Review Article
ISSN: 0974-6943

*P.M. Chaudhari et al. / Journal of Pharmacy Research 2009, 2(8),1179-1183*
**Available online through**
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# A review of carbon nanotube: Boon to osteoporosis

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**Received on: 07-04-2009; Accepted on: 30-06-2009**

## ABSTRACT

This review describes the developing potential of carbon nanotubes (CNTs) in osteoporosis. Carbon nanotubes are sheets of graphite rolled up to make a tube. They make ideal artificial scaffolds for bones as the nanotubes are lightweight, very strong and the body doesn't reject them. The carbon nanotubes are injected into the fractured bone and then the bone can be left to heal. Several chemical groups can be attached to the nanotube to assist with the growth and orientation of hydroxyapatite crystals. In this way, the treatment of bone breakages and fractures will be revolutionized by an injection of carbon nanotubes into the break or fracture. The strength of the nanotubes will hold the bones in place whilst the tissue heals. As this process of bone repair becomes more successful it will become possible that large casts won't be needed to be worn by the patient as the bone re-grows. The speed of tissue growth will be rapidly increased because the carbon nanotubes provide a scaffold for the new bone to grow back by fusing the bone together, meaning that the mobility of the patient won't be impaired for the long length of time it usually takes the bone to grow back at the present time

***Keywords:*** Osteoprosis, carbon nanotube, cell uptake.

## INTRODUCTION

Osteoporosis is a condition characterized by the loss of the normal density of bone, resulting in fragile bone. Osteoporosis leads to literally abnormally porous bone that is more compressible like a sponge, than dense like a brick. This disorder of the skeleton weakens the bone causing an increase in the risk for breaking bones (bone fracture).Normal bone is composed of protein, collagen, and calcium all of which give bone its strength[1, 2]. Bones that are affected by osteoporosis can break with relatively minor injury that normally would not cause a bone fracture. The spine, hips, and wrists are common areas of bone fractures from osteoporosis, although osteoporosis-related fractures can also occur in almost any skeletal bone[3].

Osteoporosis bone fractures are responsible for considerable pain, decreased quality of life, lost workdays, and disability. Up to 30% of patients suffering a hip fracture will require long term nursing home care. Elderly patients can further develop pneumonia and blood clots in the leg veins that can travel to the lungs (pulmonary embolism) due to prolonged bed rest after a hip fracture. Some 20% of women with a hip fracture will die in the subsequent year as an indirect result of the fracture. About 20% of postmenopausal women who experience a vertebral fracture will suffer a new vertebral fracture of bone in the following year[4, 5].

Osteoporosis is a major public health threat for 44 million Americans. Of the 10 million who have osteoporosis, 80 percent are women. A woman's risk of hip fracture is equal to her combined risk of breast, uterine and ovarian cancer. Therefore a woman is more likely to experience hip fracture than these three forms of cancer. Today, 2 million men have osteoporosis and almost 12 million more are at risk for the disease. Men with low levels of testosterone are especially at risk. This includes men being treated with certain medications for prostate cancer[6].

Osteoporosis is responsible for more than 1.5 million fractures annually, including

- Over 300,000 hip fractures
- 700,000 vertebral fractures
- 250,000 wrist fractures
- 300,000 fractures at other sites

Osteogenesis Imperfecta (OI) affects between 20,000 and 50,000 Americans. In severe cases fractures occur before and during birth. In some cases, an affected child can suffer repeated fractures before a diagnosis can be made. Undiagnosed OI may result in accusations of child abuse[6].

A routine x-ray can reveal osteoporosis of the bone, which appears much thinner and lighter than normal bones. In addition, x-rays are not accurate indicators of bone density. The appearance of the bone on x-ray is often affected by variations in the degree of exposure of the x-ray film. The National Osteoporosis Foundation, the American Medical Association, and other major medical organizations are recommending a dual energy x-ray absorptiometry scan (DXA, formerly known as DEXA) for diagnosing osteoporosis. DXA measures bone density in the hip and the spine. The test takes only 5 to 15 minutes to perform, uses very little radiation (less than one tenth to one hundredth the amount used on a standard chest x-ray), and is quite precise. The bone density of the patient is then compared to the average peak bone density of young adults of same sex and race. This score is called the "T score," and it expresses the bone density in terms of the number of standard deviations (SD) below peak young adult bone mass. Osteoporosis is defined as bone density T score of -2.5 SD or below. Osteopenia (between normal and osteoporosis) is defined as bone density T score between -1 and -2.5 SD[7, 8].

The vast majority of individuals affected by osteoporosis are women. Although the disease can strike at any age, the greatest risk

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for fractures from osteoporosis occurs after menopause. This is because women's bodies produce less oestrogen after menopause, and oestrogen plays an important role in helping to prevent bone loss[9]. The European Commission is involved in research studying the impact of diet and gene-nutrient interactions on calcium and bone metabolism, and a novel isotopic tracer method is also being evaluated to study and quantify these processes. This new method will be compared to already-established methods (bone mineral density, biochemical markers) in an effort to protect and improve the quality of life of Europe's ageing population[10]. Further research on the biomechanical aspects of bone structure and strength, and on the reliability and safety of prosthetic implants is also being carried out at the European Commission's Joint Research Centre (JRC) to address the area of post-fracture treatment strategies[3, 5].

New diagnostic measures are required to predict fragility and fracture risk better through three dimensional imaging of both the entire and the internal micro-structure of bone. Current approaches under development may lead to "virtual biopsies" – using computer modeling to avoid invasive procedures and provide critical information about bone strength and fracture risk[4].

The goal of osteoporosis treatment is the prevention of bone fractures by stopping bone loss and by increasing bone density and strength. Although early detection and timely treatment of osteoporosis can substantially decrease the risk of future fracture, none of the available treatments for osteoporosis are complete cures. In other words, it is difficult to completely rebuild bone that has been weakened by osteoporosis. Therefore, prevention of osteoporosis is as important as treatment. Osteoporosis treatment and prevention measures are:

1. **Life style changes**

2.**Medications that stop bone loss and increase bone strength** such as raloxifene (Evista), ibandronate (Boniva), calcitonin (Calcimar), and zoledronate (Reclast)[11]

3. **Medications that increase bone formation** such as teriparatide (Forteo)[12].

Until 1985, the chemical element Carbon was only known to exist in two forms - diamond and graphite. This changed when Kroto and co-workers discovered an entirely new form of carbon, which became known as $C_{60}$ or the fullerene molecule. (This discovery later led to their award of the 1996 Nobel Prize in Chemistry.Fullerenes are a family of carbon allotropes, molecules composed entirely of carbon, in the form of a hollow sphere, ellipsoid, tube, or plane. Spherical fullerenes are also called **buckyballs**, and cylindrical ones are called **carbon nanotubes**[13, 14].

Nanotubes are members of the fullerene structural family. In the ideal case, a carbon nanotube consists of one or several cylindrical layers of rolled-up graphene sheets, with an interlayer spacing of 0.34-0.36 nm that is close to the typical spacing of turbostratic graphite (graphite without epitaxial relationship between two neighbouring layers). The layers are in most cases helical, i.e., the carbon bonds form a spiral around the cylinder[14, 15]. Each nanotube is composed of shells with different helicities[16], although in most cases several shells show the same helicity. The length of a nanotube is usually over 1mm, and diameters range from ~1 nm (for single-shelled tubes) to ~30 nm. Pristine tubes are closed at both ends by fullerene-like half spheres that contain both five- and six-membered carbon rings. Seven-membered rings can also be incorporated in the hexagonal network and give raise to a negative curvature of the tube[17]. Carbon nanotubes are predicted to be stronger than any known material (even diamond), with potential applications in numerous nanoscale architectures such as in microelectronics.Their name is derived from their size, since the diameter of a nanotube is in the order of a few nanometers (approximately 1/50,000th of the width of a human hair), while they can be up to several millimeters in length[18, 19].

**Carbon nanotubes in osteoporosis:**

Nanotubes may also provide the cure for many bone disorders, such as osteoporosis and rickets[20]. Carbon nanotubes are sheets of graphite rolled up to make a tube. They make ideal artificial scaffolds for bones as the nanotubes are lightweight, very strong and the body doesn't reject them. The carbon nanotubes are injected into the fractured bone and then the bone can be left to heal. Several chemical groups can be attached to the nanotube to assist with the growth and orientation of hydroxyapatite crystals[21]. In this way, the treatment of bone breakages and fractures will be revolutionized by an injection of carbon nanotubes into the break or fracture. The strength of the nanotubes will hold the bones in place whilst the tissue heals. As this process of bone repair becomes more successful it will become possible that large casts won't be needed to be worn by the patient as the bone re-grows. The speed of tissue growth will be rapidly increased because the carbon nanotubes provide a scaffold for the new bone to grow back by fusing the bone together, meaning that the mobility of the patient won't be impaired for the long length of time it usually takes the bone to grow back at the present time.

A research team led by Laura Zanello, an associate professor of biochemistry at the University of California, Riverside, has successfully grown osteocytes on a scaffold of carbon nanotubes. The group's work shows for the first time that bone cells can adhere to, and proliferate on, a carbon nanotube scaffold.

Artificial bone scaffolds may also be used in bone grafting and in the treatment of bone diseases such as osteoporosis[23].

Hydroxyapatite (HA) is the prime constituent of bone cements because of its ability to bond chemically with living bone tissues; this is due to its similar chemical composition and crystal structure to apatite in the human skeletal system. However, the intrinsic brittleness and poor strength of sintered HA restricts its clinical applications under load-bearing conditions[24, 25]. Poly (methyl methacrylate) (PMMA) is another material commonly used as bone cement; however, its low mechanical strength makes the use of PMMA problematic. A concentration of 0.1 wt % MWCNTs in the PMMA/HA nanocomposite material gives the best mechanical properties[22].

**CHEMISTRY OF CARBON NANOTUBES:**

C-atoms placed in hexagons and pentagons form the end cap structures. It can be easily derived from Euler's theorem that twelve pentagons are needed in order to obtain a closed cage structure which consists of only pentagons and hexagons[26]. The smallest stable structure that can be made this way is $C_{60}$ the one just larger is $C_{70}$ and so on. Another property is that all fullerenes are composed of an even number of C-atoms because adding one hexagon to an existing structure means adding two C-atoms. Deformations, such as bends and nanotube junctions, are introduced by replacing a hexagon with a

heptagon or pentagon. Deformations can be inward or outward and, among others, electrical properties are seriously changed by these deformations[27].

The nature of the bonding of a nanotube is described by applied quantum chemistry, specifically, orbital hybridization. The chemical bonding of nanotubes is composed entirely of $sp^2$ bonds, similar to those of graphite. This bonding structure, which is stronger than the $sp^3$ bonds found in diamonds, provides the molecules with their unique strength. Nanotubes naturally align themselves into "ropes" held together by Van der Waals forces.

**SPECIAL PROPERTIES OF CARBON NANOTUBES:**

**1. Mechanical strength:**

Carbon nanotubes have a very large Young modulus in their axial direction. Carbon nanotubes are the strongest and stiffest materials on earth, in terms of tensile strength and elastic modulus respectively. Since carbon nanotubes have a low density for a solid of 1.3-1.4 $g \cdot cm^{-3}$, its specific strength of up to 48,000 $kN \cdot m \cdot kg^{-1}$ is the best of known materials, compared to high-carbon steel's 154 $kN \cdot m \cdot kg^{-1}$ [30].

**2. Electrical conductivity:**

Depending on their chiral vector, carbon nanotubes with a small diameter are either semi-conducting or metallic. The differences in conductivity can easily be derived from the graphene sheet properties[31].It was shown that a (n,m) nanotube is metallic as accounts that: n=m or (n-m) = 3i, where i is an integer and n and m are defining the nanotube. The resistance to conduction is determined by quantum mechanical aspects and was proved to be independent of the nanotube length[32].

**3. Thermal property:**

All nanotubes are expected to be very good thermal conductors along the tube, exhibiting a property known as "ballistic conduction," but good insulators laterally to the tube axis. It is predicted that carbon nanotubes will be able to transmit up to 6000 watts per meter per Kelvin at room temperature; compare this to copper, a metal well-known for its good thermal conductivity, which only transmits 385 $W \cdot m^{-1} \cdot K^{-1}$. The temperature stability of carbon nanotubes is estimated to be up to $2800^0$ C in vacuum and about $750^0$ C in air.

**4. Optical activity:**

Theoretical studies have revealed that the optical activity of chiral nanotubes disappears if the nanotubes become larger[33]. Therefore, it is expected that other physical properties are influenced by these parameters too. Use of the optical activity might result in optical devices in which carbon nanotubes play an important role.

**5. Chemical reactivity:**

The chemical reactivity of a carbon nanotube is, compared with a graphene sheet. Carbon nanotube reactivity is directly related to the pi-orbital mismatch caused by an increased curvature. A smaller nanotube diameter results in increased reactivity. For example, the solubility of carbon nanotubes in different solvents can be controlled this way[34].

**6. One-Dimensional Transport:**

Due to their nanoscale dimensions, electron transport in carbon nanotubes will take place through quantum effects and will only propagate along the axis of the tube. Because of this special transport property, carbon nanotubes are frequently referred to as "one-dimensional" in scientific articles.

**7. Defects:**

As with any material, the existence of defects affects the material properties. Defects can occur in the form of atomic vacancies. High levels of such defects can lower the tensile strength by up to 85%. Another form of defect that may occur in carbon nanotubes is known as the Stone Wales defect, which creates a pentagon and heptagon pair by rearrangement of the bonds. Some defect formation in arm-chair-type tubes (which can conduct electricity) can cause the region surrounding that defect to become semiconducting. Furthermore single monoatomic vacancies induce magnetic properties[35].

**TYPES OF CARBON NANOTUBES:**

**1. Single-wall carbon nanotubes:**

Single-wall carbon nanotubes (SWNTs) are made of a single graphene sheet. These are seamless cylinders, were first reported in 1993. Their diameters range from about 1 to 2 nm and their length is usually in order of the micrometers. SWNTs typically team up to form bundles. These bundles consists hexagonally arranged SWNTs to form a crystal-like structure[36].

**2. Multi-wall carbon nanotubes**

The multi-wall carbon nanotubes (MWNTs) are made up of collection of several graphene cylinders. MWNTs have a diameter of about 1-100nm and length of about 1-50 micrometers. The distance between each layer of MWNTs is about 0.36nm[37].

**3. Fullerite:**

Fullerites are the solid-state manifestation of fullerenes and related compounds and materials. Being highly incompressible nanotube forms, polymerized single-walled nanotubes (P-SWNT) are a class of fullerites and are comparable to diamond in terms of hardness.

**4. Torus:**

A nanotorus is a theoretically described carbon nanotube bent into a torus (doughnut shape). Nanotori have many unique properties, such as magnetic moments 1000 times larger than previously expected for certain specific radii.[38] Properties such as magnetic moment, thermal stability, etc. vary widely depending on radius of the torus and radius of the tube[38, 39].

**5. Nanobud:**

Carbon nanobuds are a newly discovered material combining two previously discovered allotropes of carbon: carbon nanotubes and fullerenes. In this new material fullerene-like "buds" are covalently bonded to the outer sidewalls of the underlying carbon nanotube. This hybrid material has useful properties of both fullerenes and carbon nanotubes

**6. Nanoflower:**

The first nanoflower was created in Japan and was actually the accidental outcome of an experiment on nanotubes.

**APPLICATION OF CARBON NANOTUBES:**

**A. Diagnostic Tools and Devices:**

1) Radiation Oncology:

CNTs can be used as a cathode material for generating free flowing electrons. Electrons are readily emitted from their tips either due to oxidized tips or because of curvature when a potential is applied between a CNT surface and an anode. The advantages of CNT-based x-ray devices are fast response time, fine focal spot, low power consumption, possible miniaturization, longer life, and low cost. Miniaturized x-ray devices can be inserted into the body by endoscopy to deliver precise x-ray doses directly at a target area without damaging

the surrounding healthy tissues, as malignant tumors are highly localized during the early stage of their development [40, 41].

2) Sensors:

Sensors are devices that detect a change in physical quantity or event. There are many studies that have reported use of CNTs as pressure, flow, thermal, gas, and chemical and biological sensors. CNT-based nanobiosensors may be used to detect DNA sequences in the body[42, 43]. These instruments detect a very specific piece of DNA that may be related to a particular disease[81]. CNT chemical sensors for liquids can be used for blood analysis (for example, detecting sodium or finding pH value) [44].

3) Probes:

Probes are devices that are designed to investigate and obtain information on a remote or unknown region or cavity. Application of CNTs as nanoprobes for crossing the tumor but not crossing into healthy brain tissue should also be investigated, as the presence of cancer in a brain tumor may result in weakening of the blood–brain barrier[45].

**B. Biopharmaceutics:**

1) Drug Delivery:

CNTs can be used as a carrier for drug delivery, as they are adept at entering the nuclei of cells. Researchers have found that functionalized CNTs can cross the cell membrane. Besides, they are of a size where cells do not recognize them as harmful intruders[46]. Other applications to be investigated include the use of CNTs to deliver drugs to the eye beyond the blood–retina barrier and to the central nervous system beyond the blood–brain barrier.

2) Drug Discovery:

The critical bottlenecks in drug discovery may be overcome by using arrays of CNT sensors and current information technology solutions (such as data mining and computer-aided drug design) for identification of genes and genetic materials for drug discovery and development[47].

**C. Implantable Materials and Devices**

1) Implantable Nanosensors and Nanorobots:

CNT-based nanosensors have the advantages that they are a thousand times smaller than even microelectromechanical systems (MEMS) sensors and consume less power. Implanted sensors can be used for monitoring pulse, temperature and blood glucose, and diagnosing diseases[48,49]. CNTs can be used for repairing damaged cells or killing them by targeting tumors by chemical reactions. Possible application of CNTs for treatment of retinal diseases caused due to loss of photoreceptors can be investigated. According to Bhargava implanted nanorobots can have following possible applications [50].

1) To cure skin diseases. A cream-containing nanorobot could remove the right amount of dead skin, remove excess oils, add missing oils, and apply the right amount of moisturizing compounds.

2) To protect the immune system by identifying unwanted bacteria and viruses and puncturing them to end their effectiveness.

3) To ensure that the right cells and supporting structures are at right place.

4) As a mouthwash to destroy pathogenic bacteria and lift food, plaque, or tartar from the teeth to rinse them away.

2) Actuators:

Actuators are devices that put something (such as a robot arm) in action. The CNT electromechanical actuators (also known as artificial muscles) generated higher stresses than natural muscles and higher strains than high-modulus ferroelectrics. MWNTs are excellent candidates for electromechanical devices because of their large surface area as well as their high electrical conductivity[51].

3) Nanofluidic Systems:

Tiny nanodispensing systems can dispense drugs on demand using nanofluidic systems, miniaturized pumps, and reservoirs. The nanodispensing systems using CNTs can be applied for chemotherapy .Other potential areas where fluid dispensing systems could be applied are lupus, AIDS, and diabetes[52].

D. Surgical Aids

Using CNTs can be developed that can aid surgeons by providing specific properties of tissue to be cut and provide information about performance of their instruments during surgery. As nanotweezers (that can be used for manipulation and modification of biological systems such as structures within a cell) have already been created using CNTs, they have the potential to be used in medical nanorobotics[53].

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**Source of support: Nil, Conflict of interest: None Declared**