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Advantages and Limitations of CNT-Polymer Composites in Medicine and Dentistry

Neeraja Turagam and Durga Prasad Mudrakola

Abstract

The past two decades have seen great technological advancements in the fields of optics, biochemistry, and physics allowing the fundamentals of our own human biology to be understood and controlled. At the forefront of this great understanding lies a tiny structure made of carbon called nanotube. Many studies have demonstrated that peptides, medicinal molecules, and nucleic acids, when bonded to carbon nanotubes, are delivered considerably more safely and effectively into cells than by traditional methods. Two types of carbon nanotubes have been researched for use in biomedical applications. The first is SWNT, single walled and second MWNT, multi-walled nanotube. Shell structures can be used for delivering anticancer drugs to tumors in various parts of the human body. In dentistry, the carbon nanotubes along with polymers prevent shrinkage and dimensional changes in resin and help in better fit at bone implant interface as well as in delivering well-fitting dentures. Evolution of gene therapy, cancer treatments, and innovative new answers for life-threatening diseases on the horizon, the science of nanomedicine has become an ever growing field that has an incredible ability to bypass barriers previously thought unavoidable.

Keywords: MWNT, SWNT, peptides, nanodentistry, nanomedicine, nanocomposites

1. Introduction

Carbon is an important element to various sciences, from physics, chemistry, and materials science to life science, but conventional carbon formulation in the micron scale may not be the optimal implant material [1]. Then the nanomaterial's such as the carbon nanotubes (CNTs), with unique electrical, mechanical, and surface properties, have captured the attention and aroused the interest of many scientists, since CNTs were discovered by Iijima in 1991 and up to now appear well suited as a biomaterial [2–7]. CNTs are substances with cylindrical structure of about 1 nm diameter and 1–10 m length, consisting of only carbon atoms. In general, CNTs contain single-wall carbon nanotubes (SWCNTs) and multiwall carbon nanotubes (MWCNTs).

SWCNTs are viewed microscopically as rolled-up structures of single sheets of graphene and individual carbon structures, approximately 1 nm in diameter and up to a millimeter or more in length, and MWCNTs are similar to hollow graphite fibers, except that they have a much higher degree of structural perfection, which are having a diameter of 10–200 nm [8–11]. Lu and Tsai investigated the load transfer efficiency in double-walled carbon nanotubes (DWCNTs, a hollow cylindrical structure, which contains two concentric graphene layers) using multiscale

finite element modeling, and the results showed that increasing of CNTs' length can effectively improve the load transfer efficiency in the outermost layers, while the DWCNTs with incremental covalent exhibit increasing load transfer efficiency in the inner layer. Besides, compared with single walled, the double walled nanotubes have decreased potential of load transfer efficiency [12].

Several studies proved increase mechanical properties of CNTs-based reinforced composites by the adding of carbon nanotubes (**Figure 1**). CNTs reinforced composites have been investigated thoroughly for numerous aspects of life and biomedical applications. The review introduced fabrication of CNTs reinforced composites, CNTs reinforced with ceramic and metal matrix composites their biocompatibility (in vivo), cell experiments (in vitro) and mechanical properties.

1.1 Early thinking

The late Nobel prize winning physicist Richard P. Feynman in 1959 speculated the potential of nano size devices as early as 1959. In his historic lecture in 1959, he concluded saying, "this is a development which I think cannot be avoided" [13].

1.2 Nanomaterials in dentistry

Inspite of the better understanding and use of chemistry and materials, recent developments in physical properties, no material has been found to be ideal for any kind of dental application [14]. Silver amalgam, as a dental restorative material has been used for more than a century, but for the toxicity and esthetics which has been of major concern for many many years [15–20]. In contrast the composite restorative materials have very good esthetics, and are very technique sensitive [21]. Nature has arranged complex biominerals in the best possible way from the micro to the nano-scale and no one can yet combine biological and physical properties to get ideal structures [22].

1.3 Access to nanodentistry

The practical applications in dentistry has various approaches [23, 24]. Broadly, two key approaches in nanotechnology are present for creating smaller or better materials. One being the top-down and the other is bottom-up. Top-down approach is based on solid-state processing of materials. The "top-down" approaches are used to fabricate functional structures at micro and nanoscales such as chemical vapor

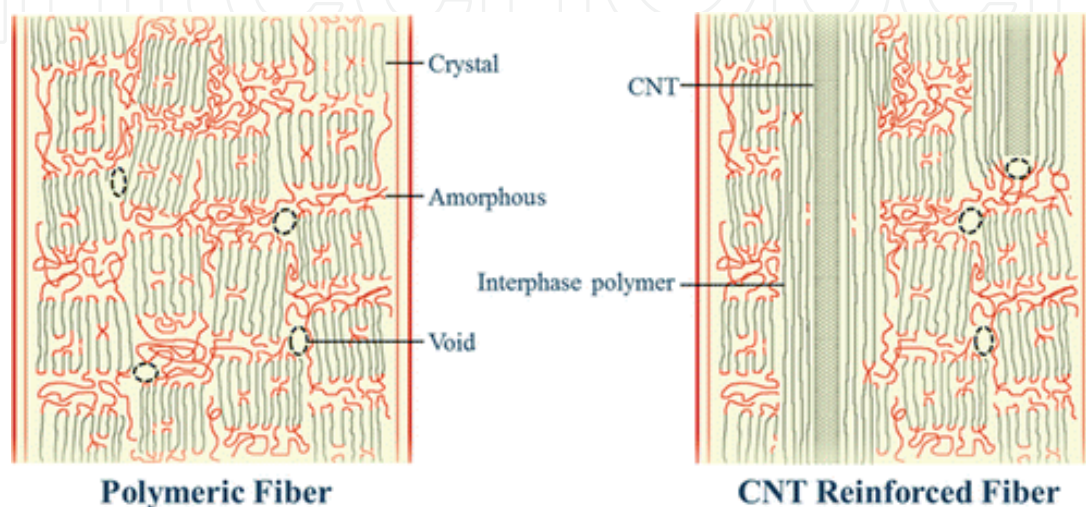


Figure 1.
CNTs-based reinforced composites

deposition (CVD), monolithic processing, wet and plasma etching [25]. These approaches are used in electronics industry as well as for coatings of medical implants and stent using chemical vapour deposition technology for increased blood flow [26].

The “bottom-up” approach entangles the fabrication of materials via edifice up particles by harvesting atomic elements. Bottom-up processing is based on extremely organized chemical synthesis and growth of materials [27] which occurs in repairing of cells, tissues or organ systems and protein synthesis as well.

Nanodentistry will make possible the maintenance of near-perfect oral health through the use of nanomaterials, biotechnology, including tissue engineering, and nanorobotics. Oral health and disease trends may change the focus on specific diagnostic and treatment modalities [28, 29].

1.3.1 Hypersensitivity cure

Dentin hypersensitivity is due to changes in pressure transmitted hydrodynamically to the pulp. Hence, teeth having hypersensitivity have eight times increased surface density of dentinal tubules and tubules with diameters twice as large than nonsensitive teeth. Dental nanorobots could precisely and selectively obstruct selected tubules in minutes using native biological materials.

1.3.2 Local anesthesia

A colloidal suspension with millions of active analgesic micron-size dental robots will be introduced in the gums of the patient. On coming in contact with the surface of tooth or mucosa, the ambulating nanorobots enter the pulp via the gingival sulcus, lamina propria, and dentinal tubules. Once introduced in the pulp, the dentist commands analgesic dental robots to stop all sensitivity and reactions in any specific tooth that needs treatment. The dentist orders the nanorobots to restore all sensation, after finishing all the oral treatments to relinquish control of nerve traffic, and to egress from the tooth by similar pathways used for ingress.

1.3.3 Orthodontic treatment

Orthodontic nanorobots could directly stimulate and manipulate the periodontal tissues, leading to rapid and painless tooth straightening, rotating, and vertical repositioning in few hours. Nanotechnology derived orthodontic wire is a new and advanced stainless steel wire which has the following properties (a) ultra-high strength (b) good deformability (c) corrosion resistance (d) good surface finish.

1.3.4 Nanoimpression

The introduction of Nanofillers into Polyvinylsiloxanes yields a siloxane impression material with properties superior to conventional impression materials.

Advantages (a) Better flow (b) Improved hydrophilic properties leading to fewer voids at margin and better model pouring (c) Enhanced detail precision.

- **Nanosolutions:** These are unique, dispersible nanoparticles with superior properties that can be produced from nanosolutions. This can be made use of dentin bonding agents (Adper™) because of better dentin bond strength and better performance.
- **Nanorobotic dentifrice [dentifrobots]:** subocclusal nanorobotic dentifrice present in tooth paste or mouthwash could monitor all supragingival and subgingival

surfaces, metabolizing the organic matter which is trapped into odorless and harmless vapors required for continuous calculus debridement. These invisibly small dentifrobots [1–10 μm], crawling at 1–10 $\mu\text{m/s}$ are purely mechanical devices which are inexpensive. They would safely get deactivated themselves when swallowed and would be programmed with strict occlusal avoidance protocol.

- Dental durability and cosmetics: durability of the tooth along with aesthetics may be improved by replacing layers of upper enamel with pure sapphire and diamond embedded carbon nanotubes as they are more fracture resistant as nanostructured composites.
- Photosensitizers and carriers: quantum dots can be used as photosensitizers and carriers as they are bound to bind to the antibody present on the surface of the target cell. They can give rise to reactive oxygen species and when stimulated by UV light and thus will be lethal to the target cell.
- Diagnosis of oral cancer.

2. Nanoelectromechanical systems (NEMS)

They transform biochemical to electrical signals. NEMS biosensors exhibit specificity and sensitivity to detect the presence of abnormal cells at molecular level.

Oral fluid nanosensor test (OFNASET) used for multiplex detection of salivary biomarkers for oral cancer.

Optical Nano Biosensor - The nanobiosensor is a unique fiberoptics-based tool which allows the minimally invasive analysis of intracellular components (Cytochrome C1).

2.1 Treatment of oral cancer

Nanotechnology in field of cancer therapeutics has offered highly specific tools in the form of multifunctional Dendrimers. Nanoshells are miniscule beads with metallic outer layers designed to produce intense heat by absorbing specific wavelengths of radiations that can be used for selective destruction of cancer cells leaving aside intact, adjacent normal cell [30].

2.2 Nanocomposites

Nanocomposites are produced by homogeneously distributed nanoparticles in resins or coatings. Nanofillers used includes an aluminosilicate powder with mean particle size of 80 nm and a 1:4 M ratio of alumina to silica and a refractive index of 1.508 [31].

2.3 Advantages

- Increased hardness.
- Increased flexural strength, translucency.
- 50% reduction in filling shrinkage.
- excellent handling properties.

2.4 Challenges faced by nanodentistry

- Precise positioning and assembly of molecular scale virus in humans [31].
- Economical nanorobot mass production technique.
- Biocompatibility.
- Simultaneous coordination of activities of large numbers of independent micron-scale robots.
- Social issues of public acceptance, ethics, regulation.

2.5 Nanomaterials used for dental tissue regeneration

Pulp stem cells are purified in the lab and grown in sheets on scaffolds composed of nanofibers of biodegradable collagen type I or fibronectin used for pulp regeneration [32, 33]. Self-assembling polypeptide hydrogels have been used for pulp tissue regeneration with the formation of a nanofiber mesh for supporting the growing cells [34]. Puramatrix proven to enhance cell growth contains amino acids repeats of alanine, arginine and aspartate [35]. Natural silk based nanomaterials are being used for various tissue regeneration applications [36]. Injectable self-assembly collagen I scaffold containing exfoliated teeth stem cells led to the formation of pulp like tissue and functional odontoblasts [37]. Collagen type I is found in the form of nanofibers in dentin (~80–90% of organic matrix) and bone with abundant fibrous protein [38]. Odontogenic differentiation and mineralization was promoted in the presence of type I collagen scaffolds [39, 40].

2.6 Nanomedicine

Nanomedicine is the application of nanotechnology (the engineering of tiny machines) to the prevention and treatment of disease in the human body. This evolving discipline has the potential to dramatically change medical science.

2.7 Current status of nanomedicine

2.7.1 Diagnostics

Nanorobots are expected to circulate in the vascular system and send out signals when imbalances appear in the circulatory and lymphatic system. To monitor brain activity fixed nanomachines could be inserted in the nervous system of the human body. Latest nanomedical heart trackers are present in the major hospitals to accurately track and treat the heart beat and its downfalls as needed in the body [41]. The present and potential diagnostic uses is large being fullerene-based sensors, imaging (cellular, etc.), monitoring, lab on a chip, nanosensors, scanning probe microscopy, protein microarrays intracellular devices, intracellular biocomputers and intracellular sensors/reporters, endoscopic robots and microscopes.

2.7.2 Protein and peptide delivery

Protein and peptide molecules form the functional units of cells. Their molecular derangements lead to many illnesses. Targeted or controlled delivery of these molecules using nano particles and dendrimers is an emerging field called nano bio pharmaceuticals.

2.7.3 Drugs dispersion and drug delivery

Drug delivery is based on developing nanoscale molecules to improve drug bioavailability. Nanomedicine based tools and devices are being developed for imaging. By the use of nanoparticle contrast agents, images such as ultrasound and magnetic resonance imaging (MRI) have improved distribution and contrast [42]. Triggered response is one way for drug molecules to be used more efficiently. The strength of drug delivery systems is their ability to alter the bio distribution and pharmacokinetics of the drug. Drugs are placed in the body and only activate on encountering a particular signal. For example, a drug with poor solubility will be replaced by a drug delivery system where both hydrophilic and hydrophobic environments exist thus improving its solubility.

2.7.4 Oncology

The small size of nanoparticles enhances their use in oncology. Quantum dots (nanoparticles with quantum confinement properties, such as size-tunable light emission), when used in conjunction with MRI, produces exceptional images of tumor sites [43]. Diagnosis of cancer at early stages can be detected from a few drops of the patient's blood by using sensor test chips containing thousands of nanowires, able to detect proteins and other biomarkers left behind by cancer cells [44]. Prof. Jennifer West has demonstrated the use of 120 nm diameter nanoshells coated with gold to kill cancer tumors in mice. By irradiating the area of the tumor with an infrared laser, which passes through flesh without heating it, the gold is heated sufficiently to cause death of the cancer cells [45].

2.7.5 Surgery

With the help of gold-coated nano shells, infrared laser and flesh welder blood-less surgery can be done with greater efficiency [46].

2.7.6 Nanomaterials for brachytherapy

BrachySil™ (Sivida, Australia) delivers 32P, clinical trial.

2.7.7 Drug delivery across

The blood-brain barrier/more effective treatment of brain tumors, Alzheimer's, Parkinson's in development.

2.7.8 Nanovectors for gene therapy

Non-viral gene delivery systems.

2.7.9 Cell repair machines

Direct cell and tissue repair can be done using molecular machines, however by using drugs and surgery only tissues can repair themselves. Access to cells by inserting needles into cells by molecular machines without killing them is possible [47].

2.7.10 Ethics and nanomedicine

Currently the most significant concerns involve risk assessment, risk management and risk communication of ENMs in clinical trials [48]. Implanting a

computing chip in humans raises many ethical concerns. The chip can diagnose diseases and can also analyze our DNA to determine the diseases to which one may be susceptible to in later stages. Ethical issues concerning a patient's right-to-know, right-not-to-know and the duty-to-know arise [49]. Increase in the current level of accuracy and efficiency of diagnostic and therapeutic procedures by augmenting the targeting and distribution by nanoparticles, the dangers of nanotoxicity becomes a paramount next step in better understanding of their medical needs [50].

2.7.11 Adverse reactions

Multiwalled carbon nanotubes led to asbestos like effects on the mesothelium due to high doses of intracavitary injection in rodents. Whether the inhalation of MWCNT will translocate to sensitive mesothelial sites has not been answered yet [51]. It will also be important to know their adverse effects, if any, in pediatric, geriatric and differing pathophysiological conditions like pregnancy, lactation, congestive heart failure, uremia, etc. (**Figure 1**).

3. Conclusions

Nanomedicine and nanodentistry will have an impact on many medical applications. The usefulness of these are not only therapeutic but also diagnostic. Development of applications of nanomedicine and nanodentistry is very complex and needs an integrated approach of all stakeholders. Future applications of nanodentistry will include nanorobotics, carbon nanotubes, nanocomposites whereas nanomedicine will include activity monitors, biochips, insulin pumps, needle less injectors, medical flow sensors and blood pressure, glucose monitoring devices and drug injecting systems. What nanomedicine and nanodentistry will be able to achieve in the future is beyond current imagination. However, it will be a tough task to handle the ethical issues which will be arising with the same pace.

Conflict of interest

Authors have no 'conflict of interest' declaration.

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