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A REVIEW ON APPLICATIONS AND TOXICITY OF NANOPARTICLES

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ABSTRACT

Nanotechnology is growing at an exponential rate and will clearly have both salutary and toxological impact on health and the environment. The unique size dependent properties of nanoparticles make these materials superior in many areas of human activities like in medicine, manufacturing, consumer products and research have raised questions about the toxicity on molecular, biochemical and physiological level. Nanotoxicological studies are intended to determine whether and to what extent these properties may pose a threat to the environment and to human beings. Data related to the toxicity of these nanoparticles still in its initial phase. This review presents application of different nanoparticles in various fields and their related toxicity on health and environment.

KEYWORDS- Application, Nanoparticles, Toxicity

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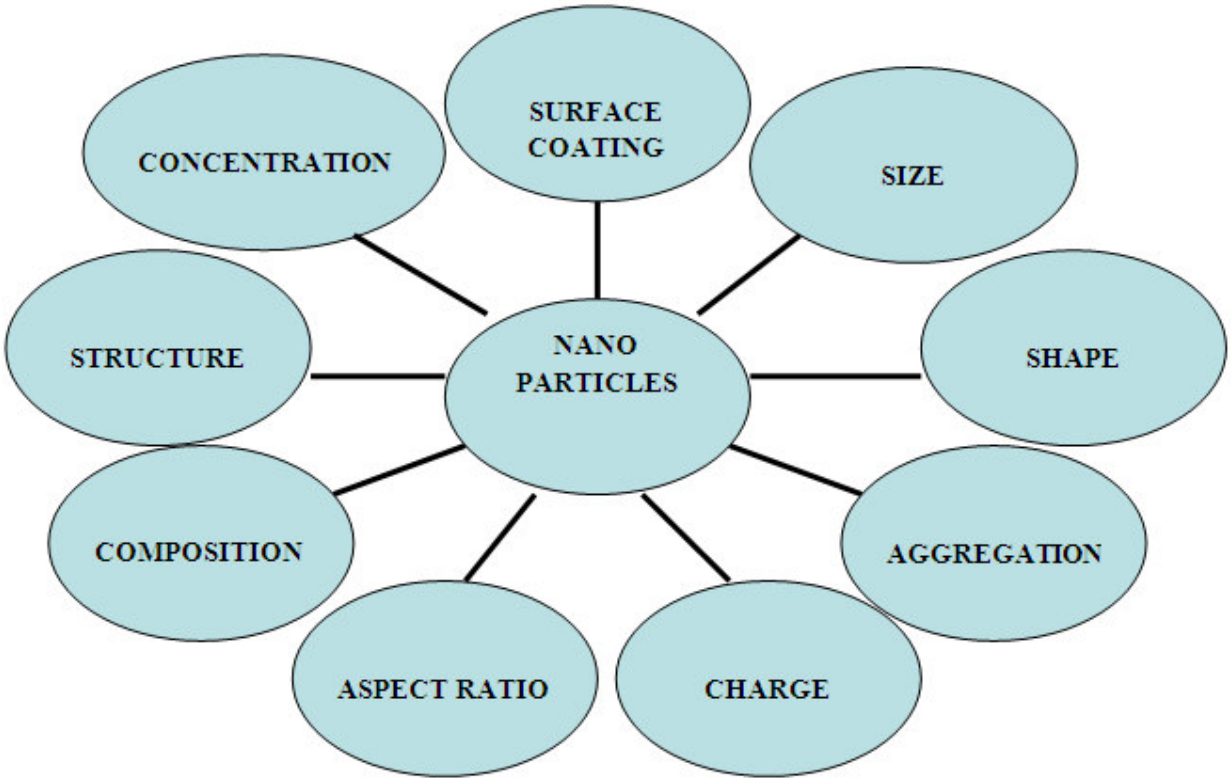
INTRODUCTION

Nanotechnology is "an understanding and control of matter at dimensions between 1 and 100 nanometers (nanometer is 1 x 10-^{9} m or one millionth of a millimeter), where unique phenomena enable its novel applications" by the creation and manipulation of materials at the nanometer (nm) scale. Nanoparticles is further classified according to size in terms of diameter; fine particles come in a range between 100 and 2500 nm, while ultrafine particles are sized between 1 and 100 nanometers. Nanomaterial's have different properties from their bulk form and some time give completely different physical and chemical properties. Due to this unexpected properties many industries and manufacturers are now introducing nonmaterials in their mainstream products to exploit its capabilities. Many types of nonmaterial's are also thriving in medical science and technological areas while related research and applications are exploring the potentials in biosensors, tissue engineering, biomaterials, drug and drug-delivery systems and DNA modification.[1,2] To create new types of analytical tools for biotechnology and life sciences recently nanomaterials such as nanotubes, nanowires, fullerene derivatives (buckyballs) and quantum dots have received enormous attention.[3,4] Nonmaterials, which range in size from 1 to 100nm, have been used to create unique devices at the nanoscale level having novel physical and chemical functional properties. [5,6] In microbiology nanoparticles show inhibitory effect on microbes as a tool to fight and control outbreaks of disease. For example, in everyday products ranging from deodorants to personalized computer devices have metallic nanoparticle systems for their anti-microbial properties.[7] However, the effect on microbes must also be checked carefully as it demonstrates the adverse effect on living organisms. It has been shown that artificial nonmaterials have highly activated surfaces which can be carcinogenic, mutagenic or cytotoxic.[8,9] With these surface properties nanoparticles are 100 times smaller than normal red blood cells, which increases the potential for interaction and the nanoparticles can interact with proteins, DNA[10] viruses and lung cells. Hence, understanding the interaction of nanoparticles with living cells and other biological systems requiring healthcare professionals and the public in general to be in closer contact with such materials. The relatively modest information on nanoparticles toxicity in various biological systems means the issue of safety still remains incomplete.

PROPERTIES RESPONSIBLE FOR TOXICITY

From the earlier studies of toxicological properties of fibrous particles, it was concluded that dimension, dose and durability will be the most critical parameters in determining adverse health effects of nanoparticles.[11] Various physicochemical properties of nanoparticles and their associated health effects, raising some uncertainties in determining the most critical factors in determining their toxicity.



The following points explain the most important characteristics of nanoparticles associated with their toxicity.

Surface to volume ratio

Larger counterparts for the same mass of particles with the same chemical composition and crystalline structure show reduced toxicity then nanoparticles. Nanoparticles with larger surface area show increased reactivity[12] and induce more reactive oxygen species and DNA damage *in vitro* experiments.[13] This suggested that the toxic effect may be dependent on the surface area of nanoparticles.

Size

From a toxicological point of view, most studies indicate that particle size has an effect on the toxicity of a material, with an inverse relation between size and toxic capability. So it can be explained by that smaller particles have a higher ratio of surface to total atoms or molecules contained by the particle. NPs below their critical size are characterized by an excess of energy at the surface and therefore, thermodynamically less stable resulting in increased surface reactivity. Consequently, a larger amount of surface molecules with a higher capability to react due to the thermodynamic instability are both in line with the increased toxicity.[14]

Aggregation

Nanoparticles aggregation mainly depends on surface charge, material type and size. It plays a critical role in determining the toxicity of nanoparticles. Larger particles more effectively removed by macrophages in compared to smaller particles. Therefore, aggregates larger than 100-200 nm[15] exhibit low toxicity. At high concentration, nanoparticles will promote aggregation and therefore reduce toxic effects in comparison to lower concentrations. Therefore, risk evaluation needs to consider concentration factor which cause the difference in aggregation and leads difference in potential toxicity of nanoparticles.

Chemistry and crystalline structure of particle

Chemistry of nanoparticles have an important role in determining toxicity but not over size of particles.[16] Particles depending on chemistry can show different sub-cellular localization,

cellular uptake and an ability to catalyze the generation of ROS.[17] Chemistry and composition of particles must be distinctly distinguished. It may be possible that the particles having the same composition may have different chemical or crystalline structure. Crystalline structure also determines the toxicity of a material. For example, allotropes of titanium oxide (rutile and anatase), rutile nanoparticles (200 nm) have been reported to induce oxidative DNA damage in the absence of light.[18]

Aspect-ratio

Aspect ratio of a particle is the ratio of the length to the width of the particle. There is a direct relationship between aspect ratio and toxicity of nanoparticles as it increase toxicity also increase. Lung cancer, mesothelioma and asbestosis were found to be induced with asbestos particles longer than 10 μm, 5 μm and 2 μm respectively. All of these particles had a minimum thickness of 150 μm.[19] Fibers longer than 20 μm not cleared from respiratory tract by phagocytosis effectively in humans by macrophages. Biopersistence of these fibers with long aspect ratio leads to long term carcinogenic effects.[11]

Surface coating and functionalization

Particle surface plays an important role in determining toxicity, as it interacts with biological components. Surfactants can change the physicochemical properties of nanoparticles such as electric, magnetic, chemical reactivity and optical, which affects their cytotoxicity. Surface coating may decide the toxicity level of nanoparticles in some cases it can make harmful nanoparticles nontoxic or increases toxicity of other harmless particles. The presence of ozone, oxygen, oxygen radicals or transition metals on nanoparticle surface leads to the creation of ROS.

Charge

In the recent development of nanomatrials in medical applications, considerable attention has gone to the effects of nanopaticles charge on cellular uptake, translocation to different tissues and cytotoxicity of NPs. In general *in vitro* condition positively charged nanoparticles are taken up more easily into the lysosomes and cause more cytotoxicity which is attributed to the acid environment.

Protein corona

When NPs come into direct contact with a biological fluid, proteins or enzymes can adhere to their surface and creates a structure “Protein Corona”. This protein corona has a large impact on the nanoparticles surface properties since it can completely change the overall charge, aggregation behavior and hydrodynamic diameter of the NP. Adhered proteins can also undergo conformational changes affecting their avidity, the epitopes exposed and functionality. The NP and protein complexes are transient relationship with a lifetime ranging from seconds to days and the corona protein layer has to be viewed as a dynamic system due to the continually changing micro-environment.[14]
Though these properties described here can be linked to nanotoxicity but there remain several other properties which are apparent at nanoscale. All these properties indicate that these nanoparticles need special and different treatment than their bulk counterparts.

APPLICATION OF NANOPRTICLES

Nanoparticles play an important role in a number of applications. Nanoparticles (NP) are attractive for various applications due to their unexpected and unique properties, like their high surface to mass ratio than that of other particles and materials. The high reactivity of the surface originates from quantum phenomena and can make nanoparticles unpredictable since. Depending on the presence of reactants and adsorbing compounds, nanoparticles surface may be modified which may instantaneously change with compounds and thermodynamic conditions. Therefore nanoparticles have a large surface which is able to adsorb, bind and transport other compounds such as probes, drugs and proteins. On the other hand, nanoparticles have more reactive surface in comparison to their analogues.[20] Different application of nanoparticles in various fields is listed in table 1.

Table 1
***Multidisciplinary application of nanoparticles in various fields.*[21]**

Field of use	Applications of nanoparticles
Automotive	Lightweight construction, Painting, Catalyst, Sensor, Tyre
Construction	Insulation, Surface coating, Flame retardant, Mortar
Electronics	Display, Fiber optic, Laser diode, Optical switch, Filter
Engineering	Machine, Protective coating for tool, Lubricant-free bearing
Food and Drink	Packaging, Additive, Storage life sensor, Juice
Medicine	Drug delivery system, Implant, Diagnostic system
Textiles	Smart clothe (Stain resistant, Anti-wrinkle, Temperature controlled)
Chemical	Filler for paint, Impregnation of paper, Composite material, Adhesive
Cosmetics	Sunscreen, Toothpaste, Skin cream, Shampoo
Energy	Lighting, Battery, Solar cell, Capacitor
Environmental	Environmental monitoring, Fuel changing catalyst, Toxic exposure sensor
Household	Ceramic coating for iron, Cleaner for glass, Odor remover, Metal, Ceramic
Sports	Ski wax, Tennis racket, Tennis ball, Goggle
Military	Bullet-proof protection, Neutralization material for chemical weapon

Some of the applications of nanoparticles are as follows:-

Targeted drug delivery

Targeting is the ability to place the drug-loaded system to the site of interest. In drug delivery, the primary requirement is the accurately targeting of the drug to tissue or cells of choice. Two most important aspects of nanoparticles using drug delivery:

1. The specific targeting nanoparticles with antibodies provides greater specificity means of enhanced delivery of drugs and reduced nonspecific toxicity to the diseased tissue.
2. The timely release of the drug to the target prevents nonspecific toxicity the drug must not disperse out of the particle while it is still in the circulatory system and must remain encapsulated until the particle hold fast to the target.[22]

Cancer treatment

Nanoparticles by functioning as a carrier for launching through fenestrations in tumor vasculature allowing direct cell access to provide a new mode of cancer drug delivery. These particles allow dainty modification for binding to cancer cell membranes, microenvironment, cytoplasmic and nuclear receptor sites. Several such engineered drugs are in clinical trial, including albumin conjugate paclitaxel and liposomal doxorubicin. The carrier mediated paclitaxel has already shown substantial efficacy in taxane resistant cancers. Other alterations including transferrin receptor and folate receptor targeted drug delivery molecules can play important role in this area. This new scheme provides many exciting therapeutic means for targeted high concentration drug delivery to cancer cells with low injury for normal cells.[23]

Gene therapy

With the development of genetic engineering, the prospect for gene therapy has grown rapidly. The transfection efficiencies of the nonviral carriers are a major challenge of gene delivery. Nanoparticles offer an ideal platform for the incorporation of all the worthy characteristics into a single gene delivery system among various nonviral gene vectors.[24] Some molecules such as antisense oligonucleotides require a delivery system since they penetrate poorly through the membranes and susceptible to nuclease attack within the lysosomes. Oligonucleotides show their action either in the cytoplasm in the case of an antisense strategy or in the nucleus for gene replacement or antigene therapy.[25] Oligonucleotides attached to nanoparticles were shown to be protected against degradation and to penetrate more easily into different types of cells.

Tissue engineering

Use of nano-sized features on the surface of the hip or knee reduce the chance of rejection and stimulate the production of osteoblasts.

Titanium widely used in orthopedics and dentistry, with a high fracture resistance ductility and weight to strength ratio in bone repairing material.[26]

Agriculture

In agriculture traditional strategies like integrated pest management are insufficient and application of chemical pesticides like DDT shows biomagnifications in animals and human beings apart from the turn down in soil fertility. In agriculture the potential benefits of nanotechnology includes insect pests management through the preparation of nanomaterials-based pesticides and insecticides, enhancement of agricultural productivity using bio-conjugated nanoparticles (encapsulation) for slow release of water and nutrients, nanoparticle-mediated gene or DNA transfer in plants for insect pest-resistant varieties. Nanomaterial's can be useful for preparation of different kind of biosensors, which would be beneficial in remote sensing devices mandatory for precision farming.[27]

Water purification

Nanotechnology provides an approach of an efficient removal of pollutants and germs in the area of water purification. Today nanoparticles, nanopowder and nanomembrane are in use for test and removal of chemical and biological substances include metals (e.g. Copper, cadmium, lead, mercury, zinc, nickel), nutrients (e.g. Ammonia, phosphate, nitrate and nitrite), cyanide, organics, algae (e.g. cyanobacterial toxins) bacteria, viruses, parasites and antibiotics. Nanomaterials reveal good results in comparison to the other techniques in water purification because of its high surface area.[28] Generally four classes of nanoscale materials that are being evaluated as functional materials for water purification e.g. carbonaceous nanomaterials, metal-containing nanoparticles, zeolites and dendrimers. Nanofibers and carbon nanotubes also show some positive result in this area. The experimental results showed that Fe_3O_4 nanoparticles could effectively reduce turbidity, total nitrogen, total organic carbon, color, phosphate, and microbial content (Enterobacter and *Escherichia coli*) at optimum conditions. Due to the magnetic properties of different NPs, rapid separation with an external magnetic field can be possible within 10 minutes whilst, it is possible to recover and separate the NPs for regeneration. This helps in reducing the treatment process time, easy to scale up the recovery process of pollutants.[29]

Cosmetic

In cosmetic products the main purpose of nanoparticles are UV filtering and delivery of active ingredients to the skin cells. In sunscreens zinc oxide and titanium dioxide are both used extensively to prevent UV damage to the skin. By reflecting visible light and absorbing UV with very high efficiency nanoformulations of these materials have been shown continually to give much better performance than larger particles. A wide range of nanostructures have been proposed as delivery mechanisms for cosmetic ingredients in anti-ageing creams, moisturizers and other skin care products. Lipid nanoparticles are particularly more effective, as they easily cross with the lipid bilayer in cell membranes, supporting the delivery of compounds which would otherwise unable to enter the cell. Silver nanoparticles were found to be very stable, having sufficient preservation efficacy against mixed fungi and mixed bacteria and unable penetrates normal human skin.[30] So silver nanoparticles appeared to be suitable for use as a preservative in cosmetics.

NANOTOXICITY

Nanotoxicity, a term coined in 2004, point out to the study of the potential toxic effect of nanoparticles on biological and ecological systems. Nanotoxicity in early studies come from aerosol studies examining size-dependent particle effects; the field continues to draw from that heritage as well as from diverse fields such as molecular toxicology, molecular biology, material science, engineering and analytical chemistry.[31] Over the past years, the field of nanotoxicity has grown significantly in response to and in hopes of introducing concerns regarding the boom in nanoparticle technology and the subsequently increased possibility of exposure through consumer and medical applications. Nanoparticles come in daily

contact as nonself particles; consume them with every drink and we inhale them with every breath. Every organism on the earth regularly face nanometer-sized entities. The immense majority causes little ill effect, and goes unnoticed, but occasionally an interloper will cause appreciable harm to the organism. Although the only size definition is no longer explicitly followed in the categorization of nanomaterials, the unique properties of nanoparticles make them subject of intense study and industrial interest. In fact, as of March 2011, nanoparticles were found in 1,317 commercially available products. On an average day, we may be exposed to commercially available nanoparticles in many seatings, including silver nanoparticles in sheets and clothing, titanium dioxide nanoparticles in sunscreens and cosmetics, carbon nanoparticles in bikes and even clay nanoparticles in beer bottles. The major toxicological concern is the fact that some of the manufactured nanomaterials are redox active[5] and some particles cross across cell membranes and especially into mitochondria.[32] The genetic complement of individuals decides the toxicity of nanoparticles, which provides the biochemical toolbox by which it can adapt to and fight toxic substances. Bronchitis, asthma, emphysema, lung cancer, and neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases are associated with inhaled nanoparticles. In gastro-intestinal tract nanoparticles have been linked to colon cancer and Crohn's disease. Nanoparticles that enter the circulatory system are the cause of arteriosclerosis and blood clots, arrhythmia, heart diseases and ultimately cardiac death. Translocation to other organs, spleen, such as liver etc, may lead to diseases of these organs as well. Exposure to some nanoparticles is associated with the occurrence of autoimmune diseases, such as: systemic lupus erythematosus, rheumatoid arthritis and scleroderma (Figure 1).[33]

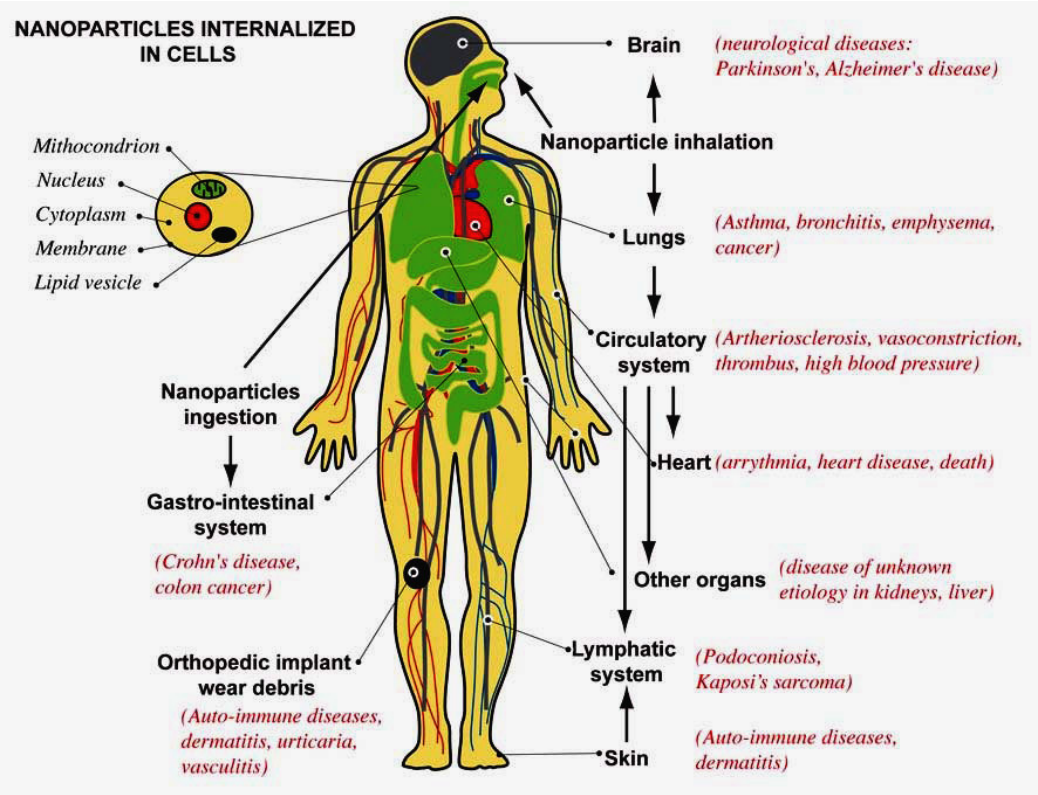


Figure 1

Schematics of human body with pathways of exposure to nanoparticles, affected organs, and associated diseases from epidemiological, in vivo and in vitro studies.[33]

TOXICITY OF DIFFERENT NANOPARTICLES

Silver (Ag)

Ag is highly toxic and the microscopic studies showed that cell exposed with nanoparticle at higher doses displaying cellular shrinkage, became abnormal in size and an acquisition of an irregular shape. To test the toxicity of silver nanoparticles further study conducted with reference to its oxidative stress. There was significant reduction in mitochondrial membrane potential, depletion of GSH level and an increase in reactive oxygen species levels, which indicates that the cytotoxicity of Ag (15nm and 100nm) in liver cells is likely to be mediated through oxidative stress.[34] Silver nanoparticle treated embryos were observed with increase in mortality and hatching delay in a concentrated manner. Additionally nanoparticles treated embryo were observed by phenotypes that had abnormal body axes, twisted notochord, slow blood flow, pericardial edema and cardiac arrhythmia. With Ag+ ions and stabilizing agents there were no significant defects in developing embryos.[35]

Titanium dioxide (TiO_2)

TiO_2 absorbs a substantial amount of UV radiation in sunscreens. However in aqueous media leads to the production of reactive oxygen species, including superoxide anion radicals, hydrogen peroxide, free hydroxyl radicals, and singlet oxygen. These reactive oxygen species can cause substantial damage to DNA.[18] Sun-illuminated TiO_2 nanoparticles catalyze damage in DNA both *in vitro* and *in vivo* conditions.[36] Nanoparticles when introduced by instillation were seen to have no inflammatory effect or genotoxicity in rats.[37] However in several other studies have reported that titanium dioxide caused chronic pulmonary inflammation in rats[38] and *in vitro* had a proinflammatory effect in cultured human endothelial cells.[39]

Vanadium oxide (V_2O_5)

Toxicity by vanadium oxide nanoparticles compared to bulk material is observed in human endothelial and epithelial lung cells might be due to the higher catalytic surface of the particles. Cell viability decreased almost ten times stronger and starts with the lowest concentrations of "nanoscaled" material (10g/mL). VnO_2 leads to an induction of heme oxygenase 1 (HO-1) in a dose-dependent manner in ECV304 cells. Reduction in protein levels was observed in the epithelial cells (A549). Lipid peroxidation can be observed also for "nanoscaled" vanadium oxide to a much stronger extent in macrophages than for bulk material. It appears to be a nanoeffect of a high surface reactivity coupled with unknown toxicity potentiating effect of a technically important catalyst.[40] Toxicity of different nanoparticles is listed in table 2.

Table 2
Toxicity of different nanoparticles

S.no.	Nanoparticles	Animal model	Dose & route	Effect
1	Silver (Ag)	Artemia nauplii	12nM of 30-40 nm AgNP In surrounding environment	DNA damage[51]
		Zebrafish embryos	5 µg/L of 10 nm AgNP,	Alterations in gene expression[52]
2	Titanium dioxide (TiO_2)	Mice	600 µg/mL, Oraly	DNA deletions[53]
3	Vanadium Oxide (V_2O_5)	Mice	0.02 M, inhalation	Testicular toxicity[54]
4	Gold (Au)	Rat	20 µg/m^3 of 4-5 nm AuNP, Inhalation	Lung toxicity[55]
		Mice	2200 µg/mL, of 13.5 nm AuNP, Orally	Spleen toxicity[56]
		Rat	50 µl of 10 nm NP, intraperitoneal injection	Lipid peroxidation in liver [57]
5	Carbon Nanotubes (CNT)	Mice	5 mg/m^3, intraperitoneal injection	Lung adenocarcinoma[58]
		Mice	0.5 mg, Intratracheal Instillation	Lung toxicity[43]
6	Zinc Oxide (ZnO)	Rat	400 mg/kg of 20 nm NPs, Orally	Lung toxicity[59]
		Rat	500 mg/kg of 20±9 nm NPs, Orally	Systemic toxic potential[60]
7	Silica (Si)	Zebrafish embryos	200 mg/Ml, whole body exposure	Developmental toxicity[61]
8	Iron Oxide (Fe_2O_3)	Zebrafish	10 – 100 mg/L, whole body exposure	Developmental toxicity[48]
		Rat	5mg kg^{-1}, intratracheal instillation	Lung toxicity[62]
9	Copper (Cu)	Zebrafish	1.5 mg/L, whole body exposure	Gill Injury[63]

Gold (Au)

Evidence of rapid translocation of metal nanoparticles from lungs into the circulation and to organs has been observed in studies of animals as experimental models. These results show the location of nanoparticles with diameters of 30 nm gold nanoparticles[15] in pulmonary capillaries and welding fumes[41] in blood, liver, kidney, spleen, brain and heart. After a half hour of exposure, large quantities of intratracheally instilled gold nanoparticles (30 nm) have been found in platelets inside of pulmonary capillaries of rats[15] motivating the hypothesis that nanoparticles may induce aggregation of platelets, leading to the formation of blood clots. The necrosis of erythrocytes in response to nanoparticles can be a measure of both membrane disruption and extreme cellular toxicity and is mainly important for nanoparticles that are intended to be directly introduced into the blood circulation. Recent studies have focused on the hemolytic potential of gold nanoparticles while assessing their effects on ROS production in neutrophils and thrombotic capabilities.[42]

Carbon nanotubes (CNT)

Cellular intake of CNTs is important in interpreting the cytotoxicity of CNTs .TEM images of cellular ultrastructure reveal the presence of cytoplasmic extensions and CNT-containing phagolysosomes, shows that CNTs increase the phagocytic activity of macrophages. Using fluorescence microscopy, also observed fragmented nuclei (apoptotic cells) and balloon-like nuclear morphology (necrotic cells) in CNT-exposed cells.[42] With single-wall carbon nanotubes in mice demonstrated that carbon nanotube products induced dose-dependent epithelioid granulomas in mice and in some cases, interstitial inflammation in the animals of the 7-day post-exposure groups.[43]

Zinc oxide (ZnO)

ZnO nanoparticles show their toxic effect due to the compound's solubility. Inhalation or instillation of the ZnO nanoparticles results in lung inflammation and systemic toxicity but intraperitoneal administration induces neurological effects. Nanoparticles show systemic distribution; targeted organs includes liver, lung, spleen, kidney and in some cases the heart. Exposure with zinc oxide *in vitro* condition to BEAS-2B bronchial epithelial cells and A549 alveolar adenocarcinoma cells results in cytotoxicity, increased intracellular Ca^{2+}, increased oxidative stress, interleukin -8 production and decreased mitochondrial membrane potential. Reduced contractility of airway smooth muscle cells poses an additional hazard.[44]

Silica oxide (Si)

SiO_2 nanoparticles of 15 nm were used to determine oxidative stress responses and time-dependent cytotoxicity. Cell viability decreased significantly as a function of both nanoparticle dosage (10–100 µg/ml) and time intervals (24 h, 48 h, and 72 h). Exposure to SiO_2 nanoparticles increased ROS levels and depleted glutathione levels. The increased production of malondialdehyde and lactate dehydrogenase release from the cells suggested that lipid peroxidation and membrane damage in cultured human bronchoalveolar carcinoma-derived cells was closely correlated to increased oxidative stress.[45] SiO_2 nanoparticles showed modulation of the cellular redox status, cytotoxic effects and the impact on DNA integrity in human colon carcinoma cells (HT29). The result shows that these SiO_2 nanoparticles induced the proliferation of HT29 cells and interfere with glutathione biosynthesis, depending on the particle size and the incubation period. The cytotoxicity by SiO_2 nanoparticles depend on the concentration, size and on the FCS content of the culture medium. Finally it can be concluded that the effects of SiO_2 NPs were not mediated by oxidative stress but by interference with the MAPK/ERK1/2 as well as the Nrf2/ARE signalling pathways.[46]

Iron oxide (Fe_2O_3)

Rats were exposed with the repeated doses of Fe_2O_3 nanoparticles and observed not only with significant inhibition in total, Mg^{2+}, Na^{+}, K^{+}, and Ca^{2+}-ATPases in brain but also significant inhibition was recorded in RBC and brain acetylcholinesterase point out that both synaptic

transmission and nerve conduction were affected by this compound. Fe_2O_3 increased the total amount of alanine amino transferase, aspartate amino transferase and lactate dehydrogenase in serum and liver, whereas in kidney these enzymes were significantly decreased indicating tissue necrosis and possible leakage of these enzymes into the blood stream.[47] Another study showed that ≥10 mg/L of iron oxide nanoparticles induces developmental toxicity in these embryos of zebrafish, causing mortality, hatching delay, and malformation.[48]

Copper (Cu)

The toxicological effects of copper nanoparticles (CuNPs) were investigated based on a stress-responsive bacterial biosensor array in E.coli. According to the responses of the biosensing strains, it was found that CuNPs induce not only oxidative stress in *E. coli*, but also protein damage, cell membrane damage, DNA damage and ultimately lead to cell growth inhibition. The toxicological effects of CuNPs are traced to H_2O_2 generation through enzyme detoxification analysis.[49] Nano and ionic copper particles both are moderately toxic, and micro-copper practically non-toxic of Hodge and Sterner Scale. In mouse , kidney, spleen and liver were found to be target organs of copper nanoparticles. Nanoparticles induce toxicological effects and heavy injuries on kidney, liver and spleen of experimental mice, but micro-copper particles do not, on mass basis a gender dependent manner.[50]

CONCLUSION

Nanoparticles present a highly attractive platform for a diverse array of biological, medical and environmental application. With increasing use in large quantity and daily exposure produce adverse effect on health and environment. With this new possibility to utilize the unique properties of nanoparticles for research, industry, medicine or any other field, there is a need to build design rules for the synthesis of safe nanoparticles; therefore, systematic studies are required and should be based on well studied physicochemical nanoparticle properties and their effects on cellular viability and function in relevant model systems.

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