

# Short Review



## A Review of Toxicity of Some Conventional Nanomaterials

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### Abstract

Increased production and use of nanomaterials has led to an ever growing exposure of living organisms to these substances. Limited knowledge about possible toxicity of nanomaterials and their potential to harm living creatures is becoming a serious concern. To address this problem, there is a need for development of diagnostic methods enabling effective determination of potential toxicity of nanomaterials. On the other hand, developing appropriate test methods are contingent on identifying the underlying cellular mechanisms of nanomaterial toxicity. This study reviews toxicity of some of the most widely used nanomaterials. According to the literature, Iron oxide nanoparticles can augment rate of cell death through oxidative stress and lipid peroxidation. Exposure to zinc oxide, gold and silver nanoparticles can result in cell death via mitochondrial dysfunction, expression of abnormal protein in cells, and altering the patterns of gene expression, respectively. Likewise, carbon nanotubes can lead to an increased rate of cell death through the reduction of membrane fluidity, thereby destroying cell membrane. Our literature review identified a lower toxic effect for nanotubes as compared with other nano-structures. Regarding the evident high toxicity of nanomaterials, caution must be exercised in irregular production and use of these substances in the industry. In addition, from the health and environmental standpoints, carbon nanotubes are the preferable nano-structures for development of nanotechnologies regarding their lower toxicity in comparison with other nanomaterials.

**Keywords:** Nano-materials, Nanoparticles, Toxicity, Cell Mortality

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## Introduction

Nanomaterials (NMs) are usually classified into four structural categories including Tube NMs, Rod NMs, Wire NMs and Ballshaped (Spheres) NMs. In another category nanomaterials are classified into five categories of Metal NMs, Metal oxide NMs, Quantum dot NMs, Fullerenes NMs and Fibrous NMs (Aguilar 2013. Sahoo et al., 2007; Singhet al., 2009).

Nanomaterials offer significant electrical, thermal, mechanical and visual advantages, which render them promising for commercial, medical and environmental applications. Among the most important commercial contexts of nanomaterials, electronics, computers, food, furniture, and health industries could be mentioned (Jeng and Swanson 2006; Romig et al.; 2007; Singh et al., 2009).

Despite the broad application of NMs, the growing production of nanomaterials has increased the exposure of living organisms to them (Hahn and Pauluhn, 2008; Jia, Li, and Chen, 2005; Jones and Grainger, 2009; Muñoz and Costa 2012). In the present study, the toxicity of several categories of some widely used nanomaterials is reviewed.

## Review

### Toxicity assessment methods

In vitro evaluation of the toxicity of nanomaterial is the most developed approach to investigate the safety of nanomaterials. In vitro studies can be classified into two categories of genomic and cellular toxicity investigations.

### In vitro cytotoxicity evaluation

There are three main methods used in the study of the potential cytotoxicity of nanomaterials (Chen et al., 2011. Huet et al., 2010. Jones and Grainger, 2009):

### Cell viability

- Determination of mitochondrial activity (Colorimetric MTT assay)
- Release of lactate dehydrogenase (LDH) after necrosis
- Annexin V and Propidium iodide (PI) staining for apoptotic and necrotic cells
- Determination of the collisions with lysosome through the neutral red absorption
- Determination of an apoptotic marker (Caspase 3)

### Stress response

In order to determine stress responses, the concentration of ROS should be measured by 2, 7 di chloro-dihydroergotaminedi acetate.

### Inflammatory response

ELISA method is used to assess the production of inflammatory markers. Important inflammatory markers used in mice and human studies include interleukin-8 (IL-8), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6) (Jones and Grainger, 2009, Seaton, Tran, Aitken and Donaldson, 2009).

### Genotoxicity assessments by in vitro models

The most common tests used in evaluating the NMs' genotoxicity include Amest test, Chromosome aberration test, Comet assay, Cytokinesis-blocked, Micronucleus assay, HPRT forward mutation assay, H2AX staining and DNA adduct hydroxyl deoxy guanosine (Jones and Grainger, 2009; Seaton et al., 2009).

### Mechanisms of toxicity

While the application of NMs is already developed, mechanisms of their toxicity are not well understood yet. However, several investigations have shown that the physicochemical characteristics of the NMs can significantly impact their cellular uptake

rate, thereby imposing undesirable physiological effects to the cells. Several risks have been identified for exposure of living organisms to NMs, including cell-environment interactions, fate and transport of NMs, agglomeration and mobility in the permeable medium, accumulation (density) and changes in the redox potential (Melanie et al., 2006, Mélanie et al., 2008).

Evidence shows that NMs leave toxic effects on cells and their genetic content through different mechanisms. A summary of the relevant studies is summarized as following:

#### **Iron oxide Nanoparticles**

The effect of iron oxide NMs has been studied in a series of cells (Ban et al., 2012, Ying and Hwang, 2010). While iron oxide NMs have shown anti-cancer properties, they also have the potential to contribute to the development of cancer regarding their ionic nature. Studies on the spindle cells of connective tissue and pleomorphic cells of the sarcoma connective tissue in mice have proposed the following mechanisms for the cell destruction (Bhasin et al., 2002):

- Increased oxidative stress followed by lipid peroxidation, which can lead to direct damage of DNA and proteins.
- Excessive availability of iron pool in the cell, which can lead to dysfunction of cell.
- Increased level of hydroxyl radicals via the Fenton reaction (Bhasin et al., 2002).

#### **Zinc oxide Nanoparticle**

Several studies are conducted on the cytotoxic effects of NPs, especially on lung epithelial cells (Chang et al., 2011). The most important mechanism of NP-related cancer induction has been identified to be increased oxidative stress, thereby damage of macromolecules essential to the cells. On the other hand, while zinc oxide nanoparticles have shown advantageous properties in treatment of human colon cancer, their use in medical applications can lead to the following undesirable effects (Guo et al.,

2013):

- Decrease in mitochondrial potential
- Increased production of superoxide
- Increased markers of apoptosis
- Cell death due to mitochondrial dysfunction (Henget al., 2010, Mooset al., 2010).

#### **Gold Nanoparticle**

Study on human lung embryonic fibroblast cells, has identified important adverse effects for exposure to gold particles with the following mechanisms (Chuanget al., 2010, Soenen et al., 2012):

- Unspecific interactions between nitrogen bases of oligonucleotides
- Disruption of the hydrogen bonds formed between oligonucleotides (Liet al., 2007)

#### **Silver Nanoparticle**

Although antibacterial and antifungal properties of silver nanoparticles have found interesting medical applications, evidence indicates toxic effects for these NPs on stem cells and embryonic fibroblasts of rats (Ahamed et al., 2010, Grosset al., 2013). Literature suggests the following mechanisms for the adverse effects of silver nanoparticles on the cells:

- Increased expression of p53 protein and phosphor-H2AX
- Decreased cell viability with respect to the time
- Lack of toxicity or changes in the production of glutathione
- Changes in the patterns of gene expression, in particular apoptotic and inflammatory genes (Ahamed et al., 2008).

#### **Cobalt Nanoparticle**

A study on the effects of Cobalt NPs on human peripheral blood leukocytes has identified the following mechanisms to be responsible for their toxicity of on cells (Colognato et al., 2008):

- An increase in DNA strand breakage at different dose levels of nanoparticle
- An extensive production of superoxide and hydroxyl radicals
- Increased percentage of comet tail and cytotoxicity
- Disruption in repairing DNA-binding proteins (enzyme), due to competition with magnesium(Colognato et al., 2008).

### Carbon Nanotubes

Use of carbon nanotubes (CNTs) has become popular in medicine regarding their antibacterial, antifungal and anticancer activities(Ji et al., 2010, Yang et al., 2011,Zare-Zardini et al., 2012, Zare-Zardini et al.,2013).Carbon nanotubes are also useful in development of novel drug delivery systems (DD system) (Chowdhury 2011, Elhissiet al., 2012, Prakash et al., 2011). Similar to other nanomaterials these compounds have the potential to leave a series of cell-specific toxic effects as well(Ghoshet al., 2011. Kayat et al., 2011. Zhao and Liu, 2012).It is evident that CNTs, in particular single-walled CNTs, can destroy the cells by reducing membrane fluidity or specific interactions with genetic material(Chen et al., 2011, Davoren et al., 2007). While some useful biological effects of carbon nanotubes has been identified to be lower than other nanostructures they have reported the lowest toxic effects among almost all other nanomaterials (Cheng et al., 2011). It has been shown that implementing of functional groups on the surface of CNTs can improve their biological activities (Amiri et al., 2012,Zare-Zardini et al., 2012, Zare-Zardini et al., 2013).

### Conclusion

The high toxicity of nanomaterials calls for caution in irregular production or use of them in the industry. Alongside with application of nanomaterial in industry and medicine, significant emphasis should be given to

the waste management of nanomaterials in the environment. Our review of literature on toxicological aspects of nanomaterials identified carbon nanotubes to be the safest nanostructures from toxicological aspects. Therefore, from the environmental standpoint carbon nanotubes are the preferable nanomaterials for future nanotechnology developments. Although biomedical application of carbon nanotubes is limited as compared with other nano-scale materials, this drawback can be alleviated by their conjugation with biological compounds including amino acids.

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