Toxicity of carbon nanotubes – Some recent studies

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Carbon nanotubes (CNTs) have recently gained popularity in the burgeoning field of nanotechnology. CNTs possess high aspect ratio with nano diameter and can be classified into two types: (i) single-walled carbon nanotubes (SWCNTs; Figure 1) consisting of a single layer of graphene sheet (a single atomic layer of graphite) seamlessly rolled into a cylindrical tube and (ii) multi-walled carbon nanotubes (MWCNTs; Figure 1) comprising two or more layers of concentric cylinders with a separation of about 0.34 nm between the adjacent layers.

CNTs exhibit unique properties like chemical stability, extremely high mechanical strength and stiffness while being light and with excellent ability to conduct electricity and heat. Because of their strength and light weight, products containing CNTs such as tennis rackets, bicycle handlebars and baseball bats have entered the market. Electronic properties of CNTs have made them as candidates for flat panel displays in TVs, batteries, etc. As the use of CNTs in engineered materials has been rapidly increasing in commercial applications, the production of CNTs will exacerbate the possible exposure of individuals to them. The public is also anxious to know about the potential health hazards of CNTs.

A superficial resemblance between CNTs and asbestos fibres, has motivated several groups in recent years to study the potential health risk of CNT exposure. Lung is the target of asbestos fibres when people are exposed to them. Inhalation of asbestos fibre is known to induce lung cancer, scarring of the lungs (asbestosis) and malignant mesothelioma. The result of a recent study of CNTs introduced into the abdominal cavity of mice has raised considerable public concern. The authors selected four samples of commercial MWCNTs, such that two of them were straight fibres longer than 20 μm and the other two consisted of low aspect ratio (i.e. shorter length) tangled aggregates. Samples were prepared for in vivo use by ultrasonication using a sterile 0.5% BSA/saline solution. Next, 50 μg dose of each of the four materials was administered by injection into the peritoneal (abdominal) cavity of mice and washed out 24 h or seven days later. In general, the response to pathogenic particles by the mesothelium, the cell layer that covers the chest (pleural) peritoneal cavities, is inflammation. This can be assessed by increased levels of polymorphonuclear leukocyte (PMN, white blood cells), protein exudation and the formation of scar-like structures (lesions) called granulomas. MWCNT samples with high aspect ratio caused significant PMN or protein exudation and granulomas on the peritoneal side of the diaphragm. However, the mesothelial lining on the pleural side of the diaphragm was normal in each case. Short CNTs do not mimic the behaviour of long CNTs. The authors state ‘our study did not address whether the mice exposed to long CNTs that developed inflammatory and granulomatous changes would go on to develop mesotheliomas’. Earlier, Warheit observed that intratracheal instillation of SWCNTs in the lungs of rats resulted in the formation of lung granuloma. This study also indicated that 5 mg/kg dose exposure to SWCNTs produced mortality in ~15% of instilled rats within 24 h post-instillation due to the enhanced blockage of the large airways. That SWCNTs can induce pulmonary injury in mice has also been recently confirmed by Chou et al. They have also demonstrated that the intratracheal instillation of 0.5 mg of SWCNTs into male ICR mice (8-weeks-old) induced alveolar macrophage activation, various chronic inflammatory responses and severe pulmonary granuloma formation.

At this juncture, it will be of interest to know the toxicity of single-walled carbon nanohorns (SNHVs), which are aggregates of thousands of graphitic tubules (similar to SWCNTs) having diameters 2–5 nm with a spherical structure of diameter of 50–100 nm (Figure 2). Extensive in vitro and in vivo toxicological assessments of as-grown SNHVs for various exposure pathways, pointed out that SNHVs have low toxicities. This may probably be due to the absence of metal catalyst in the nanohorns. SNHVs are shown to be nonirritant and a non-dermal sensitizer by skin primary and conjunctival irritation tests and skin sensitization tests. The negative mutagenic and dastogenic potentials suggest that SNHVs are not carcinogenic. The intratracheal instillation also revealed that SNHVs barely damaged rat lung tissue for a 90-day test period, although black pigments due to accumulated nanohorns were observed. These studies strongly suggest that as-grown SNHVs have low acute toxicities.

Despite the revelations that the exposure to pristine CNTs is harmful, functionalized (chemical modification) CNTs (f-CNTs) are employed both in the treatment of cancer and as drug-delivery vehicles at the target without any toxic effects.

While biological systems are transparent to 700–1100 nm near-infrared (NIR) light, the strong optical absorbance of SWCNTs in this region has been exploited to destroy cancer cells. SWCNTs

Figure 1. Molecular structure of SWCNT (left) and MWCNT (right).

Figure 2. TEM images of SNHN aggregates prepared in Ar. Scale bar represents 20 nm. Reprinted with permission from Miyawaki et al. Copyright (2008) from American Chemical Society.
are targeted to cancer cells by attaching folic acid to the surface of the nanotubes, as folic acid binds to a folic acid receptor protein found in abundance on the surfaces of many types of cancer cells. Selective ablation of tumour cells can be achieved by functionalization of SWCNTs with a folate moiety, selective internalization of SWCNTs inside cells labelled with folate receptor tumour markers, and exposure to noninvasive NIR, without harming receptor-free normal cells. In another recent study, it has been demonstrated that the specific binding of antibody-coupled CNTs to tumour cells in vitro followed by exposure to NIR resulted in the death of specifically targeted cells by the heat emitted by CNTs. Liu et al. attached a cancer chemotherapy drug doxorubicin (DOX) molecule onto prefuntionalized nanotubes, for in vivo cancer therapy. They demonstrated that DOX-loaded f-SWCNTs induced significant U87 cancer cell death and cell apoptosis, similar to free DOX. The main advantage of using f-SWCNT as a drug carrier compared to free drug is the potential to target delivery for selective destruction of certain types of cells, reducing the toxicity to non-targeted cells. In vitro studies to assess the cytotoxic capability of the MWCNT-DOX supramolecular assemblies using the MCF7 human breast cancer cells showed a statistically significant enhancement in the cytotoxic capability of the MWCNT-DOX complex compared to that of DOX alone.

It has been established that covalent functionalization, irrespective of functional group and chemistry, offers significant improvements in the toxicity profile of CNT, in vitro and in vivo. f-CNTs are employed in several investigations because of their ready solubility in water and other solvents. Dumortier et al. have addressed the question of impact of f-CNTs on cells of the immune system and demonstrated that f-CNTs are uptaken by B and T lymphocytes as well as macrophages in vitro, without affecting cell viability.

Imaging studies of intravenously administered MWCNTs functionalized with diethylentriaminopentaacetic dianhydride (DTPA–MWCNT) and radio-labelled with indium-111 showed that nanotubes enter the systemic blood circulation and within 5 min begin to permeate through the renal glomerular filtration system into the bladder. Urinary excretion of DTPA–MWCNT was confirmed at 24 h post-administration. In another recent study employing intrinsic Raman spectroscopic signatures of SWCNTs, Liu et al. measured the blood circulation of intravenously injected f-SWCNTs and detected SWCNTs in various organs and tissues of mice ex vivo over a period of three months. Raman spectral studies revealed SWCNT in the intestine, face and kidney, and bladder of mice, suggesting excretion and clearance of SWCNTs from mice via the biliary and renal pathways. This study also revealed the absence of any toxic side effect of SWCNTs to mice in necropsy, histology and blood chemistry measurements. Schipper et al. also came to similar conclusions when f-SWCNTs were injected into the bloodstream of mice. Though these studies indicate the potential toxicity with pristine CNTs, SWNHs containing no metal impurity are non-toxic. Any metal impurity that is present in CNTs would have been removed during the process of functionalization and probably due to this f-CNTs are also found to be safe. It would also be crucial to test metal-free SWCNTs. Unfortunately, such samples can only be prepared by rigorous purification procedures and studies with metal-free CNTs are needed to convincingly confirm their toxic effects. However, Poland et al. suggest the need for further studies and great caution be exercised before introducing products containing CNTs into the market, if long-term harm is to be avoided.


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Collimated particle beams from pulsars

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Flying 200 times higher than the Hubble space telescope, the Chandra X-ray Observatory has produced some stunning images of the universe. Launched by NASA in 1999, Chandra remains today the most sophisticated X-ray telescope ever built (NASA’s premier X-ray observatory was named in honour of the late Indian American Nobel laureate, Subrahmanyan Chandrasekhar). Images of spectacular cosmic activity obtained by Chandra have enthralled and inspired the public world over.

Amongst the most popular images ever obtained by Chandra are pictures of the Crab pulsar nebula. The pictures (Figure 1) show enormous swirls of tornado-like activity in the region surrounding the pulsar. These images provoked much discussion amongst astronomers. Deshpande and Radhakrishnan have attempted to explain the phenomenon causing these features. In fact, the X-ray images of Crab pulsar nebula further substantiated...