Review Paper

Nanomaterials and Nanotoxicity in the Present Scenario: A Short Review

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ABSTRACT

Nanomaterials have begun to play an integral part of our daily life as they are being increasingly used in medicines, prosthetics, engineering materials, house hold articles, clothes, paints, etc,. At present there are few studies about the hazards of nanoparticles to human health. Ecotoxicological issues due to nanomaterials have received even less attention, which is alarming since production of nanomaterials is progressing at a brisk scale. This review addresses some of the health concerns pertaining to nanomaterials in the light of their tremendous potential for extensive use in various fields.

Key Words: Nanoparticles; Nanomaterials; Ultra fine particles; Nanotoxicity

Introduction

Nanomaterials or nanoparticles (NPs) are particles with an overall dimension of less than 100 nanometres, and include gold and silver nanoparticles, metal oxides of titanium and zinc,[1] carbon nanomaterials such as fullerenes, nanotubes and buckyballs,[2] and quantum dots (QD) of cadmium telluride and cadmium selenide. Nanosubstances have gained tremendous popularity in recent times as these are useful in almost all spheres of our daily life. Nanomedicines are being designed in the form of micelles, emulsions, nanocapsules and particles, proteins, and nanosome, or liposome formulations.[3]

Manipulating biological materials, for instance by engineering blood NPs could create a synthetic blood cell that can enhance human performance by a hundred times. "Tissue engineering" can artificially stimulate cell proliferation and increase growth factors with the help of carbon nanotubes. Engineered specific nanoparticles can be equipped with a dose of taxol by attaching nanoparticles to a folic acid derivative (anticancer drug) that targets malignant tumours. Magnetic core composed mainly of iron oxide, exhibits strong fluorescence. This trait enables the particles to be easily tracked and controlled once they are inside the human body by using optical imaging /MRI. If there is no cancer found, then the biodegradable nanoparticles undergo metabolism in the liver, while the iron core is utilized by the body. Thus the NPs perform diagnostic and therapeutic functions in one blow. Engineered nanoparticles are biocompatible and biodegradable. They can be modified to almost any form, from delicate electronics to "self-cleaning" fabrics whose NPs actually "eat" stains.

Discussion

Any highly stable closed-cage structure having more than twenty carbon atoms is called a fullerene (**Fig 1**). The most stable one is the "bucky ball" which has 60 carbon atoms arranged in the form of a standard soccer ball (**Fig 2**). A fullerene allows other molecules to penetrate into it like a reservoir which may then permit a controlled release and delivery of the substance from it. A classical bucky ball is a molecule, composed entirely of carbon in the form of a hollow sphere, ellipsoid or a pipe. Bucky balls come in all sizes. The smallest one consists of 20 carbon atoms; the frequently encountered buckyballs have 60 or 70 carbon atoms. The largest has 540. Carbon nanotubes are long, hollow structures with the walls

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formed by one-atom-thick sheets of carbon (graphene). These are allotropes of carbon. Nanotubes have been constructed with length-to-diameter ratio of up to 132,000,000: 1. They exhibit extraordinary strength and unique electrical properties, and are efficient thermal conductors. Nanotubes are members of the fullerene family and spherical buckyballs having approximately 1/50,000th of the width of a human hair. Quantum dots (QDs) are fluorescent NPs that may be used to improve biomedical imaging, drug delivery, diagnostic testing and biomarkers in cancer therapy.

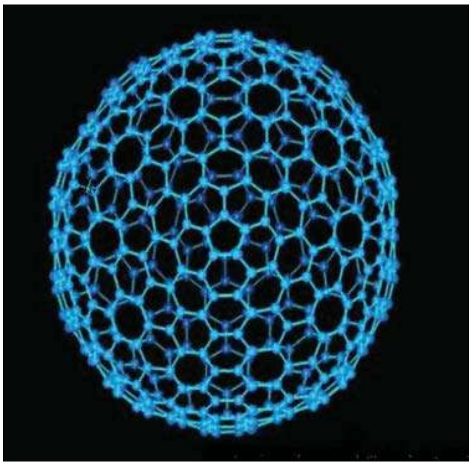

Fig 1

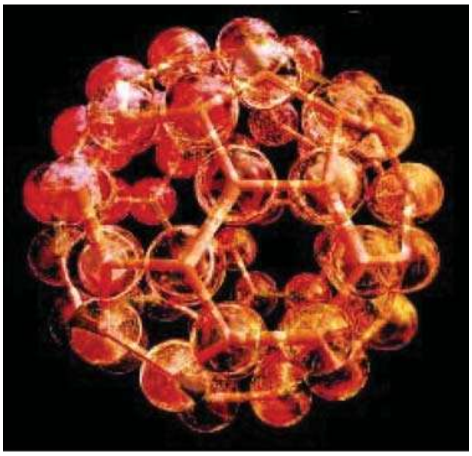

Fig 2

Numerous consumer products utilize NPs during the manufacturing process, for e.g., sunscreens contain zinc oxide or titanium oxide which protect against ultraviolet rays and skin cancer.[4] These materials can enter the environment on a continuous basis by various means.[5,6] Nanotechnology is being used in the manufacture of fabrics which are stain free, would not shrink and do not get wet in water. Paints developed with nanotechnology are of all-weather coats which repel water. Heat resistant vessels with improved smooth surface, helps in cooking in "easy to clean vessels". Self-cleaning windows are another novel product of nanoscience. "Intelligent" packaging indicates whether the contents are fit to be consumed or not. Packaging of strong smelling foods such as cheese, or food sensitive to oxygen, for e.g., meat can be done with the help of nanotechnology. Popularly used consumer products comprising nanomaterials include computer chips and smaller rapid action integrated circuits, high capacity hard disk drives and flash memories. Transport sources manufactured with nanomaterials are lighter, carry more payloads, consume less energy and are less polluting to the environment. Quantum caged atoms (light emitting diodes) for illumination offer high beam quality and help in energy conservation. Self-cleaning glasses and solar cells are cheaper.[7] NPs could enhance flame retardant properties, and also protect against corrosion.[8] Thus nanomaterials have universal applications.

Engineered nanoparticles are known to interact directly with biological membranes.[9] The cell membrane, mitochondria and cell nucleus are considered as major cell targets for nanotoxicity either by adsorbing onto the membrane, or compromising its integrity, or by providing a hole or pore. NPs increase the permeability and enhance diffusion of the phospholipid membranes.[10] Anticancer nanogel formulations have demonstrated a significantly augmented cytotoxicity in cultured cancer cells,and enhance tumour specificity, while significantly reducing systemic toxicity.[11] NPs mediated drug delivery systems are being used to target organs which undergo oxidative damage in neurodegenerative diseases (Alzheimer's, Parkinson's).[12]

Nanomaterials such as bucky balls interrupt immune response by preventing mast cells from releasing histamine by binding to free radicals. Gold nanoparticles tagged with short segments of DNA can be used for detection of genetic sequence in a sample using nanotechnology. Medical imaging, biocompatible implants and prostheses, MRI guided gene drug delivery or cell replacement, cell tracking and bioseperation are fields where nanomaterials are being used. "Laboratories-on-a-chip" that reduce the time for biomedical analyses to only a few seconds, markers to detect disease well before the primary symptoms appear are new arrivals. Intra-vascular nanosensor and nanorobotic devices, diagnostic and imaging procedures are presently under development.[13]

Properties of nanomaterials specifically depend on their physiological, morphological and biochemical characteristics.[14] Pegylation can increase cytoplasmic transport and bioavailability as well as the $t_{½}$ of the nanomaterial or the drug used.[15] Nanomedicines are designed to have optimum combination of lipophilicity and hydrophilicity so that they distribute all over the body rapidly through the circulation by diffusion through tissues and cells, and interact with their target receptors or an enzyme. It has been observed that nanoparticles can decrease semen quality by 2% per year, as per a study spanning 50 years.[16] NPs can affect gametogenesis producing heritable gene mutations, and structural and chromosomal aberrations in germ cells.[17] Nanomaterials can enter the human body through several ports, after inhalation via the lungs, and after oral uptake in the digestive system.[18] They can cross the blood-brain barrier, and even the blood-testis barrier.[19,20]

Silver NPs could be used in bone cement or other implantable devices as antimicrobial agents,[21] but nanoparticulate form could be toxic for the bone-lining cells and other tissues. Factors that make nanoparticles toxic include small size with greater surface area per mass compared with larger particles, and surface charge distribution, shape, agglomeration state, crystal structure, chemical composition, smoothness of surface, lipophilicity, ability to cross cell, tissue-barriers and resistance to biodegradation.[22-24] It has been experimentally proved that caffeine and urea diffuse more directly through the membrane bilayer in the presence of nanotubes, the property of which may be used in many other procedures for drugs diffusion.[25]

When these special properties are being explored to the advantage of mankind in different fields, it becomes necessary to know the toxic potential of these nanomaterials so that it can be used with certain amount of caution it deserves. In vivo administered magnetic nanoparticles (MNPs) are quickly challenged by macrophages of the reticulo endothelial system resulting in potential MNP toxicity. Nanomaterials have potential for antioxidant activity.[26] The surface coating of NPs with albumin clearly causes even the smallest particles to be internalized via caveolae.[27] Caveolae are plasma membrane invaginations prominent in all endothelial cells lining blood vessels that serve as membrane organizing centers. These are rich in adiposities having 50–100 nm size, and are involved in endocytosis, oncogenesis, uptake of pathogenic bacteria and certain viruses. Ultrafine particles (UFPs) produce adverse respiratory and cardiovascular effects resulting in morbidity and mortality in susceptible groups of the population.[28] Zinc oxide induced toxicity in cells results in the generation of reactive oxygen species (ROS), oxidant injury, exacerbation of inflammation, and cell death.[29] Erythrocytes treated with nano-TiO2 underwent abnormal sedimentation and changes in surface properties resulting in haem agglutination and dose dependent haemolysis, which was different from those treated with micro-TiO2. Nano-TiO2 may have potential toxicity to humans.[30]

Environmental exposure to NPs which is common in urban areas has the risk of causing pulmonary damage, seen more in older than in younger adults.[31,32] Multi-wall carbon nanotubes (MWCNTs) induce a strong immune and inflammatory response within skin fibroblasts and are internalized in keratinocytes.[33,34] The introduction of only a few strategically spaced single bonds in polar and rigid ligands markedly increases their binding to a carbon nanotube.[35] At high doses, quantum dots (QD) caused pulmonary vascular thrombosis, most likely by activating the coagulation cascade via contact activation. The study highlights the need for careful safety evaluation of QDs before their use for human applications.[36] Nano-copper produced changes suggestive of mitochondrial failure, enhanced ketogenesis, fatty acid beta-oxidation, and glycolysis which contributed to the hepatotoxicity and nephrotoxicity. An increase in triglycerides in the serum, liver and kidney tissues could serve as a potential sensitive biomarker reflecting the lipidosis induced by nano-copper.[37] Silver NPs were more toxic while molybdenum trioxide (MoO3) were the least toxic as observed in a study of the cytotoxicity of NPs in the germ line in-vitro.[38]

Conclusion

Our current knowledge does indicate different areas of concern that deserve further investigation to understand how individual nanoparticless behave and what toxicity could be expected from them. In the midst of all the benefits of the nanomaterials of the current age, the vast field of nanotoxocity is not addressed fully. Manufacturing of multi-functional NPs need to be assessed and subjected to strict quality control along with the final products. Various high throughput methods need to be developed which can predict the uptake, transport, transformation, accumulation and release of engineered nanomaterials in the human body and environment within the shortest duration. The knowledge of interactions between NPs and lipid membranes might significantly contribute to the determination of safe doses of NPs in the emerging field of nanomedicine. Data generated from recent experiments support the fact that an integrated pharmacological, biotechnological and pharmaceutical approach is promising for the development of a rapid in-vivo screening method for nanotoxicity.

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