



Carbon Nanotube: A Drug Delivery Platform in Neurological Disorder

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Abstract

Carbon nanotubes (CNTs) possess distinguished characteristics including good electrical, penetration capability across cell layer barrier, high payload capacity, good thermal conductivity, large surface area for easy surface modification which makes them worthy nanocarrier for drug delivery in tumor tissues and brain.

Keywords: Carbon Nanotubes (CNTs); Drug Delivery; Single-Walled or Multiwalled Carbon Nanotubes (SWNTs or MWNTs)

Introduction

Firstly the term carbon nanotubes (CNTs) were coined by Iijima in early on nineteen century as needle-like tubes. It comprised of several layers of graphite sheets. It can be further subdivided into single-walled or multiwalled carbon nanotubes (SWNTs or MWNTs), made of one or several layers of graphene. CNTs have potential application in industry due to their good electronic, better mechanical strength and thermal characteristics. Along with it possesses large surface area, light weight render them ideal for neuro-engineering application. The ultrahigh high surface area is highly desirable for chemical surface modification of CNTs with distinguished therapeutic moiety. Multifunctional CNTs showed high potency in targeting of specific cells, tissues, and imaging as well. The hollow tube like structure has the added advantages in drug delivery application.

The drugs can be encapsulated in their inner hollow core, while other molecules can be attached to the external surfaces to render them dispersible and biocompatible for targeting purposes. Currently, various therapeutic agents, such as anticancer drugs, central nervous system disorders therapy drugs, anti-inflammatory and anti-microbials drugs, have been successfully delivered with CNTs utilizing versatile strategies, demonstrating superior efficiency and minimized toxicity to cells or tissues.

Generally, the major obstacle in the path of drug delivery via CNTs is its hydrophobicity which gets to undesirable for biological system. However, such issues could be sorted out by surface functionalization phenomena, which makes them biocompatible, biodegradable and target oriented nanocarrier in biological system. The surface modification approach based on chemical reaction such as

conjugation, oxidation, coating with hydrophilic or biological molecules are promptly adopted in targeted drug delivery system.

Thus, Functionalized carbon nanotube (F-CNTs) are safe in nanodrug targeting with reduced or no toxicity and indeed, an excellent nano-biomaterial for application in nanomedicine. Besides this it translates promise opportunity as nanocarrier for delivery of therapeutics or DNA, mRNA, gene, antibodies, protein, and peptides both *in vitro* and *in vivo*.

Role of carbon nanotube in CNS disorder

F-CNTs enter cells by through receptor mediated endocytosis, and macropinocytosis process. However, the needle like also assisted in cell membrane penetration of the target region. The drug delivery to CNS is challenging may be attributed to blood brain barrier. Rather several studies documented the successful delivery of F-CNTs in brain.

Shityakov and associate assessed the active transport of FITC-labeled MWNTs across immortalized murine microvascular cEND cells using the Transwell® device (Corning Inc., NY, USA). The accumulation and distribution of FITCMWNTs in the target cells imaged by fluorescence microscopy. The intracellular distribution of formulation was presented in 3D structure applying dynamics simulation modeling software. The result revealed that FITC-MWNT aggregates were centralized over cell surface with prominently dispersed within the cells or nearby by the cell membrane

Another study demonstrated that the penetration characteristics of amino-functionalized MWNTs *in vitro* BBB model composed of brain endothelial cells, and primary rat astrocytes. The transmission electron study clearly indicated intracellular uptake

of amino-functionalized MWNTs. Further cell uptake was confirmed by γ -scintigraphy study. Several research works stated the significant application F-CNTs in neurological disorder including glioblastoma, stroke, Alzheimer disease and others. The first study of F-CNTs credited to Yang, et al. for brain targeting where SWNTs were given orally to mice daily for 10 days. Electron microscopy detected SWNTs in absorptive cells, neurons and macrophages but were investigated their traces in other organs viz., liver, heart and brain. SWNTs were able to deliver acetylcholine, contributing in melioration of the learning and memory in induced Alzheimer disease mouse model.

The stereotactic injection in brain although precise and direct access, however, invasive nature renders to switch over systemic route to alleviate clinical translation of functionalized carbon nanotubes. Based on this stereotactic delivery Zhao, et al. utilized F-CNT for the delivery of immunoadjuvant CpG, preceding for anti-glioma effect. F-CNTs conjugated to CpG oligonucleotides were fluorescently labeled with Cy5.5 and were injected into brain for the treatment of glioma. Results indicated enhanced the uptake of CpG oligonucleotides tumor cells and elevated levels of proinflammatory cytokines and thus lower down tumor growth. Despite these it is highly applicable in photothermal or photoacoustic therapy in cancer cells [1-10].

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