ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

The Role of Nanomaterials in Food Industry with Advantages and Risks On Human Health.

Kurapati Srinivas*.

GITAM School of Technology, GITAM University, Bengaluru-562163, India.

ABSTRACT

The Nanotechnology offers scientifically enhanced capabilities for food product development through the provision of novel functional ingredients and nutrient delivery systems, safety testing, packaging and authentication. However, there are still many uncertainties about the technology and its potential applications, as well as doubts about its efficacy and safety in the long term. As with all new sciences and technologies, rigorous safety testing and risk-to-benefit analyses will need to be undertaken in order to ensure that public and environmental concerns are addressed and any regulatory, ethical and policy challenges met. These include an assessment of the potential toxicity of nanotechnology applications in advance of any permission to market them. Problems arise if safety assessments lag behind nanoparticle development: this has the potential to damage consumer confidence and create a long-lasting mistrust similar to what has been experienced with genetic modification technology.
Keywords : Nanotechnology, Nanofood processing, Nanofood packaging.

Corresponding author

INTRODUCTION

Scientific research and the potential for use of nanotechnology in the agri-food industry has increased substantially in the last decade and it is predicted to grow rapidly over the next few years. Its potential for providing safer and more nutritious foods is important in an era when food security and sustainability are highly topical for a global population predicted to be greater than nine billion by 2050. The island of Ireland has the potential through its strong agri-food background to be a global player in the provision of high quality, safe and nutritious food. However, to date there is no collated information on the current or potential use of nanotechnology on the island of Ireland within the agri-food sector. The technology offers scientifically enhanced capabilities for product development through the provision of novel functional ingredients and nutrient delivery systems, safety testing, packaging and authentication. However, there are still many uncertainties about the technology and its potential applications, as well as doubts about its efficacy and safety in the long term. As with all new sciences and technologies, rigorous safety testing and risk-to-benefit analyses will need to be undertaken in order to ensure that public and environmental concerns are addressed and any regulatory, ethical and policy challenges met. These include an assessment of the potential toxicity of nanotechnology applications in advance of any permission to market them. Problems arise if safety assessments lag behind nanoparticle development: this has the potential to damage consumer confidence and create a long-lasting mistrust similar to what has been experienced with genetic modification technology.

Technological advances such as nanotechnology are an important means of helping the agri-food industry to successfully deal with the challenges of a globalised food system in order to meet increased food production needs and ensure sustainability. This can be done through addressing long-term issues, including global population growth, climate change, changing consumer consumption patterns and increasing competition in the global food market [1-2]. .Nanotechnology has been shown to have a wide range of current and potentially beneficial applications in the agri-food industry. These include precision-farming techniques, novel functional ingredients and nutrient delivery systems, safety testing, innovative packaging, and authenticity and traceability [3-4]. The use of nanotechnology has undoubted economic benefits for food companies, giving them a competitive advantage over competitors, which in turn can facilitate longevity of companies. However, given the level of investment required to implement this technology, there are many factors that can greatly impede the agri-food industry's willingness to adopt such technologies, including existing uncertainties regarding nanotechnology's associated risks, such as potential implications for human health and the environment. Moreover, while multinational food companies have the knowledge, skills and finances to invest in novel technologies, for small and medium-sized enterprises (SMEs), innovation may be constrained by limited resources and difficulties in accessing research and know how to implement such technologies. The traditional challenges facing SMEs are further exacerbated by existing global economic conditions. Across the island of Ireland (IoI), the vast majority of food companies are SMEs which make an enormous contribution to the economy in both jurisdictions. Government efforts are, therefore, focussing on funding research institutes to support these food companies in implementing innovative technologies to expand on their capabilities.
This research was interested in examining the agri-food industry's current level of awareness of nanotechnology and the attitudes towards it on the IoI. Furthermore, the factors supporting and impeding the uptake of such technologies for food and food-related applications were explored and documented. These data should assist in informing and guiding the agri-food industry and government strategies. If nanotechnology is presented in a positive way, and is acknowledged over conventional products, this may increase the uptake of such technologies by even the most cautious agricultural producers and food companies.

A number of reviews [5-11] have discussed the emerging applications of nanotechnology for agricultural production.

To meet this objective, the current and potential applications of nanotechnology at the primary producer and processing levels in the worldwide agri-food industry are examined. The different aspects investigated included different sectors across the agri-food sector:

- Primary production (e.g., targeted genetic engineering of crops; agrochemical delivery)
- Processing (e.g., nanoencapsulation; gelation and viscosifying agents; nanoemulsions;

sanitisation of equipment

- Products (e.g., antimicrobials; intelligent packaging; food contact materials)
- Nutrition and feed (e.g., nutraceuticals; nutrient delivery; fortification of vitamins and minerals)
- Safety (e.g., sensory diagnostics; security/anti-counterfeiting devices)
- EU legislation (e.g., what does it cover? How is it defined? What are its potential effects on industry and trade?)

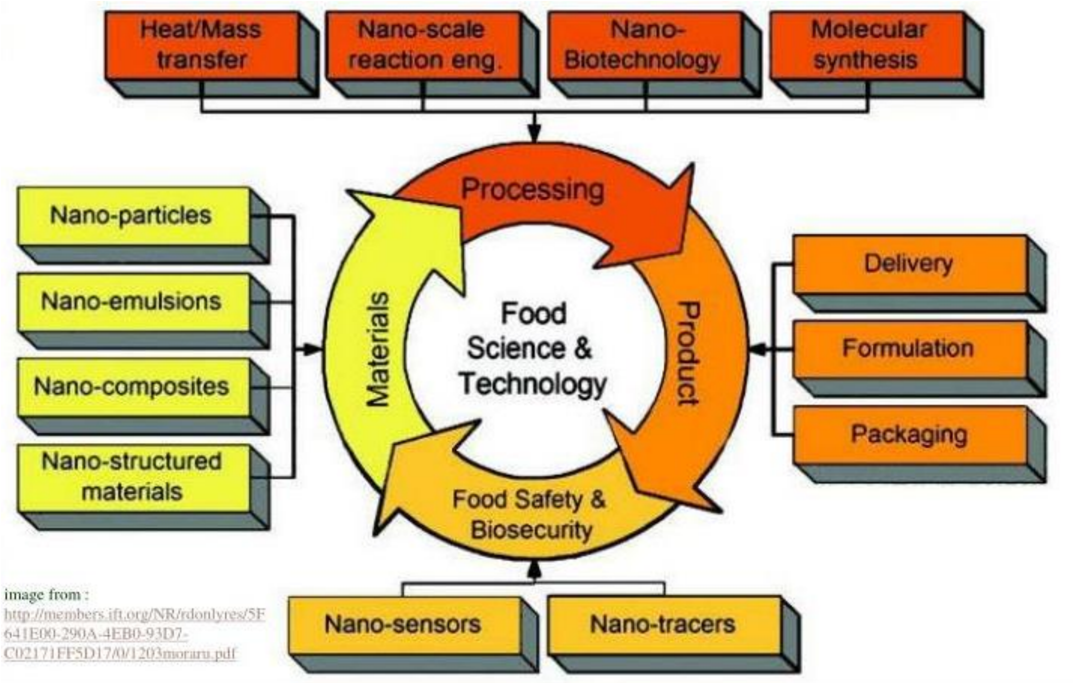

Figure 1. Food and Science using Nanotechnology

NANOFOOD PRODUCTION

Nanotechnology is expected to facilitate the next development stage of GM crops, animal production inputs, chemical pesticides and precision-farming techniques. Precision farming is one of the most important techniques utilised for increasing crop productivity by monitoring environmental variables and applying targeted action [3]. Applications of nanotechnology in agriculture are currently at the R&D stage and so may take many years before being commercialised worldwide. Such techniques are mostly intended to address some of the challenges and limitations facing large-scale, capital and chemical-intensive farming operations.

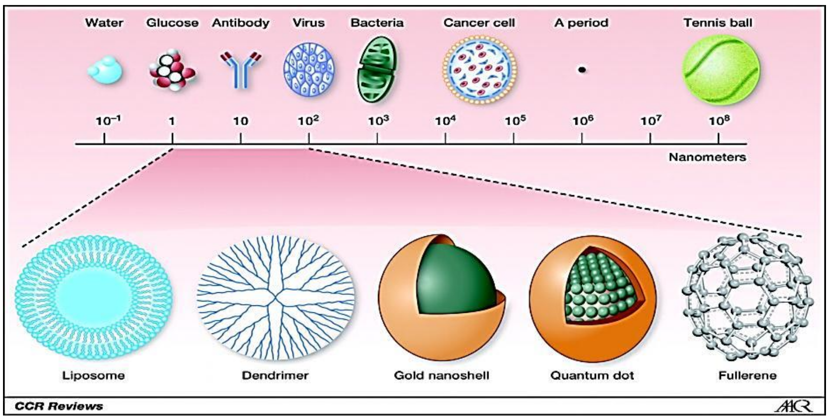

Figure 2. Shows various structures available in nanoscale.

The potential applications of nanotechnology in animal production include improved efficacy and nutrition of animal feeds (e.g., fortified with nanosupplements, antimicrobial additives and detoxifying NMs) and nanobiosensors for animal disease diagnostics. At present, there are very few examples of commercially available products where a nano-sized additive has been explicitly designed for animal feed. An example of a feed additive is one that contains a natural biopolymer from yeast cell walls that is intended to bind mycotoxins to protect animals against mycotoxicosis. The potential use of an aflatoxin-binding nano-additive for animal feed, which is derived from modified nanoclay, has also been suggested. Scientists have also developed an NP that adheres to E. coli, comprising a polystyrene base, polyethylene glycol linker and mannose-targeting biomolecule. These NPs are designed to be administered through feed to remove food-borne pathogens in the GI tracts of livestock [12]. In plant-based agriculture, emerging applications include nano-formulated agrichemicals (e.g.,fertilisers, pesticides, biocides and veterinary medicines) for improved efficiency, reduced use of farm chemicals, new toxin formulations for pest management and better control of applications (e.g., the slow release of pesticides). Nanosensors can be used, for example, for the detection of pathogens, pesticides and other chemicals. Nanosensors have been applied to pesticide residue detection such as organophosphates in fruit, plants and water [8][11] and observed that nanosensors offer high sensitivity, low detection limits, super selectivity, fast responses and small sizes. However, some issues have also been identified regarding this application, such as the accessibility of NMs sensitive to common pesticide residues, the simplicity of sensor fabrication techniques and instrumentation, the desired reliability and repeatability in trace level detection, the cost, and, finally, concerns relating to NM exposure and the environment. The outcome of this narrative review has pointed towards the need for further research in order to ensure complete success for these types of nanotechnology application[11].

Smart field sensing systems are another important application for the real-time monitoring of crop growth and field conditions, including nutritional status, light, temperature, moisture level, soil fertility, insects, weeds and plant diseases, etc.[3] have reported that networks of wireless nanosensors placed across cultivated fields provide detailed information on crop and soil conditions, enabling the best agronomic decisions to be made, with the aim of maximising agricultural yields while minimising resource inputs. This includes information on the optimal times for planting and harvesting crops, as well as the times for applying water, fertilisers, pesticides and other treatments – and their amounts – given the precise plant physiology and pathology and environmental conditions[3]. Wireless nanosensors have already been used in certain parts of the US and Australia. For instance, a Californian vineyard, Pickberry, in Sonoma County has installed Wi-Fi systems with the aid of the information technology (IT) company, Accenture. The cost of installing this system has been rationalised by the fact that it facilitates the best grapes to be grown which, in turn, results in better-quality wines being produced. These then command a premium price [13].

Agriculture	Food Processing	Food Packaging	Supplements
• Single molecule detection to determine enzyme substrate interactions • Nanocapsules for delivery of pesticides, fertilizer and other agrichemicals more efficiently • Delivery of growth hormones in a controlled fashion • Nanosensors for monitoring soil conditions and crop growth • Nanochips for identity preservation and tracking • Nanosensors for detection of animal and plant pathogens • Nanocapsules to deliver vaccines • Nanoparticles to deliver DNA to plants (targeted genetic engineering)	• Nunocapsules to improve bioavailability of neutraceuticals in standard ingredients such as cooking oils • Nanoencapsulated flavor enhancers • Nanotubes and nanoparticles as gelation and viscosifying agents • Nanocapsule infusion of plant based steroids to replaces meat's cholesterol • Nanoparticles to selectively bind and remove chemicals or pathogens from food • Nanoemulsions and particles for better availability and dispersion of nutrients	• Antibodies attached to fluorescent nanoparticles to detect chemicals or foodborne pathogens • Biodegradable nanosensors for temperature, moisture and time monitoring • Nanoclays and nanofilms as barrier materials to prevent spotlage and prevent oxygen absorption • Electrochemical nanosensors to delect ethylene • Antimicrobial and antifungal surface coatings with nanoparticles (silver, magnesium, zinc) • Lighter, stronger and more heat-resistant films with silicate nanoparticles • Modified permeation behavior of foils	• Nanosize powders to increase absorption of nutrients • Cellulose nanocrystal composite as drug carrier • Nanoencapsulation of neutraceuticals for better absorption, better stability of targeted delivery • Nanocochleates (coiled nanoparticles) to deliver nutrients more efficiently to cells without affeccting color or taste of food • Vitamin sprays dispersing active molecules into nanodroplets for belter absorption

Figure 3. Nanotechnology applications in agriculture and food

Another emerging plant-based application is nanoscale carriers (i.e., encapsulation and entrapment, polymers, dendrimers, etc.) for the efficient delivery of agrichemicals (i.e., pesticides, herbicides, fertilisers, plant growth regulators, etc.). Nanoscale delivery vehicles appear to be useful in agronomic applications by improving stability against degradation in the environment and, in doing so, improving its effectiveness while decreasing the amount to be applied. This reduces agricultural chemical runoff and alleviates environmental problems [6].. These carriers can be designed in such a way that the plant roots or the surrounding soil structures and organic matter are anchored, provided that the molecular or conformational affinity between the delivery nanoscale structure and targeted structures and matters in soil are used. These mechanisms enable the slow uptake of active ingredients, thus reducing the amount of agricultural chemicals to be used, in addition to minimising inputs and the waste produced [6]. The nanoencapsulation of pesticides involves manipulating the outer shell properties of a capsule, allowing slow and controlled release of the active ingredient, and, therefore, delivering more effective control over certain pests at lower dosage rates and over a prolonged period of time. Nanopesticides can increase the dispersion and wettability of agricultural formulations (i.e., decreased chemical runoff) and unwanted pesticide movement. Other potential benefits of nanoencapsulated pesticides include increased solubility and decreased contact of active ingredients with farm workers [11]. Globally, pesticides containing nanoscale-active ingredients are commercially available, with many of the world's leading agrochemical firms recognising their potential usefulness and conducting research into the development of novel nanoencapsulated pesticides. For example, Syngenta has incorporated nanoemulsions into its pesticide products. Primo MAXX® is one of its successful growth-regulating products, which, if applied before the onset of stress, such as heat, drought, disease or traffic, can strengthen the physical structure of turf grass, thus enabling it to withstand ongoing stresses throughout the growing seasons [13]. To summarise, while most agricultural applications are still at the R&D stage, they have the potential for adoption at a very large scale by the agricultural sector worldwide due to their ability to improve precision farming practices. Potential applications include nano-formulated agrichemicals, smart field sensing systems to monitor crop growth and field conditions, nanobiosensors for animal disease diagnostics and nanosensors for pathogen and pesticide detection. However, at present, research on methodology, identification and characterisation of NMs, testing priorities and the regulatory guidance on NP safety are still in their initial stages.

NANOFOOD PROCESSING: NUTRITION AND FEED

Nano-food implies that food has been cultivated, produced, processed or packaged using nanotechnology tools or techniques or to which NMs have been added [14]. The intentions of nano-food technology are to improve the quality, safety and nutritional value of food, as well as to reduce costs. Consumers can benefit from this application in terms of meeting individual dietary and health requirements or taste preferences, while benefits to food companies include product differentiation, new market opportunities and economic gains. A diverse range of processes are being utilised to aid with this, such as nanoemulsions, surfactant micelles, emulsion layers, reverse micelles and functionally-designed nanocapsules. Sekhon [14] has indicated that a key application of nanotechnology in food processing involves the development of nano-structured food ingredients, which offers improvements to consistency, taste and texture. Nanoemulsion technology is frequently used to create low-fat mayonnaise, spreads and ice cream, where they are claimed to be as creamy as the full-fat alternatives, thus offering consumers healthier options[14-15]. For example, mayonnaise can be nano-textured using oil in water emulsion containing nanodroplets of water inside oil droplets. The mayonnaise offers taste and texture attributes that are similar to the full-fat equivalent but with significant reductions in the fat content. Unilever is another example, producing an ice cream with reductions in fat from 8-16% to 1% while not compromising on the flavour. Consumers can also benefit from more rapid and simpler thawing of frozen foods in the microwave, as developed by Nestlé using nanoemulsion technology. It has patented water-in-oil emulsions (10-500nm), and through the addition of polysorbates and other micelle-forming substances, aims to contribute to a uniform thawing of frozen foods [16] . Food companies can greatly benefit from adding NPs to their food and beverage products in terms of making improvements to flavour, colour, flow properties and stability during processing or extending their shelf life. For instance, aluminosilicate materials are commonly used as anti-caking agents in granular or powdered processed foods, while titanium dioxide is a food whitening and brightening additive that is commonly used in confectionary, and in some cheeses and sauces[16].

Nanotechnology also offers opportunities to alter and manipulate food and beverage products to allow for more effective delivery of nutrients such as protein, vitamins and minerals, in addition to antioxidants, to specifically target the nutritional and health benefits to consumers. This application also enables food companies to gain a competitive advantage by satisfying individual dietary requirements and consumers' varied demands for foods. An important area of current nanotechnology application is nanoencapsulation of food ingredients and additives. Nanocarrier systems, including emulsions, micelles, liposomes, biopolymer matrices and association colloids, have been developed for use in food and beverage products. Nanoencapsulation can control the release of certain active ingredients (i.e., proteins, vitamins, minerals, enzymes and preservatives), mask undesirable odours and flavours such as fish oils, enhance the shelf life and stability of the ingredient and the finished food product, and improve the uptake of encapsulated nutrients and supplements [2],[5]. The modified characteristics of nanocarriers enable their use in a vast array of food and beverage products. For example, Alfadul and Elneshwy [16] have reported that George Weston Foods, one of the leading bakeries in Western Australia, has successfully incorporated nanocapsules containing tuna fish oil into their "Tip Top" UP bread for additional health benefits. The nanocapsules are designed to be secreted once they enter the stomach, thereby avoiding the unpleasant taste of the fish oil. Another example is Shemen Industries, which has used minute compressed micelles, called nanodrops, in the development of canola active oil. The micelles work as a liquid carrier, enabling the penetration of vitamins, minerals and phenolic compounds that are insoluble in water or fats. The micelles are added to food products, and so pass through the digestive system efficiently, without breaking up, to the absorption site (The Pew Charitable Trusts and Wilson Centre, 2013 [17]. Nutritional additives are an increasing source of the addition of NPs to food. The European Commission (EC) Concerted Action on Functional Food Science in Europe has defined a functional food as "a food that beneficially affects one or more target functions in the body beyond adequate nutritional effects in a way that is relevant to either an improved state of health and well-being and/or reduction of risk of disease" [18]. Nanoencapsulation technologies are being employed to protect bioactive compounds, including vitamins, minerals, proteins, lipids, carbohydrates and antioxidants, for the manufacture of foods with improved functionality and stability, thus offering huge potential for improvements to public health and nutrition[14]. The Nutralease Ltd Company has developed novel carriers for nutraceuticals to be incorporated into food systems, thereby enhancing the bioavailability of the product. Lycopene, beta-carotenes and phytosterols are some of the nutraceuticals incorporated in the carriers, and are used in the production of healthy foods, especially to prevent the accumulation of cholesterol [16]. The added health benefits arising from this application are, therefore, particularly beneficial for consumers with health concerns. Food companies can also benefit from product differentiation and new market opportunities[19]. Rishidi.et.al[19] have proposed that micelles are capable of encapsulating nonpolar molecules, including flavourants, lipids, antimicrobials, vitamins and antioxidants. Various nano-micelle based carrier systems have been developed for nutraceuticals and nutritional supplements and are available on the market. For example, LivOn Laboratories has developed Lypo-Spheric™ vitamin C, using liposomes as the supplement delivery system. Lypo-Spheric™ vitamin C is able to produce serum levels of vitamin C that are nearly twice the level of any other oral form of vitamin C. Health Plus International® Inc. have also developed an innovative nutritional product line, known as Spray For Life. The technology offers benefits of introducing nutrients into the body in a way that enables more rapid, uniform and complete absorption than pills, capsules or other liquids[17]. Dairy products, cereals, breads and beverages are now fortified with vitamins, minerals, antioxidants, plant sterols, probiotics and bioactive peptides[16]. BioDelivery Sciences International has introduced its Bioral™ nanocochleate nutrient delivery system for micronutrients and antioxidants. The nanocochleates (~50 nanometres in size) are based on a phosphatidylserine carrier derived from soya beans, and are generally recognized as safe (GRAS). The nanocochleate system appears to prevent degradation of micronutrients and antioxidants during manufacture and storage[5]. The German company, Aquanova, which has developed a nanocarrier system using 30 nanometre micelles to encapsulate two active substances for fat reduction and satiety; this is a novel innovation for intelligent weight management for consumers. Marketed as NovaSOL, it uses CoQ10 to target fat reduction and alpha-lipoic acid for satiety, thus enabling consumers to feel fuller for longer and assisting in weight loss. This technology has also been used to add antioxidants into food and beverage products through the introduction of nutrients such as vitamin A, C and E, thereby targeting the health and dietary requirements of consumers. NovaSOL also offers substantial advantages to food companies, such as cheaper ingredients, faster production process, enhanced shelf life, higher colour stability, improved uptake and bioavailability, and ready-to-use liquid form, thus resulting in overall reductions in energy usage, wastage and costs. Other examples of these include nano calcium/magnesium from Magi-I-Cal.com USA, and the nano-selenium-enriched Nanotea from Shenzhen Become Industry & Trade Co Ltd [5].

A recent trend reported by Alfadul et.al[16] is the nanoencapsulation of live probiotic microbes for the promotion of GI health. They can be incorporated into various food and drink products, including fermented milk, yoghurts, cheese, puddings and fruit-based drinks. Nanoencapsulation technology is applied to aid in the development of designer probiotic bacterial preparations which can be transited to the GI tract where they interact with specific receptors and can improve intestinal microflora and , thus, support good consumer health (Sherwood and Gorbach, 2000). Many of the large food companies worldwide (e.g., Heinz, Kraft Foods and Nestlé) are investing in nanotechnology and are on their way to commercialising food and beverage products. For instance, the development of interactive foods, which can be modified in terms of their colour, flavour or nutritional properties according to an individual's dietary requirements, allergies or taste preferences, are another function discussed by Alfadul and Elneshwy[16]. Numerous products based on nanocluster delivery systems are available commercially worldwide. For example, RBC Life Sciences® Inc. has developed a nutritional supplements line called NanoCeuticals™. This technology has been used to create a slimming product based on cocoa nanoclusters, which are coated on the surface of engineered NMs to enhance the chocolate flavour through the increase in surface area that targets the taste buds. This product offers consumers an effective solution to weight loss while appealing to their taste preferences. A nanotube is a discrete hollow fibre entity, which has two dimensions in the nanoscale[12]. The self-assembly of hydrolysed calcium binding milk protein α-lactalbumin into nanotubes is another recent development[4]. These food protein-derived nanotubes show good stability and offer potential applications in food, nutrients and pharmaceuticals. α-lactalbumin has an important role in lactose formation, which is essential for milk production; it is already used as a food ingredient in infant formula. Human breast milk provides all the essential nutrients for an infant's growth and development in balanced proportions. Infant formula feeding is the most appropriate alternative if the mother is unable or chooses not to breastfeed her infant. Infant formula is designed to bear a close resemblance to human breast milk, and so extensive research has been dedicated to improving the protein quality of infant formula so that it is more like human milk[20]. Due to the relatively high content of essential amino acids in α-lactalbumin, it is desirable for improved infant formula protein systems, by offering similar protein content to that of human milk, and , thus, helping to meet the nutritional needs of infants[20].

NANOFOOD PROCESSING: EQUIPMENT

The food processing system is faced with a number of challenges relating to the control of chemical contaminants, microbiological hazards and pathogens in order to promote food safety. A number of research initiatives are in the process of investigating the use of NPs as antibacterials for improving food safety. Silver NPs are being incorporated into food processing systems to kill food pathogens and bacteria[16]. Silver's effective antimicrobial properties are due to its intense antimicrobial activity and low toxicity to mammalian cells and tissues[21]. Therefore, silver NPs are being considered as an important means of overcoming the growing problem of antibacterial resistance. At present, these are being used as antimicrobial agents in foods, with the aim of developing food-related applications, such as microbe-resistant fabrics or non-biofouling surfaces[16]. In food manufacturing, the greatest energy requirements are from the process heating and cooling systems, which are an essential part of the maintenance of food safety. Nanotechnology-based equipment insulation coatings have been developed to enable manufacturers to reduce heat loss and lower their energy costs. Nansulate has developed thermal insulation coatings using award-winning, patented technology, which integrates a safe, nano-sized internal structure into a low-volatile, organic compound, water-based, acrylic latex coating. Nansulate offers manufacturers an easy method of coating a number of difficult-to-insulate food and beverage processing equipment (i.e., heat exchangers, ovens, dryers and cookers), as well as protecting equipment from corrosion and mould growth. Furthermore, the clear coatings allow for easy visual inspection of the substrate surface. The overall benefits to food manufacturers include significant cost savings and improved profit margins . Another nanotechnology-based coating system is Bioni, which was also developed to satisfy the requirements of the food industry. The patented solution uses a two-layer system that can be applied directly to mould-affected substrates and other surfaces. The system also provides a permanent protection against the growth of new mould, mildew or bacteria on the coating film, thereby providing cost-saving benefits. A further advantage to Bioni is that it is eco-friendly as it does not require any other chemicals for disinfectant and pre-treatment of affected surfaces[22]. In summary, nanotechnology has promising applications for the sanitisation of food processing equipment (i.e., silver NPs), which can offer effective solutions to food safety issues and reduce resource costs. Moreover, many companies have already demonstrated successful nanotechnology applications in the development of nano-foods and beverage products, due to the various potential benefits they offer in terms of improvements to flavour, texture, consistency and nutritional value.. Some of the processes being utilised for the production of nano-food include nanoencapsulation, nanoemulsions, surfactant micelles, emulsion layers and functionally-designed nanocapsules.

NANOFOOD PACKAGING

Nanopackaging applications as food contact materials are growing rapidly; this is now considered to be the most active area of nanotechnology in the food sector. At present, approximately 400 to 500 nanopackaging products are available on the global market, with predictions that nanopackaging will account for 25% of all food packaging within the next 10 years[23]. Manufacturers claim that nanopackaging can extend product shelf life, as well as assist in the maintaining, improving or monitoring of the quality and safety of foods. For instance, the use of NPs in food packaging can improve the mechanical and heat resistance properties, thereby affecting gas or water vapour permeability, and , thus, increasing shelf life. Improved packaging has been described by Silvestre et al.[24] as incorporating NPs in the polymer matrix materials, with improved packaging properties in terms of temperature/moisture stability, flexibility, durability and gas barrier properties (e.g., nanocomposites, silicate NPs and nanosilver). Han et al. [25] have also suggested that the application of NPs in food packaging has additional functions. such as antibacterial properties. Elgin, IL Multifilm Packaging has developed an ultra-thin coating known as N-Coat®, which is applied to a 48-gauge polyester film, resulting in a clear laminate with an excellent gas barrier that can compete with most metallised structures. N- Coat® has been primarily developed for nuts, coffee and dry foods[17]. Active and intelligent food packaging are novel concepts of packaging compared with traditional materials. Polymer nanocomposites, integrating metal or metal oxide NPs, have been developed for active packaging. These include silver, gold, zinc oxide, silica, titanium dioxide and iron oxides. Chaudhry et al.[5] have indicated that active packaging has the ability to remove undesirable tastes and flavours, and improve the colour or odour of the packed food. For example, carbon black NPs incorporated into polymer packaging can absorb odours released from the food or packaging. An emerging active packaging application integrates NPs with antimicrobial or oxygen scavenging properties; this packaging is designed to stop microbial growth once the package is opened by the consumer and rewrapped with an active-film portion of the package[4]. A number of food contact materials have been developed using nanosilver, which, it is claimed, preserves the food for longer and inhibits the growth of microorganisms. For example, Blue Moon Goods LLC has introduced new silver NP fresh box super airtight food storage containers that can reduce bacteria by up to 99.9%. Foods can easily be stored for up to four times the length of time than traditional food containers, thus offering consumers the benefits of fresher, higher quality food for a longer period of time, and, subsequently, reduced food wastage. Other examples include “FresherLonger™ Miracle Food Storage Containers” and “FresherLonger™ Plastic Storage Bags” from Sharper Image® USA, “Nano Silver Food Containers” from A-DO Global and “Nano Silver Baby Mug Cup” from Baby Dream® Co Ltd[17]. Nanosilver has also been used to provide an antibacterial coating on kitchenware and tableware (Changmin Chemicals, Nano Care Technology Ltd, Pro-Idee GmbH & Co KG) to kill attached bacteria and maintain permanently clean and hygienic surfaces, thus benefiting consumers in terms of reduced risks of foodborne illnesses[17]. Furthermore, nanosilver has been integrated into the interior coating of domestic refrigerators (LG, Samsung and Daewoo) for effective disinfection, deodorisation and antibacterial effects[17]. Intelligent or smart-food packaging incorporates a nanobiosensor for sensing and signalling microbial and biochemical changes, and releasing antimicrobials, antioxidants, enzymes, flavours and nutraceuticals to extend shelf life. A diverse range of devices has been developed to detect food spoilage organisms in food packaging (e.g., nanowires and antibodies), thus enabling versatility and much cheaper production[8]. Examples of some of the companies developing intelligent packaging for their food and beverage products include the nanotechnology company, pSiNutria, which is developing nano-based tracking technologies, including an edible BioSilicon, which can be placed in foods for monitoring purposes and pathogen detection. Another example is Kraft, which is working with Rutgers University (US) to develop engineered nanosensors in food packaging, which change colour to warn the consumer of food spoilage or, if the food has been contaminated by pathogens. These nanosensors use electronic ‘noses’ and ‘tongues’ to ‘taste’ or ‘smell’ scents and flavours[4]. AgroMicron has developed the NanoBioluminescence Detection Spray, which encompasses a luminous protein that is intended to bind to the surface of bacteria such as salmonella and E.coli [8]. Biodegradable nanocomposites food packaging has been described by Momin et al.[4] as incorporating inorganic particles, such as clay, into the biopolymeric matrix, which can improve the delivery of micronutrients. The nano-layered structure also restricts the access of gases, and offers considerable improvements in terms of the gas barrier properties of nanocomposites. Biodegradable materials have potential use in a wide range of food packaging applications, including processed meats, cheese, confectionary, cereals and boil-in-the-bag foods, as well as extrusion-coating applications for fruit juices and dairy products or co-extrusion processes for the production of bottles for beer and carbonated drinks [5]. For example, Voridan has developed a nanocomposite containing clay NPs, called Imperm. This is ideal for beer, as the resultant bottle is lighter and stronger than glass and is less likely to shatter. Furthermore, the nanocomposite structure minimises loss of carbon dioxide from the beer and keeps oxygen out of the bottle, thereby retaining the freshness of the beer and extending its shelf life. This technology has been adopted by various companies, including the Miller Brewing Co [13]. Aegix® OX (Honeywell Speciality Polymers) has also successfully engineered plastic beer bottles that integrate nanocomposites to enhance the barrier properties and extend shelf life by up to 26 weeks. This technology has been used in the Hite Pitcher beer bottle from Hite Brewery Co in South Korea[13]. Durethan KU2-2601 (Bayer AG) is another example. This a hybrid plastic that is enriched with numerous silicate NPs. The plastic incorporates Nanocor's clay to produce a film that is lighter, stronger and more heat resistant than traditional packaging materials. The film is intended to prevent the entrance of oxygen and other gases, and the exit of moisture, thus preventing food spoilage[5]. Conversely, Durán and Marcato [8] have suggested that biodegradable materials demonstrate poor barrier and mechanical properties and require substantial improvements before replacing traditional packaging materials. Nanopackaging has the potential to provide manufacturers with a vast range of benefits, including the ability to keep packaged food fresher for longer[23]. This may enable food to travel further and remain in storage for an extended period of time, thus resulting in a more reliable food supply. By increasing the shelf life of food products, manufacturers will also be able to sell food that would have otherwise been discarded due to spoilage, and hence contribute to reductions in food waste. Innovative and novel packaging that is lightweight, stronger and functional can also significantly reduce transportation costs and packaging materials in the environment. Smart labels on food packaging are likely to appeal to manufacturers due to the ability to effectively monitor the safety, quality and security of food and beverage products during transportation and storage, reducing the risks of foodborne illnesses. Consumers may also benefit from attractive new products on the market, which are safer and of better quality. In summary, improved packaging, active and intelligent packaging, and biodegradable nanocomposites food packaging are the three main types of innovative packaging identified. The application of NPs to food packaging can extend shelf life and improve product quality and safety. However, for complete success, certain materials require further improvements before replacing traditional plastics.

NANOFOODS AND NANO AGROCHEMICALS POSE NEW HEALTH RISKS

The incorporation of manufactured nanomaterials into foods and beverages, nutritional supplements, food packaging and edible food coatings, fertilisers, pesticides and seed treatments creates a host of new exposure pathways and a whole new array of risks for the public, workers in the food industry and farmers[26]. However, since there is no register of which nanomaterials are used and in what quantity or what food products and food contact materials they are used in[27]. The evidence of potential harm associated with certain nanomaterials has become stronger.

Why nanomaterials pose new risks

- Nanomaterials are generally more chemically reactive than larger particles of the same chemicals
- Nanoparticles have greater access to our bodies than larger particles
  - Greater bioavailability and greater bioactivity may introduce new toxicity risks;
  - Nanomaterials can compromise our immune system response;
  - Nanomaterials may have long term pathological effects.

Absorption through the digestive tract Numerous in vivo experiments using rats and mice have demonstrated gastrointestinal uptake of nanoparticles[28-32] and small microparticles[33-35]. Pathological examination of human tissues suggests ingestion and translocation of microparticles[36-37]. The absorption rate of substances via the gastrointestinal tract appears to depend on their properties such as size and surface structure. In one study looking at rats, the smaller the nanoparticles the higher the uptake via the digestive tract[38]. In another study mice were fed 4 nm gold particles. These were later detected in the liver, kidney, spleen, lung and brain. Larger 58 nm particles remained in the gastrointestinal tract[39]. Studies have shown that nanomaterials may affect the human intestine. When human colon cells were treated with nano-sized polystyrene, which is commonly used in food packaging, these became more permeable to iron[40]. It has been observed that the daily exposure of people in the Western world to submicrometre-sized mineral particles has resulted in 'pigmented cells' loaded with these particles in parts of the intestinal tract. The particles have been observed to be composed of aluminosilicates, titanium dioxide and a small percentage of non-aluminium-containing silicates such as silica (SiO2) and magnesium trisilicate(talc)[31]. Preliminary evidence suggests that existing levels of nanoparticles up to a few hundred nanometres in size in processed food may be associated with rising levels of immune system dysfunction and inflammation of the gastro-intestinal tract, including Crohn's disease[42-45]. Individuals with Crohn's disease or colon cancer have been found with nanomaterials in their intestinal tissue[46]. Nanomaterials in the human body Our bodies' defensive mechanisms are not as effective at removing nanoparticles from our lungs, gastrointestinal tract and organs as they are with larger particles[47]. Nanoparticles are also more adhesive than larger particles to surfaces within our bodies[48]. As a result of these factors and their very small size, nanoparticles are much more likely to be taken up into our cells and tissues than are larger particles. A growing body of evidence demonstrates that some nanomaterials are more toxic per unit of mass than larger particles of the same chemical composition[49-52]. Nanomaterials have been detected in the heart, liver, spleen, lung, kidney, brain and bone marrow. Insoluble nanomaterials may accumulate and remain in the body for extended periods[53]. In one study, particles of 200-300 nm reached the foetus via the placenta. It is not known whether this causes harm to the placenta or the unborn child[54-55]. Currently there is no data on whether it is possible for nanomaterials to pass into breast milk[56]. The cell membrane is no obstacle to nanomaterials penetrating into cells, unlike larger particles. Studies show that 30 nm nanoparticles can even penetrate into the nucleus[57]. Non-degradable nanoparticles may lead to long-term health damage, even in the absence of acute toxicity.

A small number of clinical studies suggest that nondegradable nanoparticles and small microparticles which do not provoke an acute toxic response can accumulate in our bodies and over time result in the development of 'nanopathologies', such as granulomas, lesions (areas of damaged cells or tissue), cancer or blood clots[58-60]. The Federal Institute for Risk Assessment and the Federal Environment Agency in Germany believe there is clear evidence that some nanomaterials have greater carcinogenic potential then microscale particles of the same material[61]. Health concerns with nanomaterials in food and food contact materials

Nano Silica

Uses: Used as a 'trickle and flow' aid in powdered food products, as a clearing agent in beer and wine, as a food additive and a food coating. Health concerns:

• Several recent studies have shown liver toxicity when animals were injected with nanosilica[62]. Animal studies suggest that nanosilica can be absorbed from the gastrointestinal tract as nanoparticles, become systemically available, and accumulate in tissues. Once systemically available nanosilica appears to be mostly distributed to the liver and spleen, and to a lesser extent other tissues. Some studies suggest that nanosilica can cross the blood-brain barrier and possibly the placenta[63];
• A recent study where rats were fed synthetic amorphous silica (SAS) - a form of nanostructured and that the nanostructured silica accumulated in the spleen[64].
• Recently a consumer intake of silica from food was estimated at 9.4mg/kg of body weight per day of which 1.8mg/kg body weight per day was estimated to be in the nano size range[65]. **Nano-silver**

Uses: In the Woodrow Wilson inventory of nano products, silver is the most common nanomaterial mentioned in product descriptions[66]. A recent court case in the US found that the use of nano-silver was 'ubiquitous' and that there was no way for consumers to avoid exposure[67]. Food and food contact products food containers, packaging, cutting boards, salad and collapsible coolers. In agriculture, it is used in poultry production and agricultural and aquacultural disinfectants[68]. Health concerns:
• There is mounting evidence that nano-silver may have greater toxic effects when compared with bulk silver. Nano-silver can better penetrate biological barriers and attach itself to the outside of cells[69]. Nanoscale silver can also enter the bloodstream and reach all organs of the body including the brain, heart, liver, kidneys, spleen, bone marrow and nervous tissue;• Animal studies have shown placental transfer and foetal uptake of nano-silver[70]. is disturbing when one considers a recent study which found that exposure to nanosilver widely used as a model organism for the study of embryological development in other vertebrates including humans[71];

• Health experts have also raised concerns that the widespread use of nano-silver in consumer

products will further increase the problem of superbugs[72].
NanoTitanium dioxide

Uses: A whitener and brightener in a range of food products Health concerns:

• ECHA is currently reviewing the safety of titanium dioxide (including the nano form) because of concerns it may be harmful to the environment and human health[73];
• In contrast to bulk particles of titanium dioxide, nanoscale titanium dioxide is biologically very active. Studies show that titanium dioxide can damage DNA[74], disrupt the function of cells, interfere with the defence activities of immune cells and, by adsorbing fragments of bacteria and 'smuggling' them across the gastro-intestinal tract, can provoke inflammation[75-80]. A single high oral dose of titanium dioxide nanoparticles kidneys and livers of female mice;
• In a 2010 study the German Federal Institute for Risk Assessment (BfR) and the German Federal Environment Agency (UBA) concluded that nanoscale titanium dioxide is a possible carcinogen if inhaled[81];
• Nano titanium dioxide is highly mobile in the body and has been detected in both humans and animals in the blood, liver and spleen[82]. A study using pregnant mice found that they transfer nanoparticles of titanium dioxide to their offspring. This resulted in brain damage, nerve system damage and reduced sperm production in male offspring[83];
• A human exposure analysis of titanium dioxide age range as having the highest exposure because the titanium dioxide content of sweets is higher than any other food products. It also calculated that a typical exposure for a US adult may be of the order of 1 mg of titanium per kilogram of body weight per day[83].

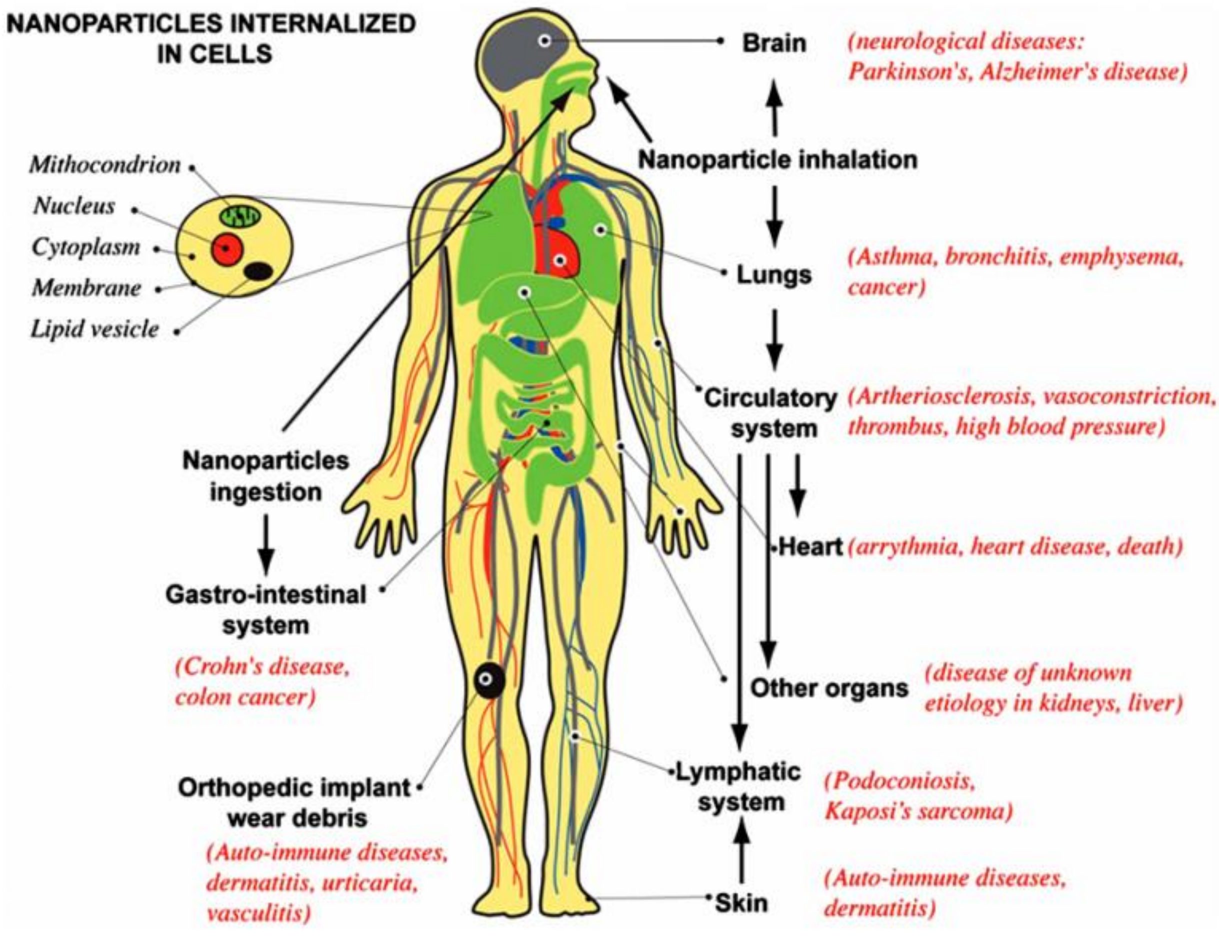

Fig. 4. Pathways of exposure with affected organs and associated diseases (reprinted from Buzea et al. 2007) Buzea, C., Pacheco, I. I., and Robbie, K. (2007). "Nanomaterials and nanoparticles: Sources and toxicity." Biointerphases, 2(4), MR17–MR71.

ISSN: 0975-8585

NanoZinc oxide

Uses: Surface coatings

Health Concerns:

• Nanoscale zinc oxide (ZnO) is toxic when ingested and has been found to cause lesions in the liver, pancreas, heart and stomach. A recent review of the safety of nano zinc oxide by the European Safety stated that "clear positive toxic responses in some of these tests clearly indicate a potential for risk to humans."[84] Inhalation exposure of nano zinc oxide induces lung inflammation, leading the SCCS to conclude that "the use of ZnO nanoparticles in spray products cannot be considered safe."[84]

Nano Copper

Uses: dietary supplements[85]

Health Concerns:

• The German Federal Institute for Risk Assessment compared the acute toxicity of micro- and nanoscale copper. No adverse effects were observed with microscale copper – however, nanoscale copper showed adverse effects on the kidney, spleen and liver of mice[86].

Carbon nanotubes

Uses:

food and food contact products containing carbon nanotubes, food packaging and food sensors containing carbon nanotubes have been developed[87-88]. The use of carbon nanotubes in fertilisers is also being researched but does not yet appear to have been commercialized[89].

Health Concerns:

• The Australian National Industrial Chemical and Safe Work Australia, which reviewed the safety of carbon nanotubes, found that multi-walled carbon nanotubes "have been shown to induce mesothelioma in rodents"[90].

Nano supplements

The head of the nanotechnology research group at the United Kingdom's Central Science Laboratory warns of unpredictable effects of nanoparticles and nano encapsulated additives: "They can be absorbed faster than desired or affect the absorption of other nutrients. We still know very little, if anything at all"[91]. In 2009, based on the growing number of commercially available nano supplements, the Woodrow Wilson International Center for Scholars' project on emerging nanotechnologies found that the United States Food and Drug Administration had neither the regulatory supplements were safe[92].

Health risks associated with nano packaging

It is possible that nanomaterials could migrate from food packaging into foods. Polymers and chemical additives in conventional food packaging are known to migrate from the packaging into food products[93-94]. The Institute of Food Science and Technology has expressed concern that manufactured nanomaterials are already being used in food packaging, despite migration rates and exposure risks remaining unknown[95]. To date there are only a few studies that have investigated the migration of nanomaterials from food packaging into food and the results have been inconclusive.

Health risks posed by nano agrochemicals

There is a risk that the development of nano formulations of existing agrochemicals which are more reactive and bioactive may in turn increase the risk to human health. Many developments seem to be currently at the R&D stage and it is likely that the agriculture sector will see some large-scale applications of nanotechnologies in the future. Should this occur, this will increase the potential exposure to agrochemicals used in the agriculture sector[96]. Data on the health risks associated with agrochemicals is voluminous[97] but scarce for nano agrochemicals. In addition to concerns relating to worker inhalation and exposure, there are concerns regarding potential risks associated with bioaccumulation of nanoparticles in food crops[98] and the health impacts produced by interactions between both active and inactive ingredients in the new pesticide formulations[99].

Recognising that many of these nanoscale reformulations are new, EU regulation (1107/2009) requires that "coformulants must not exhibit harmful effects on human and animal health." Occupational health and safety (OHS) concerns In the food sector, workers may come into contact with nanomaterials during production, packaging, transport and waste disposal of food and agrochemicals[100]. To date, there is very little data relating to the exposure of workers to nanomaterials.

A number of nanomaterials used in the food industry such as zinc oxide and titanium dioxide have been shown to be harmful when inhaled, raising OHS concerns for workers handling these materials. However the lack of a mandatory register and product labelling means that many workers may be unaware that they are handling nanomaterials and of the need to use protective equipment. Studies have also shown that nanomaterials can enter the bloodstream via the lungs raising major OHS concerns[101]. Based on a 2009 review of carbon nanotubes by Safe Work Australia and NICNAS, carbon nanotubes were declared a hazardous chemical for purposes of health and safety laws[102].

CONCLUSIONS

An overview of the current and potential applications of nanotechnology in food and related products indicates that it offers a range of benefits to the entire agri-food sector, from improved precision farming practices to food products with enhanced flavour, texture and nutrition, as well as novel packaging which can extend product shelf life and increase the quality and safety of food. Many of these benefits will enhance the range, quality and quantity of food products, enable new international market opportunities to be taken and improve profit margins. It also offers great potential for improvements to food and water safety and nutrition in developing countries. The current level of nanotechnology development in the global food sector is still relatively small, with most products still at the R&D stage, and limited successful applications of nanotechnology to food. It is particularly important to ensure that consumers are able to exercise choice in the use of the products of nanotechnology and that they have the information to assess the benefits and risks of such products. The success of these advancements will be dependent on consumer acceptance and the exploration of regulatory issues. Food producers and manufacturers could make great strides in food safety by using nanotechnology, and consumers would reap benefits as well. At present, there are uncertainties regarding food companies' levels of awareness and attitudes towards the use of nanotechnology for food application. Existing scientific gaps in knowledge in relation to potential health risks and environmental safety are impeding the implementation of effective legislation. These issues must be addressed in order for the technology to be successfully adopted by industry.

ACKNOWLEDGEMENTS

I would like to acknowledge Prof. Vijaya Bhaskara Raju, Director of GITAM Institute of Technology, GITAM University Bengaluru Campus, India and Prof. R. Venkatanadh, Research Coordinator, GITAM University, Bengaluru for their constant encouragement to finish this work.

REFERENCES

[1] Godfray, H.C.J., Crute, I.R., Haddad, L., Lawrence, D., Muir, J.F., Nisbett, N., et al., The future of the global food system. Philosophical Transactions of the Royal Society B: Biological Sciences, 365: 2769-2777,2010.

[2]. Sastry, R.K., Anshul, S. and Rao, N.H., Nanotechnology in food processing sector- An assessment of emerging trends, Journal of Food Science and Technology, 50: 831-841, 2013.
[3] Chen, H. and Yada, R., Nanotechnologies in agriculture: New tools for sustainable development. Trends in Food Science and Technology, 22(11): 585-594, 2011.
[4] Momin, J.K., Jayakumar, C. and Prajapati, J.B., Potential of nanotechnology in functional foods. Emirates Journal of Food and Agriculture, 25(1): 10-19, 2013.
[5]. Chaudhry, Q. and Castle, L., Food applications of nanotechnologies: An overview of opportunities and challenges for developing countries. Trends in Food Science and Technology, Volume 22, Issue 9, September 2011, Pages 498.
[6] Ditta, A., How helpful is nanotechnology in agriculture? Advances in Natural Science.: Nanoscience and Nanotechnology, 3: 1-10, 201222(11): 595-603, 2011.
[7] . Duncan, T.V., Applications of nanotechnology in food packaging and food safety: Barrier materials, antimicrobials and sensors. Journal of Colloid and Interface Science 363 (2011a) 1–24.
[8]. Durán, N. and Marcato, P.D., Nanobiotechnology perspectives. Role of nanotechnology in the food industry: A review. International Journal of Food Science and Technology, 48(6): 1127-1134, 2013.
[9]. Garcia, M., Forbe, T. and Gonzalez, E., Potential applications of nanotechnology in the agro-food sector. Ciencia E Tecnologia De Alimentos, 30(3): 573-581, 2010.
[10]. Grobe, A. and Rissanen, M.E., Nanotechnologies in agriculture and food - An overview of different fields of application, risk assessment and public perception. Recent Patents on Food, Nutrition and Agriculture, 4(3): 176-186, 2012.
[11]. Khot, L.R., Sankaran, S., Maja, J.M., Ehsani, R. and Schuster, E.W., Applications of nanomaterials in agricultural production and crop protection: A review. Crop Protection, 35: 64-70, 2012.
[12] FAO/WHO expert meetings on the application of nanotechnologies in the food and agriculture sectors: potential food safety implications. Meeting report. 2010Available from: http://www.fao.org/docrep/012/i1434e/i1434e00.pdf.
[13]. Joseph, T. and Morrison, M., Nanotechnology in Agriculture and Food. Institute of Nanotechnology, Nanoforum Report 2006: 1-13 Available from: ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/nanotechnology_in_agriculture_and_food.pdf.
[14]. Sekhon, B.S., Food nanotechnology- an overview. Nanotechnology, Science and Applications, 3: 1-15, 2010.
[15]. Cushen, M., Kerry, J., Morris, M., Cruz-Romero, M. and Cummins, E., Nanotechnologies in the food industry - Recent developments, risks and regulation. Trends in Food Science and Technology, 24(1): 30- 46, 2012.
[16]. Alfadul, S.M. and Elneshwy, A.A., Use of nanotechnology in food processing, packaging and safetyreview. African Journal of Food Agriculture, nutrition and Development, 10(6): 2719-2739, 2010.
[17]. The Pew Charitable Trusts and Wilson Centre. Nanotechnology Consumer Products Inventory. The Project on Emerging Nanotechnologies. Available from: http://www.nanotechproject.org/cpi/browse/categories/food-and-beverage/.
[18]. European Commission, Directorate-General for Research, Food, Agriculture & Fisheries & Biotechnology. Functional Foods. 2010 Available from: ftp://ftp.cordis.europa.eu/pub/fp7/kbbe/docs/functional-foods_en.pdf.)
[19]. Rashidi, L. and Khosravi-Darani, K., The Applications of Nanotechnology in Food Industry. Critical Reviews in Food Science and Nutrition, 51: 723-730, 2011.
[20]. Lien, E.L., Infant formulas with increased concentrations of α-lactalbumin . American Journal of Clinical Nutrition, 77(1): 1555S-1558S, 2003.
[21]. Araújo, E.A., de Andrade, N.J., da Silva, L.H.M., Bernardes, P.C., de Carvalho Teixeira, A.V.N., Queiroz Fialho, J.F., de Sá, J.P.N. and Fernandes, P.E., Modification of stainless steel surface hydrophobicity by silver nanoparticles: strategies to prevent bacterial adhesion in the food processing. Journal of Adhesion Science and Technology, 27(24): 2686-2695, 2013.
[22]. Bioni-USA. The first effective and efficient solution for food and beverage processing facilities.2013http://bioni usa.com/bionisystem/food_and_beverage_processing_solution/.
[23]. Lyons, K., Scrinis, G. and Whelan, J., Capacity. Section II: Capacity. Nanotechnology, Agriculture, and Food. In: Maclurcan D, Radywyl N, editors. Nanotechnology and Global Sustainability. CRC Press, Taylor & Francis Group; 2011.
[24]. Silvestre, C., Duraccio, D. and Cimmino, S., Food packaging based on polymer nanomaterials. Progress in Polymer Science, 36(12): 1766-1782, 2011.

[25] Han Wei, Yu Yan Jun, Li Ning Tao and Wang Li Bing. Application and safety assessment for nanocomposite materials in food packaging. Chinese Science Bulletin, 56(12): 1216-1225, 2011.
[26]. TA Swiss (Zentrum für Technologiefolgen-Abschätzung) (2009) Nanotechnology in the Food Sector, http://www.ta-swiss.ch/ nanofood/#downloads (accessed 10 March 2014)
[27]. EFSA (2009) The Potential Risks Arising from Nanoscience and Nanotechnologies on Food and Feed Safety, http://www.efsa.europa.eu/en/efsajournal/doc/958.pdf .
[28]. Chen Z, Meng H, Xing G, Chen C, Zhao Y, Jia G, Wang T, Yuan H, Ye C, Zhao F, Chai Z, Zhu C, Fang X, Ma B, Wan L. (2006b) Acute toxicological effects of copper nanoparticles in vivo. Toxicol Lett 163:109-120.
[29]. Desai M, Labhasetwar V, Amidon G, Levy R. (1996) Gastrointestinal uptake of microparticles: Effect of particle size. Pharm Res 13(12):1838-1845.
[30]. Hillyer J, Albrecht R. (2001) Gastrointestinal persorption and tissue distribution of differently sized colloidal gold nanoparticles. J Pharm Sci 90(12):1927-1936.
[31]. Wang B, et al. (2007) Acute toxicological impact of nano- and submicro-scaled zinc oxide powder on healthy adult mice. J Nanopart Res 10(2):263-276.
[32]. Wang J, et al. (2007) Acute toxicity and biodistribution of different sized titanium dioxide particles in mice after oral administration. Toxicol Lett 168(2):176-185.
[33]. Hazzard R, Hodges G, Scott J, McGuinness C, Carr E. (1996) Early intestinal microparticle uptake in the rat. J Anat 189:265-271.
[34]. McMinn L, Hodges G, Carr K. (1996) Gastrointestinal uptake and translocation of microparticles in the streptozotocin-diabetic rat. J Anatom 189:553-559.
[35]. Wang B, Feng W-Y, Wang T-C, Jia G, Wang M, Shi J-W, Zhang F, Zhao Y-L, Chai Z-F. (2006) Acute toxicity of nano- and micro-scale zinc powder in healthy adult mice. Toxicol Lett 161:115–123.
[36]. Ballestri M, Baraldi A, Gatti A, Furci L, Bagni A, Loria P, Rapana R, Carulli N, Albertazzi A. (2001) Liver and kidney foreign bodies granulomatosis in a patient with malocclusion, bruxism, and worn dental prostheses. Gastroenterol 121(5):1234–8.
[37]. Gatti A, Rivasi F. (2002) Biocompatibility of micro- and nanoparticles. Part I: in liver and kidney. Biomaterials 23:2381–2387.
[38]. LUBW (Landesanstalt für Umwelt, Messungen und Naturschutz Baden-Württemberg) (2010) Nanomaterialien: Toxikologie/Ökotoxikologie, http://www.lubw.baden wuerttemberg.de/servletƒNGname=U10-S05-N10.pdf .
[39]. SRU (Sachverständigenrat für Umweltfragen) (2011) Vorsorgestrategien für Nanomaterialien, http://www.umweltrat.de/ SharedDocs/Downloads/DE/02_Sondergutachten/2011_09_ SG_Vorsorgestrategien%20f%C3%BCr%20Nanomaterialien. pdf?__blob=publicationFile .
[40]. Spiegel online (2012) Nanopartikel verändern Eisenaufnahme im Darm, http://www.spiegel.de/wissenschaft/medizin/ diskussion-um-gefahren-nanopartikel-veraendern-eisenaufnahme-im-darm-a-814794.html.
[41]. Powell JJ, Faria N, Thomas-McKay E, Pele LC. (2010) Origin and fate of dietary nanoparticles and microparticles in the gastrointestinal tract. J Autoimmun 34:J226–J233.
[42]. Ashwood P, Thompson R, Powell J. (2007) Fine particles that adsorb lipopolysaccharide via bridging calcium cations may mimic bacterial pathogenicity towards cells. Exp Biol Med 232(1):107-117.
[43]. Gatti A, Tossini D, Gambarelli A. (2004) Investigation Of Trace Elements In Bread Through Environmental Scanning Electron Microscope And Energy Dispersive System. 2nd International IUPAC Symposium, Brussels, October 2004.
[44]. 'Hƒ-cacy and tolerability of a low microparticle diet in a double blind, randomized, pilot study in Crohn's disease. Eur J Gastroenterol Hepatol 13:101-106.
[45]. Lucarelli M, Gatti A, Savarino G, Quattroni P, Martinelli L, Monari E, Boraschi D. (2004) Innate defence functions of macrophages can be biased by nano-sized ceramic and metallic particles. Eur Cytok Net 15(4):339-346.
[46]. SRU (Sachverständigenrat für Umweltfragen) (2011) Vorsorgestrategien für Nanomaterialien. http://www.umweltrat.de/ SharedDocs/Downloads/DE/02_Sondergutachten/2011_09_ SG_Vorsorgestrategien%20f%C3%BCr%20Nanomaterialien. pdf?__blob=publicationFile .
.[47]. Oberdörster G, Oberdörster E, Oberdörster J. (2005) Nanotoxi Environ Health Perspect 113(7):823-839.
[48]. Chen, Z. et al. (2006) Acute toxicological effects of copper nanoparticles in vivo. Toxicol Lett 163:109-120.
[49]. Brunner T, et al. (2006) In Vitro Cytotoxicity of Oxide Nanoparticles: Comparison to Asbestos, Silica, and the Effect of Particle Solubility. Environ Sci Technol 40:4374-4381.
[50]. Chen Z. et al. (2006) Acute toxicological effects of copper nanoparticles in vivo. Toxicol Lett 163:109-120.

[51]. Long T. et al. (2006) Titanium dioxide (P25) produces reactive oxygen species in immortalized brain microglia (BV2): Implications for nanoparticle neurotoxicity. Environ Sci Technol 40(14):4346- 4352.
[52]. Magrez A. et al. (2006) Cellular toxicity of carbon-based nanomaterials. Nano Lett 6(6):1121-1125.
[53]. Panel on Plant Protection Products and their Residues (PPR), http://www.efsa.europa.eu/de/efsajournal/doc/1171.pdf (accessed 17 July 2012)
[54]. Eidgenössische Materialprüfungs- und Forschungsanstalt (2011) Ten Years of Assessment of Nanomaterials, http://www.biozid.info/deutsch/aktuelles/meldung/?tx_ttnews[tt_news]=89&-cHash=77f53ff8b00b1dd02f12dcbc0a78c798 .
[55]. Umweltbundesamt (2009) Nanotechology for Humans and the Environment, http://www.umweltdaten.de/publikationen/ fpdf-l/3765.pdf .
[56]. Panel on Plant Protection Products and their Residues (PPR), http://www.efsa.europa.eu/de/efsajournal/doc/1171.pdf (accessed 17 July 2012)
[57]. Umweltbundesamt (2009) Nanotechology for Humans and the Environment, http://www.umweltdaten.de/publikationen/ fpdf-l/3765.pdf .
[58]. Ballestri M. et al. (2001) Liver and kidney foreign bodies granulomatosis in a patient with malocclusion, bruxism, and worn dental prostheses. Gastroenterol 121(5):1234–8.
[59]. Gatti A, Rivasi F. (2002) Biocompatibility of micro- and nanoparticles. Part I: in liver and kidney. Biomaterials 23:2381–2387.
[60]. Gatti A. (2004) Biocompatibility of micro- and nano-particles in the colon. Part II. Biomaterials 25:385-392.
[61]. . Bundesinsitut für Risikobewertung und Umweltbundesamt (2010) Beurteilung eines möglichen Krebsrisikos von Nanomaterialien und von aus Produkten freigesetzten Nanopartikeln, http://www.bfr.bund.de/cm/343/beurteilung_eines_moeglichen_ krebsrisikos_von_nanomaterialien_und_von_aus_produkten_freigesetzten_nanopartikeln.pdf .
[62]. Nishimori H, Kondoh M, Isoda K, Tsunoda S, Tsutsumi Y, Yagi K. (2009) Histological analysis of 70-nm silica particles-induced chronic toxicity in mice. Eur J Pharm Biopharm 72:626–629.
[63]. Dekkers S, Bouwmeester H, Bos P, Peters RJ, Rietveld A, Oomen AG (2013) Knowledge gaps in risk assessment of nanosilica in food: evaluation of the dissolution and toxicity of different forms of silica. Nanotoxicology 7:11
[64]. Van der Zande, M. et al. (2014) Sub-chronic toxicity study in rats orally exposed to nanostructured silica. Particle and Fibre Toxicology 11:8
[65]. Dekkers S, Krystek P, Peters RJ, Lankveld DX, Bokkers BG, van Hoeven-Arentzen PH, Bouwmeester H, Oomen A.G. (2011) Presence and risks of nanosilica in food products. Nanotoxicology 5:393–405.
[66]. Risks (2013) Preliminary Opinion, Nanosilver: safety, health and environmental effects and role in antimicrobial resistance, December 2013, p 21, emerging/docs/scenihr_o_039.pdf .
[67]. NRDC vs. US EPA and Heiq Materials AG (2013), http://cdn.ca9. uscourts.gov/datastore/opinions/2013/11/07/12-70268.pdf .
[68]. Risks (2013) Preliminary Opinion, Nanosilver: safety, health and environmental effects and role in antimicrobial resistance, December 2013, p 21-22, 24.
[69]. BfR (Bundesinstitut für Risikobewertung) 2010. BfR rät von Nanosilber in Lebensmitteln und Produkten des täglichen Bedarfs ab, http://www.bfr.bund.de/cm/343/bfr_raet_von_nanosilber_in_ lebensmitteln_und_produkten_des_taeglichen_bedarfs_ab.pdf .
[70]. Correia Carreira, S. (2013) The toxicity, transport and uptake of nanoparticles in the in vitro BeWo b30 placental cell barrier model used within NanoTEST, Nanotoxicology 1-14, http://informahealthcare.com/doi/pdf/10.3109/17435390.2013.833317.
[71]. Browning, L.M. (2013) Silver Nanoparticles Incite Size- and Dose-Dependent Developmental Phenotypes and Nanotoxicity in Chem. Res. Toxicol. 26(10):1503–1513.
[72]. FoEA (2011) Nano-silver: policy failure puts public health at risk, Aus%20v2%20web.pdf .
[73]. ECHA (2013) -CoRAP substance – Titanium Dioxide, http://echa.europa.eu/ documents/10162/37e258fd-f57a-4957-b978-4f18fe593938.
[74]. ChemEurope.com (2009) Nanoparticles used in common household items caused genetic damage in mice, http://www. chemeurope.com/en/news/109581/nanoparticles-used-in-common-household-items-caused-genetic-damage-in-mice.html .
[75]. Ashwood P. et al. (2007) Fine particles that adsorb lipopolysaccharide via bridging calcium cations may mimic bacterial pathogenicity towards cells. Exp Biol Med 232(1):107-117.

[76]. Donaldson K. et al. (1996) Free radical activity associated with the surface of particles: a unifying factor in determining biological activity? Toxicol Lett 88:293-298.
[77]. Dunford R, Salinaro A, Cai L, Serpone N, Horikoshi S, Hidaka H, Knowland J. (1997) Chemical oxidation and DNA damage catalysed by inorganic sunscreen ingredients. FEBS Lett 418:87-90.
[78]. Long T, Saleh N, Tilton R, Lowry G, Veronesi B. (2006) Titanium dioxide (P25) produces reactive oxygen species in immortalized brain microglia (BV2): Implications for nanoparticle neurotoxicity. Environ Sci Technol 40(14):4346-4352.
[79]. Lucarelli M, Gatti A, Savarino G, Quattroni P, Martinelli L, Monari E, Boraschi D. (2004) Innate defence functions of macrophages can be biased by nano-sized ceramic and metallic particles. Eur Cytok Net 15(4):339-346.
[80]. Wang J, Zhou G, Chen C, Yu H, Wang T, Ma Y, Jia G, Gai Y, Li B, Sun J, Li Y, Jiao F, Zhano Y, Chai Z. (2007b) Acute toxicity and biodistribution of different sized titanium dioxide particles in mice after oral administration. Toxicol Lett 168(2):176-185.
[81]. Bundesinsitut für Risikobewertung und Umweltbundesamt (2010) Beurteilung eines möglichen Krebsrisikos von Nanomate http:// www.bfr.bund.de/cm/343/beurteilung_eines_moeglichen_ krebsrisikos_von_nanomaterialien_und_von_aus_produkten_ freigesetzten_nanopartikeln.pdf .
[82]. Landesanstalt für Umwelt, Messungen und Naturschutz Baden-Württemberg (2010) Nanomaterialien: Toxikologie/Ökotoxikologie, http://www.lubw.baden-wuerttemberg.de/servlet/ƒNGname=U10-S05-N10.pdf .
[83]. Weir, A. et al. (2012) Titanium dioxide nanoparticles in food and personal care products. Environmental Science and Technology 46:2242-2250.
[84]. Nowack, B., Mueller, N. C., Krug, H. F., and Wick, P. (2014). "How to consider engineered nanomaterials in major accident regulations?" Environ. Sci. Eur., 26(1), 2..
[85]. Allied Biotech Europe GmbH (2012), http://www.altratene.com/dietary.php .
[86]. Bundesinsitut für Risikobewertung (2012) Nanosilver: Progress in analysis, gaps in toxicology and exposure, http://www.bfr.bund.de/ de/presseinformation/2012/08/nanosilber__fortschritte_in_der_ analytik__luecken_bei_toxikologie_und_exposition-128936.html .
[87]. ElAmin, A. (2007) Carbon nanotubes could be new pathogen weapon, http://www.foodproductiondaily.com/Safety-Regulation/Carbon-nanotubes-could-be-new-pathogen-weapon .
[88]. Whitworth, J. (2014) Carbon nanotube sensors detect food dye, http://www.foodqualitynews.com/Innovation/Carbon-nanotube-sensor-detects-food-dyes
[89]. Bourzac, K. (2009) Carbon nanotubes are super fertilizers, http://www.technologyreview.com/view/415456/carbon-nanotubes-are-super-fertilizer/ .
[90]. Safe Work Australia (2012) http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/725/ *WOCPA*GCNVJA*C\CTFA#UUGUUOGPVACPFA%NCUUKƒECVKQPAQHA%CTbon_%20Nanotubes.pdf .
[91]. Miller, G. & Senjen, R. (2008) Out of the Laboratory and onto our Plates: nanotechnology in food and agriculture, Friends of the Earth Australia.
[92]. Woodrow Wilson International Centre for Scholars (2009) A Hard Pill to Swallow: Barriers to Effective FDA Regulation of Nanotechnology-based Dietary Supplements,http://www.nanotechproject.
[93]. Franz R. (2005) Migration modelling from food-contact plastics into foodstuffs as a new tool for consumer exposure estimation. Food Additives and Contaminants 22(10): 920–937.
[94]. Das R., Selke S. & Harte J. (2007) Development of electronic nose method for evaluation of HDPE flavour characteristics correlated with organoleptic testing. Packaging Technology and Science 20:125-136.
[95]. IFST (2006) Information Statement: Nanotechnology. Institute of Food Science & Technology Trust Fund, London, http://www.ifst. pdf .
[96]. FAO/WHO (2010) Expert meeting on the application of nanotechnologies in the food and agriculture sectors: potential food safety implications, http://whqlibdoc.who.int/publications/2010/9789241563932_eng.pdf, p18.
[97]. See e.g. Evangelia E Ntzani, Chondrogiorgi M, Ntritsos G, Evangelou E, Tzoulaki I. Literature review on epidemiological studies linking exposure to pesticides and health effects. EFSA supporting publication 2013:EN-497, http://www.efsa.europa.eu/ en/supporting/doc/497e.pdf.
[98]. Nanomaterials in Agricultural Pesticides. Center for Nanotechnology in Society. Arizona State University, http://nice.asu.edu/nano/ nanomaterial-applications-agricultural-pesticides .

[99]. Kah, M. et al. (2013) Nanopesticides: State of Knowledge, Environmental Fate, and Exposure Modeling, Critical Reviews in Environmental Science and Technology 43:16, 1823-1867.
[100]. EFSA (2009) The Potential Risks Arising from Nanoscience and Nanotechnologies on Food and Feed Safety, http://www.efsa.europa.eu/en/efsajournal/doc/958.pdf .
[101]. Oberdörster G, Maynard A, Donaldson K, Castranova V, Fitzpatrick J, Ausman K, Carter J, Karn B, Kreyling W, Lai D, Olin S, Monteiro-Riviere N, Warheit D, Yang H. (2005) Principles for characterising the potential human health effects from exposure to nanomaterials: elements of a screening strategy. Particle Fibre Toxicol 2:8.
[102]. Safe Work Australia (2012) http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/725/Nanotubes.pdf .