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Characterization and Functionalization of Carbon Nanotubes(CNTs) Intended for Bioapplications

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ABSTRACT

A carbon nanotube is a tube-shaped material, made of carbon ,having a diameter measuring on the nanometer scale. A nanometer is one-billionth of a meter, or about one ten-thousandth of the thickness of a human hair. Carbon nanotubes have many structures differing in length, thickness, and in the type of helicity and number of layers. Although they are formed from essentially the same graphite sheet, their electrical characteristics differ depending on these variations, acting either as metals or as semiconductors.

Since their discovery in 1991, carbon nanotubes have generated huge activity in most areas of science and engineering due to their unprecedented physical and chemical properties. No previous material has displayed the combination of superlative mechanical, thermal and electronic properties attributed to them; these properties make nanotubes ideal, not only for a wide range of applications but as a test bed for fundamental science.

The discovery of carbon nanotubes has the potential of revolutionizing biomedical research as they can show superior performance because of their impressive structural, mechanical, and electronic properties, such as small size and mass, high strength, higher electrical and thermal conductivity, etc.

Recently, carbon nanostructures are proposed as promising candidates to develop neural scaffolds. There are different types of carbon nanostructures. The three most popular ones are single-walled carbon nanotubes, multiwalled carbon nanotubes, and carbon nanofibers.

Carbon nanostructures have excellent mechanical, electrical, and conduction properties, and have nanostructure similar to neuritis. Hence, they have been utilized to improve neural activities and guide severed ends in a nerve through each other.

The tubular, vesicle-like character of carbon nanotubes has been used for drug containment and focused drug delivery in clinical trials (e.g., for the dispersal of cancer drugs for localized tumor treatment). Consequently, carbon nanotubes are also amenable for nano-sized platforms, whereby functional groups that would normally not coincide (e.g., like antibodies, polyethylene glycol, and cancer medication) can be brought together. Functionalization, through the attachment of different functional groups, has also made it possible to create nanotube-based moieties with complex behavior (e.g., a drug-delivery vehicle that can traverse the plasma membrane, and release the drug in a target organelle).

Since the discovery of carbon nanotubes composed of graphite, there has been a remarkable increase in determining the possibility of using it for treating disease and promoting tissue regeneration.For example, as described, Mattson et al. provided the first evidence that multi-walled carbon nanotube can be used to support neuronal cell attachment and growth. Furthermore, studies have shown that carbon nanotube chemically functionalized with various bioactive molecules can improve neural regeneration activity including neurite branching, outgrowth and attachment of growth cones.Matsumoto et al. demonstrated that multiwalled carbon nanotube can regulate and promote neurite out-growth when covalently bonded with neurotrophin .

Using carbon nanotubes-mediated gene delivery and treatment for in vivo studies is still in its infancy. All the reported in vivo studies were administrated by local intratumoral injection. Targeted delivery of DNA / siRNA to specific disease sites can greatly enhance therapeutic efficiency and eliminate side effects, while there is no such effort found in literature for in vivo targeted delivery of DNA/siPvNA medicated by carbon nanotubes. Systematic

studies on the stability, blood circulation, and pharmacokinetics of DNA-carbon nanotubes conjugates or complexes are urgently needed. In vivo delivery of chemical anticancer drugs by carbon nanotubes, and targeted delivery of carbon nanotubes alone to tumor sites have been reported. The studies of pharmacokinetics, blood circulation, and biodistribution of carbon nanotubes/drug conjugations have demonstrated the powerful detection and imaging capabilities of carbon nanotubes.

The medical applications of carbon nanotubes are determined by the following properties: biocompatibility in contact with blood, bone, cartilage and soft tissues; biofunctionality understood as the ability of taking over certain functions of tissues by a mutual adjustment of implants and tissues properties.

Carbon nanotube (CNT) materials display superior properties in electric current carrying capacity, thermal conductivity, and thermal stability. Due to the unique CNT structure with high-aspect ratio, CNT may show unusual toxicity and complicate its safe use in a target tissue. To test nanotoxicity of CNT, we describe a set of protocols of prior knowledgebased physical and chemical characteristics to develop 3-dimensional in vitro models of the intact skin, and a 3D in vitro model of the human airway using a co-culture of normal human bronchial epithelial cells and normal human fibroblasts. The human airway 3 D model served as a tool of health risk assessment of CNTs on the human respiratory systems. To test functionality at different CNT concentrations in a 3D model, physical characteristics of multiwalled CNTs and production of nitric oxide (NO) served as cell viability and inflammatory marker; mitochondrial activity (MTT assay) served as the cytotoxic response of the epithelial cell layers; transepithelial electrical resistance (TER) measured nanotoxicity in the changes in airway physiological function. Cytoxicity and inflammatory responses of CNTs were dependent on different size, mass, shape, and functionality of CNTs as viable in vivo tests were conducted to evaluate the toxicity of engineered CNTs. We monitored the transport across skin, and the physiological perturbation of transepithelial electrical resistance (TER) during the exposure of different concentrations of CNTs. The mechanisms of CNTs' toxicity are closely related to their structure, functional group, and surface charge on the molecule. We established the nanoscale toxicity fullerenes of CNTs.

Keywords: Carbon Nanotubes, Nanotoxicity, silver nanoparticles,fullerene,Cytotoxicity ,Surface Functionalization ,Metal Nanoparticles , covalent functionalization, Surface amidation, Zwitterionic linkages *Microwave assisted solubilization,* epoxide ring-opening polymerization

1. INTRODUCTION

Nanomaterials have emerged as potential tools in almost every field from space to the environment and from health to robotics.With the increasing demand for nanomaterials it is necessary to evaluate toxicity carefully before accepting new nanomaterial in wider bioapplications. In this chapter, technical developments on carbon nanotubes are described with an account of their historical development, experimental models and potential applications.The first section describes the carbon nanotubes-based nanocomposites. This chapter is divided in subsections on the toxic nature of CNT, model CNT-metal and collagen composites, structure of carbon nanotube materials, physical principles of CNT-biosurface interaction, nanoindentation testing and the mechanism of inflammation in epithelial cells induced by CNT with an account of biophysical experiments on CNT exposed to mesenchymal cells, 3D human lung prototype, skin tissues and prototype scaffold nanomaterials. A possibility of CNT as a safer drug delivery system is explored that describes the future of possible bioapplications of carbon nanotubes and nanocomposites.

Carbon nanotubes were discovered in 1991 and their use expanded to make conductive and high-strength composites, energy storage devices, sensors and actuators, field emission displays, nano-scale semiconductor devices, probes with unique physical, mechanical,electrical, and thermal properties. Initially CNTs in powder form were considered to be cytotoxic and DNA mutagenic with risk of inhalation-induced toxicity to workers due to direct skin contact. Several studies recently indicated possible toxicity of CNTs based on the facts that: 1) CNTs and fullerenes have produced toxic effects on biological systems ; 2) CNTs can translocate to bloodstream ; 3) CNTs can