



# Role and adverse effects of nanomaterials in food technology

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## Abstract

Food processing is related to the practice adopted by the food and beverages industries to change raw plant and animal materials in to 'ready to eat form'. Nanomaterials are applied to food technology with respect to their properties and predetermined set goals such as taste, flavor, shelf-life, appearance, likes and dislikes of the consumers. Nanomaterials have specific potentials depending on their physicochemical properties such as surface effect, small size effect, quantum size effect and quantum tunneling effect. These properties regulate their behavior in the biosystem for they may be either tolerated or be the cause of disturbance to biochemical and/or physiological homeostasis. Mostly nanomaterials have the ability to reach target tissues or organs where their counterparts fail to reach in the organism. Nanoparticles like zinc, calcium and silver are found to be biocompatible and antimicrobial in nature. Hence, these are used in the form of edible film incorporated with cinnamon or oregano oil in the packaging of food. Generally, polymers are incorporated with the nanomaterials and are used in food packaging and food processing. Food processing is aimed at good food quality and safe evaluation by improving food sensing and better nanostructured ingredients. These nanomaterials improve the flexibility and durability of the food contents. The nanomaterials enter the body along with the food products, beverages and other drinks for consumption. Understanding the mechanism involved in toxicity due to nanomaterials may provide necessary information about the nanomaterials which will act as guide lines for their appropriate use in food technology and its related aspects. This will also help to develop more innovative devices to meet the future challenges in food technology. This overview is intended to evaluate the extent of overall role of nanomaterials in food technology.

**Keywords:** Nanomaterials, biocompatibility, food-packaging, food safety, food processing

## Introduction

The food industry is one of the prime industries and a major target of application of nanomaterials. Food processing refers to the practice adopted by the food and beverages industries to convert the raw plant and animal materials in to ready to serve or eat form of food for consumers [1]. Media has played its significant role to build a strong public opinion in favor of the processed food products. As a result of this impact on public, the market has been infiltrated with huge number and varieties of processed food products [2]. Nanomaterials play an effective role in food preservation, packaging process and packaging material [3]. Candies, sweets, and chewing gums have gained popularity because of the use of nanomaterials [4]. This success is based on the sensitivity and efficiency of the products of nanoscience. Uses of nano-scale materials in

the food industry are likely to improve the processed food [5]. Nanomaterials are being used as coated materials in treatment and as diagnostic tools [6].

Nanomaterials have unique properties such as surface effect, small size effect, quantum size effect and quantum tunneling effect. These have the ability to exist in aerosol, suspension, make them worthy of application in enhancing the utility of the food products. The surface and interfacial properties of nanomaterials can be modified with surfactants; these engineered nanomaterials exhibit flexibility. This facilitate in fabricating nanomaterials for various uses. Various types of nano-objects are involved in the formulation of nanomaterials such as nanoparticles, nanorods, nanotubes, nanocomposites, and nanofilm etc. These are used as per the need of applications in varied industries. Mostly nanopowder may include  $\text{TiO}_2$ ,  $\text{SiO}_2$ ,  $\text{ZnO}$ ,

CeO<sub>2</sub> colloidal dispersions and nano-suspensions involve gold, silver, silica etc. Food nano-sensing is related with food quality and safe evaluation while nanostructured ingredients help to improve food processing [7]. In a broadly sense, the nano-food processing is accomplished in three major aspects namely production (this pertains to over all conversion of raw food materials in to edible form), processing (it is related to modify the processed food with respect to taste, shelf life, protection against possible pathogens etc, as per the need of consumers) and to retain required nutritional values [8]. Agriculture and agrobased industries are the sources of raw materials for food industries. The involvement of nanomaterials in agriculture, food and food technology appears to be inevitable to meet the current demand of human population.

## Review

### Applications of nanomaterials in food processing

Food cycle includes all phases of food industry which are exploited in bringing food from field to table. It includes agro-practice, post harvest practice and processing of raw food in to ready to eat-form. Agro-practice aspect is out of the current discussion but can be envisaged that use of pesticides, fertilizers on crops etc., are likely to be facilitated by some of the nanodevices. Post harvest aspect includes storing, aggregating the agriculture produce while processing of raw food deals with procuring grains, vegetables, fruits, and other ingredients in to processed food or ready to eat-form. Food nanotechnology goes a few steps ahead in making food palatable and its pleasant aftereffects by using nanomaterials in different forms at various stages of food processing.

Broad outline of the various stages of processing of food are packaging, designing and formulation, keeping the food fresh and usable form during storage, transportation, supply and disposal of the unused products beyond expiry period or spoiled food. The role of nanotechnology in these phases of the food industry has been established; it is becoming prominent, demanding and enduring day by day. Food processing implies that raw food is transformed in to pleasing, palatable, digestive, nutritive and hygienic form that can be consumed by humans. Elementarily, food processing remains relatively same though food and feeding habits are different in different parts of the world. The food processing has undergone varied changes in due course of time in accordance to the needs of the individual, life style and society. Application of the nanomaterials in food and food technology is based on the behavior of the nanoparticles; this behavior is primarily dependent on the scientific evidences obtained during the primary research. Ag and ZnO NPs play an effective role in maintaining the shelf-life of fresh orange juice and have recommended these NPs as safe material for food technology [9]. The major applications of nanotechnology in food engineering are as food nanosensing and nanostructured ingredients. Nanosensing pertains to better food quality and safety evaluation while nanostructured ingredients help to

improve food processing. Improved food processing includes appropriate delivery of nutrients, bio-separation of proteins, fast sampling of biological, chemical contaminants and nanoencapsulation of nutraceuticals, stabilization, delivery and coloration of the food system [7]. Nanomaterials play an effective role to attain better encapsulation and release efficiency of active components of food in comparison to the traditional encapsulating agents. Some of the important food supplements are to be retained during the food processing and it is accomplished by using nanomaterials. Nanosized powders are used to elevate the degree of absorption of nutrients, nanoencapsulation of nutraceuticals which are used to increase absorption, better stability and targeted delivery, cellulose nanocrystal composites as drug carrier, vitamin spray dispersing active molecules as nanodroplets for efficient absorption and nanococheles as coiled nanoparticles, are employed to ensure nutrients delivery to the cells without disturbing the color and taste of the food. Other varied modifications of nanomaterials include development of nanoemulsions, liposomes, micelles, bipolar complexes and cubosomes are effective in protection of bioactive ingredients, controlled delivery system, food matrix integration and masking the flavors that are undesirable [10]. Such manipulated enzymes are administered to enhance the bioavailability of essential nutrients that include essential minerals and vitamins and hydrolyze antinutrients. This practice of adding formulated enzymes ensures appropriate enzyme-substrate support system because this brings about higher surface to volume ratio as compared to traditional support system.

ZnO NPs are used in many nanostructures and have the ability to be fabricated in a wide range of morphological varieties [11]. Gelatinization of starch plays key role in processing of food based on starch because it influences the nutritional benefits (if starch used gets contaminated it can be the source of adverse effect) [12]. During the process of filtering beer from mother solution and procuring cheese from milk, nanoseives or nanomembranes are most commonly used [12]. Nanoparticles like zinc, calcium and silver are found to be antimicrobial in nature; hence, these are used in the form of edible film incorporated with cinnamon or oregano oil in the packaging of food. Nanofibers are fabricated from the shell of lobster and organic corn which are antimicrobial and can be easily biodegraded, thus, becomes preferred material for food processing. Prime concern of using nanomaterial is that the nano-additives should not carry insoluble biopersistent matter in the circulation of the consumer. Quite often food is spoiled because of oxidation of the organic and/or added components. A fabricated electrochemical biosensor (a redox biosensor) is able to detect phenolic compounds in the food within range 37nM to 4.33 μM [13]. Nanoencapsulates, silver and TiO<sub>2</sub> are among those nanomaterials that have been applied to the maximum extent [14]. Nanocomposites in the form of novel food, food or feed additives, biocides, pesticides and food contact materials have bright future in the field of food processing.

During food processing nanotechnology assures many benefits such as safety, security, quality and shelf life of the food products [15]. This interaction between nanomaterials and processed food can cause unknown and unexpected hazard to the consumer. Nanomaterials are used as nanocapsules to enhance bioavailability of nutraceuticals, standard ingredients like cooking oil, to encapsulate flavor enhancers, to infuse plant based steroids to replace cholesterol of meat; nanoemulsions and nanoparticles are employed to increase availability and dispersion of nutrients. Nanotubes and nanoparticles are used as gelation and viscosifying agents while nanoparticles are involved in selective binding and removal of chemicals and pathogens from food under consideration. The potential application of nanomaterial science is being carried out with reference to nanoscaled biomaterial, packaging, sensors to increase shelf life, to detect development of undesirable factors [16]. Inorganic nanomaterials are used in healthy food products [17]. Transition metals and metals like Ag, Fe,  $\text{TiO}_2$ , alkaline earth metals such as calcium, magnesium, and non-metals like silicates and selenium are extensively used in food processing. When children, at health center were fed ultra processed food, children aged 2-10 years, elder children (5-10 years) were found to consume relatively more ultra processed food in comparison to younger ones [18]. Silver zeolite is used as coated ceramic form; silver produced ROS which are responsible for the antimicrobial action [19]. Nano-iron is a suitable health supplement because it breaks down the contaminants and destroys microbes. Modified magnetic nanoparticles ( $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-NH}_2$ ) has been found to be relatively better agents for eliminating microbes and virus from water [20]. Further, nanomicelle based formulation involving natural glycerin is a very suitable option to remove pesticides residue from fruits and vegetables up to 99.9%.

### Nanomaterials used in food packaging

In general nanomaterials used in food packaging include nanofilms as barrier materials to prevent spoilage and oxygen absorption, electrochemical nanosensors to detect ethylene, antibodies linked with fluorescent nanoparticles to detect chemical and food borne pathogens. Common packaging for processed food, beverages and other related products in which nanomaterials are exploited sandwich bags; salad bowl, carry bags, bear bottles, aluminum foils, etc. The polymers incorporated in the nanomaterials improve the flexibility and durability of the food contents. The engineered nanomaterials (ENMs) used nullify the effects of temperature, humidity and act as barriers for the potential organisms to harm or spoil the food thereby enhancing the stability of food. The ENMs incorporated with plastic polymers have antimicrobial properties that are used to monitor the condition of packed food. The fabricated packaging materials with such specific qualities are termed as improved nanocomposite/active nanocomposite and smart packaging [12]. When such types of engineered nanomaterials are used for food packaging there

are chances of migration of the nanomaterial towards food, drinks, or any edible matter packed therein, this migration is prevented to a greater extent. The bottles or the containers to be used for packing drinks, beverages, and other edible material contains nanoclay composite; these composites are embedded in the layers of polyethylene terephthalate (PET). There are no detectable movements of nanoclay from PET to the food contents or drinks packed. Those engineered nanomaterials that have smaller size than 1nm could migrate through packaging because polymer matrices materials exhibit relatively lower dynamic viscosity and no interaction between the two [21]. When nanocomposite specifically involving silver and polyolefines were used for packaging then there seemed to be some chances of migration of very small nanomaterials but not the bigger ones. The bigger nanomaterials get bound to the polymer matrices such as polystyrene and polyethylene terephthalate because of the relatively higher dynamic viscosity. Very low degree of migration of Ag NPs occurred from containers made of polypropylene nanosilver-composite. There was no transfer of non-nanocomposite material from the intelligent, smart and active packaging fabricated nanotechnologically like inks, reactive nanolayers and analyte at nano scale. These packaging materials provide non-toxicity, safety standards as per the legislations, reliability of products and after-use disposal issues are taken care [12]. Research and development both are aimed to maintain specific safety standards keeping the expectations of consumers and to maintain the environment. The label on the packages are improvised with radiofrequency identification display (RFID), this technique is able to track the food product during its transportation and distribution. Antimicrobial activity of ZnO powder coated PVC film with respect to food pathogens revealed that electrostatic interaction between bacterial cell surface and nanoparticles inhibited the growth of pathogens [22]. Nanomaterials like CNT, silicon nanowires, ZnO-nanorods etc, elevated the detection capability of biomolecules [23]. Those nanomaterials that have small dimensions and unique physical, chemical and optical properties ensure the safety of food and other contents of processed products along with the detection of spoilage in packed conditions. Hence, these are most suitable and ideal as bioprobes and biosensors [13]. Nanomaterial such as cubosomes (5-10 nm), liposome (20 nm), micelles (5-500 nm) have the ability to encapsulate biopolymeric nanoparticles like starch, chitosan, polylactic acid, gum Arabic, carrageenan, and alginate etc, and fabricated to be used in smart packaging material [23]. The new generations of such nanoencapsulation system are double layered liposomes, solid-lipid-nanoparticles, colloidosomes, nanolaminates and composite nanofibers, incorporated while plastic polymers are combined with nanoclay to fabricate stronger and cleaner, flame resistant material with a higher degree of reliability. These materials meet the requirements of the manufacturer, consumers of the food and food technology.

Bayer Polymers have fabricated a film involving silicate



nanoparticles. It prevents the movements of oxygen and other gaseous material and transfer of heat, retaining the moisture contents of food packed [12]. In the recent past nanoparticles like silver, ZnO, MgO are being used in beer packaging to prevent contamination of food and beverages because of their antimicrobial nature. Polylactic acid when incorporated with small concentration of silica nanoparticle becomes biodegradable material, cost effective, available commercially, and acted as a suitable packaging material [24]. If the resultant polymer matrix were incorporated with nanofillers its physicochemical properties were enhanced due to small size and increased area, its efficiency was observed to be increased many folds. Nanowheels are the devices which are bimetallic and in the form of 2D nanostructure. These are good materials to maintain heat and catalytic reactions of the food contents in packaging because these exhibit well-defined tunable surface resonance [25]. Food and crops are most vulnerable to microbial and fungal infection at any stage of food technological cycle and there is a dire need to protection where nanomaterials can be very useful [26,27]. Studied on antimicrobial activity of ZnO NPs with respect to *E. coli* and *Pseudomonas aeruginosa* and antifungal activity against *Aspergillus niger*, revealed that maximum inhibition was found to be at 100  $\mu$ l, with concentration of ZnO NPs in 100 $\mu$ l was 100 $\mu$ g and 400 $\mu$ l respectively; because of the specific antimicrobial nature of ZnO NPs against food borne pathogens hence, these are used in food packaging and food preservation [28]. Nanoscaled electrospun fibers and encapsulated active compounds very effective in increasing the shelf life of the packed food [16]. Eugenol (a phenylpropene, an alkyl chain substituted guaiacol compound clear to pale yellow in appearance), it is a stable and preferred and successful preservative. Eugenol has antibacterial and antifungal properties. This compound is advantageous as it has the ability to regulate the release of the active encapsulated contents and is advantageous for effective pay-loads [29]. Nanocellulose (microfibrillated cellulose)–another biomaterial, used for packaging of food is preferred and other applications because the fabrication is relatively much easier than production of CNT [16]. Nanotechnology is involved in developing nanomaterials which have a specific degree of permeability, nanomaterials with enhanced barrier characteristics and mechanical features, antimicrobial and anti fungal surfaces and higher degree of biodegradability [19,30]. These new generations of nanomaterials are expected to meet most of the requirements of the future.

### **Fate of nanomaterials used in food-distribution and elimination**

The nanomaterials enter the body of consumer along with food, beverages and other drinks. The ingested nanomaterials along with food undergo physiological changes. Some of these are likely get absorbed either directly or with absorbed food components. Size, shape and structure predispose them

to cross the biological barrier of the gastrointestinal tract. These nanomaterials remain in the system either in bounded or unbounded form at least for some duration. During this period these interact with biomolecules either beneficially or adversely. Their elimination from the body is brought about by different modes depending on their interaction with biomolecules and physicochemical features. Specifically the engineered nanomaterial designed for specific purpose may pose a problem during their elimination from the body depending on the type of fabrication and material used.

The investigation related to elimination of quantum dots *in vivo* indicated that the behavior of QDs depended on the size, and surface chemistry. Those QDs which had coating of cysteine and 5.5nm diameter were eliminated through kidney while QDs with different dimension and surface properties need further investigation [31-33]. Opsonization (a process that prepares foreign materials or marks the pathogen for phagocytosis) occurs depending on their size and surface features during the process of elimination of nanomaterials [34]. Orally administered nanomaterials get absorbed and move across gastrointestinal tract and distributed in the body parts like kidney, liver, spleen, brain and respective target organs. Most of the orally administered nanomaterials were eliminated along with the feces and/or urine [35]. Higher concentrations of nanomaterials were excreted via kidney, hepatobiliary pathway. When neural and neuronal cell lines were exposed to carbon nanotubes, these grew and were better differentiated [36,37]. The nanomaterials were found to be cleared by macrophages by phagocytosis; the phagocytosis was enhanced by chemotactic attraction at least in the alveolar zone [35,38]. Clearance of nanomaterials occurred as soon as these materials reach various organs of the body or circulatory system; clearance process was accomplished by live and phagocytotic process of macrophages in spleen and other organs [39]. When nanomaterials like polysorbate (used in food and pharmaceuticals) 80-coated PBCA and pegylated PLA immunonanoparticles, were administered intravenously, could move through blood brain barrier and were found to be accumulated in the brain tissue resulting in neurotoxicity due to the respective physicochemical features [40]. ZnO nanoparticles (50 $\mu$ g/g wt of egg, 50 $\mu$ g/g wt of egg) reach in the embryonic hepatic tissue within 24 to 48 hr when administered in chorio-allantoic fluid in the egg (chicken) on 18/19 day during the incubation [41]. The human red blood cells exhibited viability and hemolytic response against ZnO nanoparticles (20 $\mu$ g/ml, 30 $\mu$ g/ml and 40 $\mu$ g/ml) [42]. ZnO nanoparticles, 20 nm and 70 nm sized ZnO NPs were administered orally in male and female rats. The concentration in plasma, liver, lung, and kidneys was found to be increased within 24 hr after administration following dose-dependent pattern. Degree of renal elimination of these nanoparticles was very less as compared to fecal elimination. ZnO NPs were unevenly absorbed in to blood circulation form gastrointestinal tract [43]. The excretion of TiO<sub>2</sub> and ZnO nanoparticles in Spargue-

Dawley rats using dose (1041.5 mg/Kg body weight, for 13 days). The tissues considered for excretion were blood, liver, kidney, spleen, brain, and urine and feces.  $\text{TiO}_2$  was observed to be less in these tissues in comparison to ZnO nanoparticles. ZnO NPs were observed to be very low in brain and spleen as compared to ZnO NPs;  $\text{TiO}_2$  NPs exhibited lower renal excretion was in comparison to ZnO NPs while ZnO NPs were excreted in greater amount via urine but in feces it was very low in comparison to  $\text{TiO}_2$  NPs [44]. Intestinal goblet cell secretion path way is one of the modes to eliminate the nanoparticles from the biosystem. This was investigated by injecting 30-200 nm sized activated carbon nanoparticles in the yolk of Zebra fish, these nanoparticles were excreted directly in the lumen if intestine and hepatobiliary path was not preferred [45].

Most of the nanomaterials present in circulation in the body are cleared by reticuloendothelial cells. Those nanomaterials which degrade slowly and show a low degree of renal clearance get accumulated in liver and spleen. Nanomaterials having size around 5 nm and present in blood circulation undergo renal clearance. Those having 10-20 nm are separated by liver; 200nm sized NPs get picked up by Kupffer's cells and sinusoidal spleen. Others are taken care of by macrophages, opsonin assisted NMs undergo phagocytosis [46]. All of these varied observations related to various nanomaterials prove that most of these get distributed in biosystem and also follow a specific path for their elimination irrespective of the selected and intended purposes.

### **Evaluation of nanomaterials before their use in food technology**

There have been tremendous applications of nanomaterials in the occupational, environmental and consumer sectors. This has elevated the public concern with respect to adverse effects and health hazards. This concern is expressed as risk factor in consumers. Intense use of engineered nanomaterials in almost every aspects of human life has raised the concern in the minds of the consumers. The nanomaterials at the work place are effective and likely to cause adverse effects (poor working conditions or because of the negligence) either immediately or at a later stage of life. Worker may suffer from the derogative effects of these nanomaterials (either acute or chronic toxicity) depending on his/her general health. The worker may experience this impact either during the tenure of the job or latter part of the life.

The toxicity of pristine and functionalized carbon nanotubes were observed from mild to moderate levels of toxicity; there are many issues that demand for research approach complementary to *in vivo* investigation related to understanding the biochemical, physiological aspects and health hazard related to nanomaterials [47]. There are specific techniques to engineer safe nanomaterials for the varied uses [48]. There is a need to understand the risk and beneficial aspects of the nanomaterial to be used. This whole approach should be nano-relevant. During the analysis one should consider the effect

of nanomaterials with respect to heterogeneity, morphology, complexes formed (after nanomaterial is mixed with food). Thus, there should be clear protocol related to collection of the sample, strategies concerned with consumed food, type of processed food, amount of food consumed and the movement of food in the alimentary canal from where food sample is to be procured for analysis [49]. These precautions will ensure the safety from the nanomaterials while being exploited in the field of food technology and related agrobased industries. The evaluation of safe use of nanomaterials is of great significance to ensure most of the beneficial effects rather than adverse. Nanomaterials like ZnO, Ag, Au,  $\text{TiO}_2$ , quantum dots, dendrimers, nano-prosthetic, nanocomposite etc, if judiciously exploited will result in beneficial impact. Ampelopsin is a major flavonoid, a potential antioxidant that prevents rancidity in diets; hence, can be used in food products [50].

### **Tolerance of nanomaterials used in food technology**

Nanomaterials to be used in food technology should be tolerant to the consumer and if these result in adverse impact their use in food products is futile. Biocompatibility of nanoparticles is their ability to coexist within the body of a biosystem without disturbing the biochemical or molecular integrity of cell or tissue. Biocompatibility is regarded as the 'ability to be in contact with living system without causing adverse effects or biohazards are safely manipulated,' [51,52]. Compatibility has been redefined as the ability of a chemical to carry on its designed function with respect to a biochemical/medical therapy without causing any local or systemic adverse effect in the body of the recipient and have potential to create beneficial cellular and/or tissue response in the given conditions with optimum performance [53]. Biosystems include microbes, wild varieties and domestic organisms; domestic organisms encompass agriculture crops, poultry, animal husbandry, organisms of aesthetic value and others used for scientific research. This ability of coexistence depends on the interaction between the specific nanomaterial and the specific species; this interaction is likely to be varied depending on the specie specificity. Biocompatibility may show fluctuations, beneficial and derogative state; these associations are related to nurturing the survival of a biosystem in given environmental conditions.

The compatibility of nanomaterial depends on the dose, type, size, physicochemical nature, type of the tissues, number and the duration of exposure and the photoperiod. Regulated lower doses of nanomaterials are preferable for survival and to evaluate their biocompatibility in a biosystem. It is appropriate to avoid those interactions which disturb the biocompatibility such as surface oxidation, photosensitivity etc, to ensure appropriate tolerance. The biocompatibility can be ensured or enhanced by taking preventive steps such as coating the suspected surface, evaluating photo-effect (in-case photosensitive nanomaterials) etc, of the nanomaterials under consideration. Zinc is one of the inorganic elements

which are needed by human body; zinc oxide is non-toxic to man but it is toxic to microorganisms. ZnO nanoparticles are biocompatible to man, hence, can be suitable in the role of biosensors [54]. Biocompatibility of nanomaterials can be enhanced by self assembly with chitosan and modified lecithin [55]. Biocompatible gold nanoparticles can be formulated with green chemistry approach [56]. Inorganic nanoplate for of nanomaterials can be used as theranostics for cancer [46].

### **Biological adverse effects due to nanomaterials used in food**

Nanomaterials are used in abundance in food technology. The processed food products have been infused with nanomaterials. These carry nanomaterials in the gastrointestinal tract of the consumers. These in turn undergo physiological changes. As a result there is every possibility that these nanomaterials are likely to interact with the tissue, cellular organelles, and biomolecules. This interaction may be beneficial and/or adverse physiologically, biochemically, cytologically, histologically or genetically. Some of the nanomaterials like metallic and metallic-oxides nanoparticles, quantum dots, fullerenes, and fibrous nanomaterials have been found to cause adverse effects that include fragmentation of chromosome, breakage of strands of DNA, changes in gene precision etc. There are reports on clinical toxicity but major studies indicate that nanomaterials are able to initiate adverse biological interactions leading to untimely physiological disruption and toxicological outcome in due course of time.

Silica nanoparticles cause oxidative stress and resulted in cytotoxicity *in vitro* and *in vivo*; elevated lipid peroxidation, LPO, ROS, and declined level of cellular glutathione [57,58]. There is every possibility of known and unknown varied hazards based on systemic investigation on cells treated with nanomaterials with respect cytotoxicity and inflammation [59]. AuNPs and Ag NPs have potential to caused depolarization of  $\alpha$ -tubulin-major component of microtubule, affecting adversely the cellular structure and associated cytoskeleton of the cell [60]. The mechanism involved in the interaction between nanomaterials and living biosystems is still ambiguous [61]. The efficacy of nanomaterials with which these interact with biological molecules in the ambient atmosphere and the formation of varied end products is highly complex phenomenon. This complexity becomes more challenging with the slight changes brought about in the nanomaterials due to coating, charge, size, surface properties, dispersion, agglomeration, concentration and matrix.

Nanomaterials have the potential to cause mutagenicity, clastogenicity, aneugenicity (causing the possession of abnormal chromosome numbers), apoptosis, autophagy and mitoptosis (death of mitochondria) etc, [6]. There is lot of toxicological data related to cytotoxicity, genotoxicity, repeated dose toxicity and biokinetics are available related to silica, titanium dioxide, and silver; there are limited records concerned with the use of nanomaterials in agriculture, food,

feed application [14]. The resume of legislation and regulations in European and non-European countries have adopted EU legal acts and formulated the guide lines to be followed for the related industries.

Mostly iron oxide nanoparticles enter mammalian cells via endocytosis, sometimes by pinocytosis, through reticuloendothelial system, while in blood circulation opsonization of nanoparticles to cell surface was also involved. Internalization of iron oxide nanoparticles was observed to be directly related to their size [62]. Graphene induced toxicity and apoptosis in cell culture has been observed; this adverse response was found to be in relation to dose and duration dependent. Graphene (100-110nm) also caused cytotoxic state and damage to mitochondria in case of neural cells also [63]. Carbon nanotubes cause varied toxic response depending on the type and the applications [64]. The toxicity of dendrimers depended on their size and shape as these nanomaterials exhibit closeness/resemblance to the components of the cells like DNA, proteins etc. Their structural aspects were found to be very suitable to provide space for encapsulation of food ingredients and therapeutic drugs, imaging molecules and conveniently regulated the release. This specific feature was also able to reduce toxicity. However, these nanomaterials exhibit hemolytic and hematological toxic responses in a given biological system. Their features such as cationic surface charge and the negative charge on the biological membrane interact leading to the toxicity *in vivo* [65-67]. To counteract this adverse effect these are engineered to be biocompatible and biodegradable. During the experimentation with quantum dots, the observation indicated oxidative stress; influencing signaling pathway between macrophages. The interaction of QDs was found to be dose dependent and exhibited adverse effects on cell division and the growth of the cell [68]. Engineered nanoparticles relevant to various industries like SiO<sub>2</sub>, ZnO, Fe<sub>2</sub>O<sub>3</sub>, Ag, CeO<sub>2</sub>, had exhibited dose dependent elevated cytotoxicity and damage of DNA, affected cell proliferation in human lymphoblastoid and adherent ovary cell culture [69].

The metal oxide NPs, metallic NPs, quantum dots, SiO<sub>2</sub> NPs, CNT and other nanomaterials with respect to size, shape, surface charge, type of coating material, reactivity, dose, exposure, route of administration exhibit toxic behavior. Further, it was found that stable metallic oxides, mostly have not shown toxicity but metallic NPs bring a change in reduction potential which causes cytotoxicity and genotoxicity. Those NPs which were in soluble form were definitely found to be toxic in comparison to non-soluble [70]. C60 got linked with the DNA at its minor grooves and initiated unwinding; when it got linked with RNA it inhibited replication of DNA [71]. When C60 bound to nucleic acid the range of energy involved varies within -56 to -10 kcal.mol<sup>-1</sup> depending on the different genomic fragment [71]. There are views with respect to optimization of immobilized enzymes, immunodiffusional limitations, maximum surface area per unit mass and high effective enzyme loading. Further, nanoparticles affect the behavior of the



enzymes in transitional region/phase between heterogeneous (immobilized) enzymes and homogeneous (with soluble free enzyme) enzyme catalysis. These nanoparticles influenced the reaction particle mobility related to the particle size and solution viscosity [72]. Polystyrene particle when used on an enzyme model  $\alpha$ -chymotrypsin it got attached to NPs covalently up to 6.6 wt%. Factors such as change in particle size, viscosity of the reaction medium affect the mobility of the enzyme catalyst; there is a change in the intrinsic activity of the said enzyme (the particle attached enzyme), Km, Kcat were found to be affected because of the particle size and viscosity [72]. Structure and function of an enzyme can be changed by nanoparticles; the enzyme–nanomaterial interaction is governed by the key properties such as structure, size, shape, surface chemistry and charge. This is because of the electrostatic complementarities between carboxylate end group and cationic residues present around the periphery of the active site [73].

When the surface of the nanoparticles was modified, these NPs affected the enzyme function in comparison to traditional materials. This factor could be modified with organic molecules via covalent or non-covalent modification to prepare functional nanoparticles. Suitably functionalized nanoparticles possess some specific abilities like preventing non-specific binding and recognizing specific biomacromolecules; this aspect of modified nanomaterials could specifically regulate enzyme activities [48]. The effects of iron oxide NPs on tissue and the

enzymes of live in rats, caused hepatotrophic effects; the levels of alkaline phosphatase, aspartate amino transferase and alanine amino transferase enzyme activities were elevated [73]. Single enzyme NP of celluloclast B G, cellulose enzyme (SEN-CK) has the ability to degrade great substrate like cellulose and the stability of the SEN-CK enzyme has been found to be significantly better than that native enzyme [74].

Moderate doses of gold, silver and ZnO NPs (50 ppm, average size of NP 10nm; 25, 50 100ppm) elevated LDH activity with all concentrations of the three nanoparticles used [75]. Specific and unique features of nanomaterials are the factors that affected toxicity and their interference during the assessment processes. Nature of nanomaterials and the mode of the behavior of the respective nanomaterials in the biosystems remain ambiguous in the current scenario of the toxicity assessment pattern [76]. One of the physiological and biochemical disturbances caused is related to change in the redox potential in the affected cell/tissue; reactive species of oxygen and nitrogen caused lipid oxidation and this condition can be created by nanomaterials [77]. SPION showed uniform distribution endothelial cells; this distribution was affected by the parameters like shape, size and other geometrical aspects and conditions related to hemodynamics [78]. Nature, type of coating on quantum dots the major parameters that played an effective role in their toxic activity; features like size, charge and the surface coating are the deciding factor of their uptake, mechanism of internalization and toxic behavior **Table 1** [79].

**Table 1. Some of the adverse responses of nanomaterials.**

Nanomaterials and parameters	Tissues/cells and Responses	References
CNT (single walled C-nanotube; 24 mg/ml)	Plasma membrane destabilized, declined viability, oxidative stress induced and caused change in ultra structural morphological changes	[80]
Single walled C-nanotubes 200µg/ml	Inhibited cell proliferation, induced apoptosis, reduced the ability of cell adhesion, viability loss of embryonic renal cells	[81]
Single walled C-nanotubes and multiwalled nanotubes, 22.6µg/ml, 226µg/ml	High toxicity in macrophages in alveolar tissue, loss of viability, detachment of cells and change in protein expression	[82]
Single walled nanotubes 24 hr	Morphological changes in lamellar structures, microvilli, tonofilaments and desmosome junctions in relation to cell membrane	[83]
Al <sub>2</sub> O <sub>3</sub> , CeO <sub>2</sub> , TiO <sub>2</sub> metal oxides nanoparticles	Change in membrane potential, induce lipid peroxidation and oxidative stress, cytotoxicity was observed,	[84]
Cationic nanoscale materials (related to surface charge)	Spherical NPs were taken up 500% more readily than rod shaped NPs, internalized NPs bombarded the endosomes and reached cytosol machinery, cationic NPs move across the cell membrane by forming transient opening and due to hydrophobicity, induced cytotoxicity	[85]
Silica NPs	Resulted cytotoxicity, caused oxidative stress in vivo and in vitro, elevated lipid peroxidation resulting rise in ROS and decline in cellular glutathione (GHS)	[58,86]
Gold NPs (AuNPs), Silver NPs (AgNPs), CoCrNPs	Depolarization of $\alpha$ -tubulin, disturbing the cellular structure, partial fragmentation of Protein	[60]
Silver zeolite NMs	Produces reactive oxygen species	[19]
Carbon nanotubes	Causes inflammation in neural cells (glial cells), cytokine	[87]
Dextran coated SPION(20nm and 60 nm)	Induced proinflammatory cytokine	[86]
Colloidal gold NPs (1µM/5µL)	Affected electrical activity in retina but no morphological changes	[87]

Continuation of Table 1.

Nanomaterials and parameters	Tissues/cells and Responses	References
ZnO NPs (50µg/g, 150µg/g)	Atrophy of embryonic hepatic tissue (chicken)	[41]
ZnO NPs (20µg/ml, 30µg/ml)	Hemolysis of human red blood cells	[42]
Copper NPs 413mg/K <sup>-1</sup> 5000mg/K <sup>-1</sup>	Pathological damage to liver, kidney, spleen	[39]
CdSeQD with ZnO shell 0.014µg/kg/day	Increased gastric toxicity in presence of simulated gastric fluid, induce accumulation in body tissues	[88]
Silver NPs 125mg/kg, 60nm	Elevated cholesterol and cholestric enzyme	[88]
Coated QD (bidentatethiolatedhydrocarbonic acids, silica, lipid micelles)	Induced the release of proinflammatory cytokines leading to cytotoxicity	[79]
Gold, silver and ZnO NPs 10 nm; 25, 50 and 100ppm	Caused increase in LDH activity	[75]
TiO <sub>2</sub> (in respiratory tract)	Caused oxidative damage to DNA and inflammation genetic instability,	[89]
TiO <sub>2</sub> (industrial grade)	Higher degree of deletion of DNA, pups exhibit dose dependent DNA strand breaks	[88]
SiO <sub>2</sub> , ZnO, Fe <sub>2</sub> O <sub>3</sub> , Ag, CeO <sub>2</sub> ,	Caused dose dependent DNA damage	[69]
SWNT, MWNT (less than 2.5 micron Particulate Matter)	Damaged mtDNA, increased aortic plaque	[90]
C60 Nanoparticle	Bind to DNA and RNA and damages them	[71]
Polystyrene particles (110nm to 1000nm	Affected the intrinsic activity of enzyme model α-chymotrypsin,	[72]
anionic MMPCs (protected nanoclusters)	Effectively inhibited the chymotrypsin activity.	[91]
Silicon nanowires (SiNW-SiO <sub>2</sub> -functionalized with carboxyl group and highly reactive hydrogen modified (SiNW-H)	Inhibited the enzyme activity of restriction endonuclease and <i>Taq</i> DNA polymerase.	[92]
Iron oxide NPs	Increased the levels of alkaline phosphatase, aspartate amino transferase and alanine amino transferase enzyme activities	[93]
Iron oxide NPs, 30-35 nm diameter, 7.5,15, 30mg/kg	Enzyme activity of GSH, SOD and CAT declined as the concentration of NPs increased	[94]

## Conclusion

Nanotechnology is a multi-interdisciplinary technology having multifaceted applications. Its products are exploited in the formulation of personal care, health care, commercial and industrial applications. This ability is in relation to the structure, function and functionalization of either some groups of a molecule or molecule as a whole. Nanomaterials are being exploited in the processing of raw food to 'ready-to-eat state'. This journey of food involves conversion of raw food in to prepared food (preprocessing), processing, packaging, transporting, supply, storage and disposal of expired or spoiled food and the packaging material. Nanomaterials are applied to food technology with respect to their properties and predetermined set goals such as taste, flavor, shelf-life, appearance, likes and dislikes of the consumers and the financial and commercial aspects. Prior to use of the nanomaterial it is quite essential to evaluate their biocompatibility to establish their utility in food or the consumer's intention to attain and maintain good active health. Processing and packaging is an essential aspect; its efficiency and effectiveness depends on the material used to pack the food to keep it fresh, usable, retention of nutritional values for the varied age groups. Biosensors are the devices which help to detect any derogative

changes, infection or degree of spoilage of food packed. It is quite important to know distribution, fate and elimination of the nanomaterial from the body of the consumer. Various forms of nanomaterials devised, fabricated such as nanoparticles, nanofibers, nanomembranes, nanotubes, liposomes, nanofilms, etc, are used in food and food technology. It is very essential to estimate the over or abuse of these materials to avoid adverse effects. Study related to nanotoxicity is an appropriate approach to find an optimum, beneficial doses of nanomaterials to be used and their elimination from the biosystem. Even though it is claimed that the amount used of these products is within safe limits but the amount released directly or indirectly in the environment is comparatively much higher. Perspective of use of nanomaterials lies in the hands of personals involved in the field of nanotechnology, food technology and those trying to understand the adverse effects. The insight of the mechanism involved in interaction of nanomaterials and biosystems will guide the appropriate and effective manipulation for the good of man-kind and environment.

## Competing interests

The author declares that he has no competing interests.



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