

Combating Nanotoxicity: A Long Way To Go!

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Humans are exposed to engineered nanomaterials through different routes like inhalation, ingestion, dermal and ocular [1]. Since a couple of decades it is known that the cell vision i.e., the interactions between nanomaterials and cells of animals, humans and the plants are remarkably complex. The physiochemical properties and the interaction with biomolecules and cell surface determine the toxicity of nanoparticles to the biological system. Carbon and metallic nanomaterials are among the most widely used types of engineered nanomaterials. Among carbon nanomaterials, the production of Carbon Nanotubes (CNTs) is alarmingly increasing [2]. CNTs, discovered by Sumio Iijima in 1991 are cylindrical molecules composed solely of carbon atoms typically ranging in diameter from few nm up to 50 nm [3]. Owing to their promising properties (structural, mechanical, and electronic) CNTs dominates in the field of materials science and electronics including conductive and high-strength composites, sensors, field emission displays and radiation sources, semiconductor devices and nanosize probes [4]. Moreover, CNTs due to their high drug loading efficiency play a main role as drug carrier. In addition, functionalized CNTs were used in cancer therapy, in tissue engineering, as implants, as biosensors, and as a bone growth support material facilitating healing of fractures [5]. As a result, the global production of CNTs is rising considerably

and it exceeds several thousand tons per year as per recent reports [6]. The excess production of CNT in turn increases the exposure of the environment including humans to CNTs. Therefore, CNT toxicity becomes a critical issue to be addressed before their further applications in multiple fields. In this situation it is necessary for the scientific community as well as the general public to get awareness about the toxicity of CNTs and other related nanoparticles.

Recent studies have demonstrated the *in vitro* and *in vivo* toxicity of CNTs. The penetration of CNTs into the cellular membrane of rat macrophages leads to the alteration of physiology and cellular function of macrophages. A dose-dependent increase in the intracellular reactive oxygen species and a decrease in the mitochondrial membrane potential was observed in both rat macrophages (NR8383) and human A549 lung cell lines after treatment with commercial CNTs [7]. Moreover, the toxicity of CNTs in human MSTO-211H cell lines was due to different degree of cellular agglomeration. Cytotoxic effects of CNTs dispersion in surfactant was less than those of asbestos, but the effects of agglomerated CNTs in string form (more voluminous, more rigid and more solid) showed greater cytotoxicity than asbestos [8].

Recent reports on CNT toxicity studies confirmed its toxic potential due to the fibrous nature [9]. Intra-tracheal administration of CNTs showed pulmonary inflammation in mice and rats, characterized by alterations in cellularity and enzyme activities of Broncho-Alveolar Lavage Fluid (BALF) and microscopic findings like infiltration of macrophage, granulomas, and fibrosis were observed after intra-tracheal administration of SWCNTs or MWCNTs [10-12]. Previous

studies revealed the variation in polymorphonuclear neutrophils, macrophages, lymphocytes and expression of inflammatory cytokines in BALF of rats exposed to CNTs [13, 14].

Even though CNTs produce severe biological changes, the production and usage is inevitable due to their auspicious applications. Hence there is a need i) to explore the toxicity mechanism and ii) to find out a remedy for the CNT-induced toxicity. Literature survey reveals that the toxic potential of CNTs is mainly due to its retention in the tissue and subsequent free radical (ROS) generation. These findings suggest that the toxicity of CNTs can be reduced using a compound with anti-inflammatory and antioxidant activity. Interestingly, other nanomaterials like metals, metal oxides and inorganic nanoparticles were also reported to induce toxicity via oxidative stress and inflammation [15, 16]. Polyphenols are the best natural candidates with anti-oxidant and anti-inflammatory properties, which can be used to reduce the inflammation and oxidative stress without side effects [17, 18]. With this view, we are working towards the development of an antidote for CNTs-induced toxicity using naturally occurring polyphenols. Also, the research community and the general public should get awareness about the nanotoxicology in terms of mechanism of action, biocompatibility, biodegradability and biological fate of any target nanomaterial and move towards the development of proper tool to ameliorate the toxicity. All these will be possible on exploring the molecular mechanism along with a systematic understanding on the method of combating the toxicity. Obviously, there is a long way to go ahead and fill the gap!

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