage, and most are aimed at high-value products, at least in the short term. Like any other new technology, public confidence, trust, and acceptance are likely to be the key factors that will determine the success or failure of nanotechnology applications for the food sector.
Pharmaceutical nanotechnology has emerged as a discipline having enormous potential as carrier for spatial and temporal delivery of bioactives and diagnostics and provides smart materials for tissue engineering. Pharmaceutical nanotechnology is now well-established as specialized area for drug delivery, diagnostics, prognostic and treatment of diseases through its nanoengineered tools. Few nanotechnology based products and delivery systems are already in market. Pharmaceutical nanotechnology provides opportunities to improve materials, medical devices and help to develop new technologies where existing and more conventional technologies may be reaching their limits.

References

1. Roco MC, Bainbridge WS. (Eds). 2001. Societal Implications of Nanoscience Nanotechnology. Kluwer Academic Publishers Boston, pp 3-4.
2. Chen H, Weiss J, Shahidi F. 2006. Nanotechnology in nutraceuticals and functional foods. Food Technology 603:30–6.
3. Cho Y, Kim C, Kim N, Kim C, Park B. Some cases in applications of nanotechnology to food and agricultural systems. *Biochip J*. 2008;2(3):183–185.

4. Chaudhry Q, Scotter M, Blackburn J, et al. Applications and implications of nanotechnologies for the food sector. *Food Addit Contam* 2008;25(3):241–258.
5. Hoppe PP, Krämer K, van den Berg H, Steenge G, van Vliet T. Synthetic and tomato-based lycopene have identical bioavailability in humans. *Eur J Nutr*. 2003;42(5):272–278.
6. Huang Q, Given P, Qian M. 2009. Micro/nano encapsulation of active food ingredients. Vol 1007.Washington, DC: Oxford Univ. Press.
7. Solans C, Izquierdo P, Nolla J, Azemar N, Garcia-Celma MJ. 2005. Nano-emulsions. Curr Opin Colloid In 10(3–4):102–10.
8. Wildman REC. 2001. Handbook of nutraceuticals and functional foods. Boca Roton, Fla.: CRC Press.
9. Advances in Controlled and Novel Drug Delivery. Jain NK, editor.. CBS publisher New Delhi, 2001.