Understanding the toxicity of nanotubes and nanoparticles in the environment: Are nanotubes and nanoparticles safe?

Marjan Assefi[1]*, Khadijeh Onsory[2], Alireza Iranbakhsh[3]

[1]University of North Carolina, Greensboro, USA

[2]Department of Biology, Faculty of Science, Islamic Azid University, Parand, Iran

[3]Department of Biology, Science and Research Branch, Azad University, Tehran, Iran

Abstract

Nanoparticles measures from 1 to 100 nanometers in diameter are chemically different from their corresponding bulk materials and their potential toxicity can vary according to dozens of characteristics, such as size, surface area and coating. In 2009 researchers claimed that nanoparticles were responsible for lung damage. Two workers in a printing factory in China in Beijing died (Nature 460,932/2009). Researchers at a meeting said that safety testing was needed for products containing nanoparticles, products that can be absorbed by the body like; food, cosmetics and perfumes in which nanoparticles are used in their colors or in their textures. The workers who work in an occupational exposure to nanotubes and nanoparticles are at great risk.

The nanoparticles like: carbon nanotubes and nanoparticles of titanium dioxide and silver are under investigation to find out about the most toxic one *via* high–through put screening. Nowadays a lot of products that we have in marketplace which are labeled "nano-enabled" mean that they contain nanoscale particles. They are designed with nano to give them some beneficial features. In 2007, approximately $147 billion worth nano-enabled commercial and consumer products were sold. Nanotechnology has spread widely in the market, but it has shown mounting concerns over the human health effects. They have a very small size 100 nano-meters or less.

Keywords: Nanotubes, Nanoparticles, Carbon Nanotubes (CNTs), Single Wall Carbon Nanotubes (SWCNTs).

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Introduction

Nowadays, in many different industrial areas, an increasing and uncontrolled use of nano materials are being shown *via* carbon nanotubes in cars to nanoparticles in cosmetics and pharma. The consumers and customers show an increasing concern about the safety of nanomaterials and potential risks for health and environment [1]. We have it on the title of some new papers as “dangerous Nano”. Cosmetics and pharma use NCS “nanotoxicological classification system”, but other products should prove their safety. The NCS places the nanomaterials in 4 groups. Group (I,II,III) medium risks, and group (IV) as higher risk [2].

Nanomaterials have unique physical properties. These properties influence their uptake, distribution, and behavior in the body. Some nanoparticles have shown the ability to penetrate cells, where they can trigger inflammatory responses and oxidative stress.

There are safety features that should be tested:

A: We cannot deny this fact that nanoparticles can pass lung and gastrointestinal tract. A small portion of it can reach the blood stream and target the other organs. Most of NMs are cleared from lung by macrophages and are excreted through faces. On the whole more, studies are required.

B: Instillation and inhalation experiments: Following instillation studies, high local doses should be used. Transient inflammatory effects have been reported in both types of lung exposure.

C: In fluids: the studies show an unspecific particle effect. The biological response is comparable to the exposure to fine dust. Carbon Nanotubes (CNT), induce a severe tissue reaction(chronic inflammation) which leads to tumor formation. Studies have shown that NMs can dissolve in body fluids either slowly or fast. This is a new situation that should go under severe studies with nano toxicity. One of the outcomes of the study shows that the studies are not toxicological.

On the other side experiments carried out with high toxicological end points are very misleading. Toxicity parameters are size, biocompatibility, and degradability [3]. Nanoparticles larger than 100 nano meter to 1000 nano meter have access to a limited number of cells, so they are less risky. Nanoparticles smaller than 100 nano meter can internalized *via* endocytosis [3].

There are so many studies that have been published on the topic of nano safety. There have been a lot of articles on nano safety and it is increasing day by day [4]. Most of these studies, do not offer any kind of clear option on nano safety [5]. Now, they took the chance in this article to go through what are nanoparticles, the benefits, usages, hazards, and toxicology of nanoparticles, and how we can follow the nano safety rules as far as we can.

To guide scientists and engineers in nano material researches and applications as well as the use of nano materials in a safe way; a decision support system has been proposed [6]. The classification system is based on both toxicity and physicochemical characteristics of nanomaterials as well as their environmental impacts are subjects to more studies [7].

By January 2011, a load of 5000 papers were published on the topic of nanotoxicology and in 2016 they have been doubled. They show that we can study the possible negative effects of nano materials on human health and environment [8].

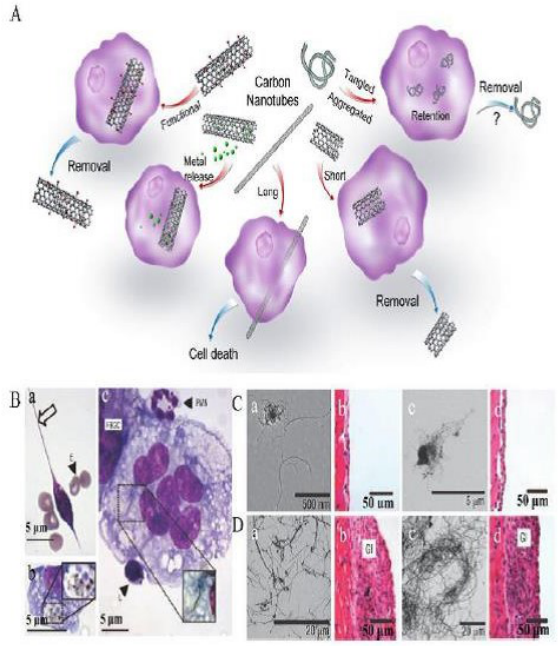

Figure 1. Physiochemical properties of CNTs can influence cell uptake and responses. (A) The varying types of CNTs can affect phagocytosis and cytotoxicity; (B) Ab long MWCNTs can lead to frustrated phagocytosis, while short MWCNTs are readily phagocytosed. (c) Foreign Body Giant Celis (FBGCs} are present after injection of long MWCNTs (PMN, olymorphonudear leukocyte; L, lymphocyte) (D) Diaphragms show the presence of Granulomatous Inflammation (Gl) in méce exposed to tong MWCNTs, while (C) A small granuloma response is seen in mice treated with tangled MWCNTs. Reproduced from ref 27. Copyright 2008 Nature Publishing Group.

Nano technology is a field of research that is growing very rapidly, and it has a great impact on different products. This field of study can be defined as the production and use of materials at the nanoscale as smaller than 100 nano meter in one dimension [9]. Nano materials are formed through both natural and synthetic processes [10]. Despite their benefits, nanotubes and nano materials have been identified as toxic *in-vivo* and *in-vitro* tests.

Carbon nanotubes are being classified in two main groups. Single Wall Nanotubes (SWCNTs) and Multi Wall Carbon Nanotubes (MWCNTs). It depends on the number layers. They are used in nano technology, optics, electronics, materials science, biology, and medicine. There are a lot of factors affecting the carbon nanotubes and nano materials like silver nano particle, and gold nano particle experiments which lead to toxify them. There are some factors as impurities, surface modification, structure, and exposure routes.

Carbon nanotubes toxicity from impurities:

One of the most important factors to carbon nanotubes toxicity is impurities. The most important catalyst metal contaminants such as the transitional metals Fe, y, Ni, Mo, and Co; some other impurities such as amorphous carbon, and other carbon nano materials; might also lead to carbon nanotubes toxicity. Presence of metal impurities could lead to conflicting data about the bio compatibility, toxicity, and the risk assessment of carbon nanotubes.

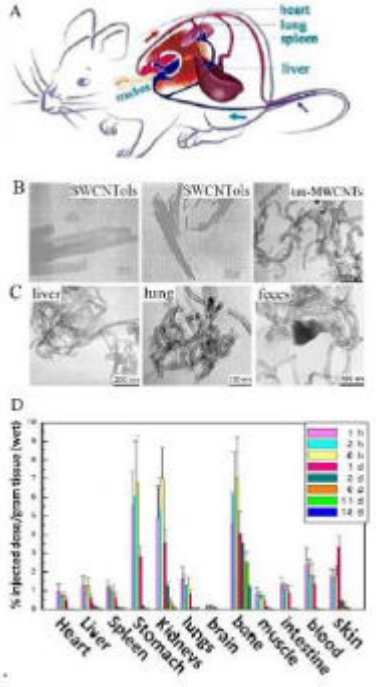

Figure 2. Distinct biodistribution of CNTs *in-vivo* resufting from different surface modifications. (A) CNTs could arrive at almost all organs, including heart, lungs, liver, kidneys, spleen, stomach, and intestine; (B) TEM images of SWCNTols21 and tau-MWCNTs22; (C) TEM images of MWCNTs in digested sotutions of liver, bung, and feces after tait intravenous injection, intratracheal injection and gavage, respectively; 22 (D) 1251-SWCNTok were distributed throughout the entire body Quickly after intraperitoneal injection (ip), except brain, accumulated In the bone for a long time.21 Reproduced from refs 21 and 22. Copyright 2004 American Scientific Publishers and Copyright 2007 by Elsevier B.V., respectively.

Commercial Single Wall Carbon Nanotubes (SWCNTs) and Multi Wall Carbon Nanotubes (MWCNTs) with contents of Fe, Co, Mo, and Ni as well as acid treated Single wall carbon nanotubes were able to cross the cell membrane. The studies have indicated that respiratory exposure to single wall carbon nanotubes which contains Fe, Co, Mo, and Ni could induce acute pulmonary and cardiovascular responses. Carbon nano

tube toxicity derived from the chemical and structural characteristics.

In the figure 3, it shows the competitive binding of blood proteins on the single wall carbon nanotubes surface could greatly alter their cellular interaction pathways and reduce the cytotoxicity of single wall carbon nanotubes. The schematic diagram of interactions between single wall carbon nanotubes and human blood cell and proteins. B and E showed Atomic force microscopy images of proteins after incubation with single wall carbon nanotubes for 5 hours.

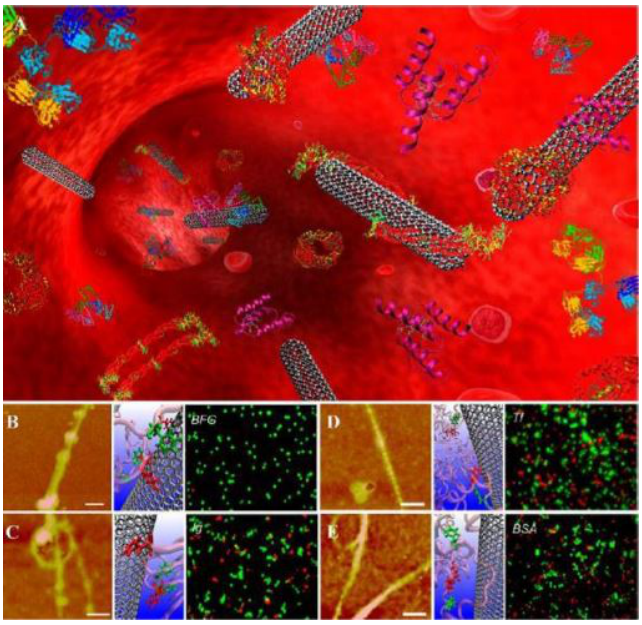

Figure 3. The competitive binding of blood proteins on the SWCNT surface could greatly alter their cellular interaction pathways and reduce the cytotoxicity of SWCNTs. (A) The schematic diagram of interactions between SWCNTs and human blood cells and proteins. (B E, left) AFM images of proteins after incubation with SWCNTs for 5 h, including BFG. (B) ig (C) Tf (D) BSA. (E) The interactions were estimated using both experimental (B E, right) and theoretical (B E, middle) approaches. Abbreviations: BFG: Bovine Fibrinogen; Ig: Gamma Globulin; Tf: Transferrin; BSA: Bovine Serum Albumin. Reproduced from ref 2. Copyright 2011 National Academy of Sciences.

Surface charge and modifications

For medical application, we should first wash Carbon Nanotubes well, and thoroughly in the water to remove all impurities.

Functional groups and surface areas are highly related to toxicity of carbon nanotubes. Hydroxylated Single wall carbon nanotubes are quickly distributed throughout the entire body and accumulate in the bone. Taurine covalently Multi wall carbon nanotubes accumulate in the liver over a period of 3 months with liver toxicity.

Shape of Carbon nanotubes are single, cylinder or multi cylindrical structures. Poland et al. warned that carbon nanotubes that was used in the abdominal cavity had asbestos like pathogenicity because of their needle like shape. So, it is very important to have more investigations related to needle like shaped nano products. In this way, we can reduce the health harm to the society and environment.

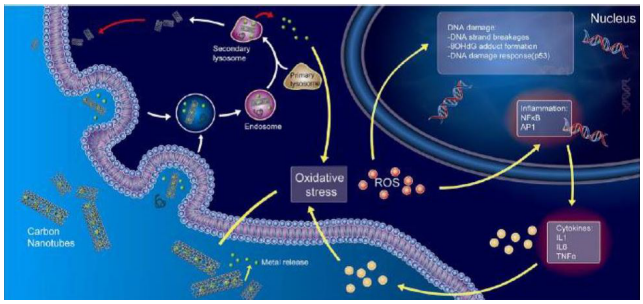

Figure 4. The mechanisms by which CNTs induce cell damage and inflammation.

Carbon nanotubes different lengths caused various degrees of toxicity. The degree of inflammation caused by 825 nano meter long; carbon nanotubes were stronger than that was induced by 220 nano meter long carbon nanotubes. Yamashita et al. indicated that long Multi Wall Carbon Nanotubes induced the strongest DNAA damage, and increased the total cell number in abdominal lavage fluid.

Agglomeration

The agglomeration state can affect the shape and surface area of carbon nanotubes, and determines the toxic potential of Carbon nanotubes. Wick et al. reported that suspended carbon nanotubes bundles were less toxic than asbestos. The toxicity partially depends on the state of tubes.

Mechanisms of Carbon Nanotubes induced toxicity

After carbon nanotubes enter the body thorough inhalation or derma, or oral routes the toxicity is shown as oxidative stress, inflammatory responses, malignant transformation, DNA damage and mutation, formation of granuloma, and interstitial fibrosis. Numerous studies have documented that the metals that are released from carbon nanotubes can cause H_2O_2 and superoxide anions to hydroxyl radicals [11].

When multi wall carbon nanotubes were injected into mice, inflammation was observed. It was also able to activate the secretion of cytokines and chemokines which cause inflammation.

Chronic exposure to single wall carbon nanotubes caused malignant transformation of human lung epithelial cells and caused tumorigenesis in mice.

Genotoxicity is the deadliest cause of cytotoxicity. Carbon nanotubes not only enter the cytoplasm, but also localizes within the cell nucleus and cause cell mortality by activating the tumor suppressor protein P53. Carbon nanotubes may get in contact with DNA when nuclear membrane breaks down during mitosis if they accumulate in cells [12]. They may destroy DNA indirectly by oxidative stress and inflammatory responses.

The toxicity of nano materials can be impact by material's physicochemical characteristics [13]. For example, toxic "Nanoparticles" one of nanoparticles that bind to soil surfaces tightly show limited movement through the environment [12]. Thus, these kinds of materials may be accepted to some extent safe for certain uses [10].

This information is very important, so the misunderstandings on nanoparticles functions related to their toxicity may delay the industrial application of nano technologies [14,15]. Nano material research should be guided with a systematic characterization of factors which lead to toxicity in the absence of definitive data [16]. There are errors due to solvents and dispersion agents during the experiments: their dosage; interference effects with test system, and the complete lack of references for comparisons. Numerous errors occur when unsuitable concentrations are used during experiments [15]. WittMaack showed that a minor overdose of nano material in petri dishes leads to a complete coverage of cells by agglomerated nanoparticles [16]. So, the supply of nutrients and oxygen lead to the death of the cell [17].

Drug Delivery

Magnetic nanoparticles have been used as makers in biomedical diagnosis [31]. Magnetic Nanoparticles can be used for achieving drug and radiation delivery. Small magnetic particles can be engineered to carry chemicals to tumors. The early detection of a disease remains the primary goal. Nano technology has great promises for evaluating the achievement of these goals [8,10]. This technology allows the detection of individual cancer cells months or years earlier than traditional tools; it is also being used for early detection of Alzheimer disease.

There are many other applications for nano materials I the medical and pharmaceutical sector. The only fact currently under investigation is the toxicity of these materials and their toxic effect on body, genes, cells, and DNA [4,8,31].

Nanotechnology and food production

Nanotechnologies may have a positive effect on pesticides and fertilizer to boost crop [18]. In undeveloped countries, they have started to use nanotechnology in animal husbandry [3]. These nano materials may help farmers reach their goals, but nano materials can also create adverse effects in the environment and on human health [5].

Food processing

The chitosan nano carrier is one of the systems that delivers nutrition to specific places [19]. With rapid spreading technology, new techniques are being considered to replace the old ones [20]. Nano technology is going to have a major rule in food processing [20]. Nano technology will help to decrease waste and spoilage of nutrition [19].

To prevent adverse effects on consumer health, nutrition delivery system must be made with bio degradable materials [5].

Water purification

Many scientists use nano membrane technologies in water purification like Carbon Nanotubes (CNT) [21]. (CNT) is considered a high-risk material for human health and food industry for the environment [22]. They use nano structures to remove microorganisms or toxins from the water. Broad use of some nanoparticles, like fullerene and carbon nano structures; have received protests from environmental activities [23].

Food packaging and safety

Materials like plastics and nano biodegradable materials have been used in food packaging [24-27]. With the advent of smart packaging (containing sensors and nano composites) or even edible packaging (using lipids, proteins, polysaccharides, and etc.), this field have faced with major problems; including poor properties, humidity, temperature low degradation, and gas permeability which prevent expansion [23].

Herein we confront with the unique properties of nano materials; nano composites such as in organic phase and biodegradable polymers can address a lot of problems [28]. To increase the shelf life and improve storage condition; they use manganese oxide, zinc oxide, and silver nanoparticles [29]. Gold nanoparticles, Quantum Dots (QD), carbon nanotubes, and other active nano structures are being used as sensors of microbes and food safety [27].

A) Size: One of the important characteristics for nanoparticles is size. They have announced that the size is an important factor in observed dermal cell toxicity [30]. The small nanoparticles permits them to penetrate through various biological barriers and settle in tissues like central nervous system. The size of nanoparticles should be considered in assessing the safety of nanoparticles [30-33].

B) Chemical composition: Many reagents which are used in the production of nanoparticles could be toxic. Sometimes, the toxicity is not related to nanoparticles, but is related to the process of productivity and its exposure to the toxins of the material while being produced [34-37].

C) Solubility: Solubility is a very important issue in the toxicity of nanoparticles [2]. For example; soluble titanium oxide nanoparticles are more toxic than insoluble titanium oxide [2]. A detailed report on the solubility of the oxide nanoparticles' toxicity has been published [4]. So, a lot of studies are required related to toxicity and biological activities of nanoparticles in food, health, and environment [3,4].

Nanoparticles in food and related products can penetrate the human body [2]. They disperse in the air during the production process [4]. Nanoparticles in the packaging and in pesticides and fertilizers may enter the respiratory system of workers, and sometimes they can enter the digestive system through mucocilliary clearance [4]. Another and most main important route of contact which should be considered is skin [2,4].

MCDA approaches to classification

MCDA refers to a group of methods to impart structure to thee decision making process. MCDA consists of four steps:

- Structuring the problem by identifying stakeholders and criteria.
- Eliciting the parameters of the model (weights, etc.)
- Executing the model through computer software
- Interpreting results of model and possibly re-iterating process from step 1 and 2 by reevaluating the model.

The goal of the above-mentioned MCDA is to select a single best alternative through a structured process [1,6]. A review of MCDA applications to environmental management can be found in Linkov et al.

Nano safety in Korea

The SMAA-TRI sorting method is a well-suited classification system of available information regarding the physico-chemical characteristics of nano materials [8,10]. The Electre TRI assigns the alternatives [7,8]. The three types of thresholds are used to construct the relationships by defining references [38].

Factors that may influence the potential hazards of engineered nano materials include bioavailability, bioaccumulation, and translocation potential, and potential for toxicity.

It is difficult to predict the behavior of nano materials; however, future approaches are expected [35].

Bioavailability: Describes the likelihood of nano material to be absorbed across cell membranes from the various exposure routes like; (oral, inhalation, dermal exposures) into system circulation in an organism [16,18]. However, several pathways enable nanoparticles to cross cell membranes including pinocytosis, endocytosis, and diffusion. The mechanism by which particles are absorbed is highly dependent on particle composition, surface modification, size, shape, and agglomeration [21,36].

Bioaccumulation potential: Bioaccumulation is the net accumulation of particles absorbed from all sources like; (Soil, water, air, and food) [7,4]. They must consider the kinetic factors such as exposure concentration, duration of exposure, clearance, biotransformation, and degradation [6].

Toxic potential: Toxicological effects of nano materials occur through oxidative stress, inflammation from physical irritation, dissolution of free metal nanoparticles [8,9]. The characteristics of nanoparticles that influence toxicity include size, surface area, morphology, and dissolution [9,5]. Screening studies showed toxicity from metal nanoparticles at lower concentration [5,8].

Results

A survey done on nano materials over 6000 published papers in Switzerland on nano toxicity has opened a new field in research standards and qualities [18]. Nanotechnology research has grown in the last decades [23]. Now we have a lot of health, beauty, house hold items that nanoparticle are used in them [23]. Nanotubes and Nanoparticles (nano-silver, nano-iron, nano-gold, etc) are being used in cosmetics, fibers, kitchen ware, biomedical drug delivery or tissue engineering applications and many other fields [39]. The fields are increasing day by day. The size and amount of nano materials play major rule in studies. Their unusual chemical behavior represents potential health issues or environmental hazards [21]. Wiesner acknowledges, scientists have yet to develop widely accepted methods and safety issues, for introducing nano material into living systems such as cell cultures etc, [21]. In a nano material surfaces interact with cell macromolecules and salts, can change their properties in a mysterious way [39]. Still we assume that the growth trends will continue, and nanoparticles will be needed at ever-increasing quantities [34]. So, more researches on nanoparticles are required. To obtain reproducible and accurate results, researchers must establish standards and reliable detection methods and use of CNT, nano material samples as a reference to control, and study the impact of various factors systematically [39]. To make results comparable among different institutions and countries researchers need to standardize the choices in toxicity testing [39].

Conclusion

The field of nano science has been growing rapidly in the last decades. Recently, more and more attention is being focused on nano carbon tubes and nanoparticles. It is emerging as an enabling technology with high potential impact on all fields of mankind activity [34,35,16].

There has been a significant progress in nano safety in recent years. The main objective of this study was to toxicity of carbon nanotubes and nanoparticles.

The use of nano carbon tubes and nanoparticles in food, cosmetics, kitchen ware, drug delivery, and agriculture require more studies on their safety levels. To care about the consumers, customers, patients, and their environment safety. They recommend more studies to be done on their safety, and they recommend a scientific research and evaluation group to control the experiment results [1,3,35,34,16].

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*Correspondence to

Dr. Marjan Assefi

University of North Carolina at Greensboro

North Carolina

USA

Email: m_assefi@uncg.edu