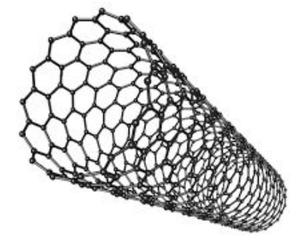

Carbon Nanotubes in Medical Technology
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One of the more important classes of material to emerge from the recent developments in nanotechnology has been the carbon nanotube. A variety of nanoscale carbon tube structures have been prepared and this article discusses their structure, properties and potential medical applications.

The versatility of nanomaterials
Nanotechnology has been discussed a few times in this column in recent years, perhaps not surprisingly because the products of nanotechnology seem to be finding applications in almost every sector of manufacturing and consumer goods. The defining character of a nanomaterial, or a nanostructured material, is that the material has a physical form that may be measured in one or more dimensions at the nanoscale, which is usually taken to mean from atomic diameters up to 100 nanometers. At these dimensions, two factors determine that the nanomaterial has properties extremely different from those of the same chemical substance in bulk form. These are the exceptionally high surface area to volume ratio and that quantum effects may be displayed. Some nanomaterials are virtually identical to commonly used bulk materials, but are prepared by specific techniques to provide the nanostructured features, for example, nanocrystalline silver and nanoparticulate titanium dioxide. In other cases, the actual molecular structure at the nanoscale may be different from that of any other form of this substance. Into this category comes carbon. Several forms of bulk carbon exist, including diamond and graphite, which obviously have different properties depending on the manner in which the carbon atoms are arranged. It has been known for more than twenty years that some special structures of carbon can be prepared with nanoscale features to provide a unique range of physical properties. Included in this range are carbon nanotubes.

The concept of carbon nanotubes
Carbon nanotubes were discovered by Iijima in 1991.[1] They are essentially one-dimensional tubes, arranged as one or more rolled sheets of carbon atoms in a honeycomb-lattice-like structure. In their simplest form, these nanotubes consist of one rolled sheet: a single atomic tube of approximately 0.4 nm in diameter and up to approximately 100 nm in length. In this form, they are known as single-walled carbon nanotubes. More usually, the tubes contain a number of concentric cylinders of carbon atoms, with overall diameters of up to 100 nm and lengths up to several hundreds of microns. These are known as multi- walled carbon nanotubes (MWNT). In this latter case, the different constituent cylinders may have different orientations and, depending on the way in which the hexagonal cells of the honeycomb are aligned with respect to the long axis, the tube may have electrical properties ranging from those of a metal to those of a semi-conductor. This versatility has given rise to a wide variety of applications, both real and projected, for the carbon nanotubes, including many in the medical field.

A couple of important points about the preparation of carbon nanotubes should be mentioned here. A variety of techniques are available including laser ablation and arc discharge, but it is now acknowledged that commercially viable, reproducible, large-scale production of nanotubes can be best achieved with chemical vapor deposition methods. These processes typically involve reacting a hydrocarbon feedstock at high temperatures with a metal catalyst, often nickel. As a result, carbon nanotubes produced in this way are contaminated with metallic nanoparticles, which, especially in the case of nickel, presents a potentially severe problem from functionality and toxicological perspectives. Recent improved manufacturing methods and new purification methods have resulted in much purer carbon nanotubes.

Medical possibilities

Endo et al. have recently published a review of the potential applications of carbon nanotubes,[2] including uses in electrochemical systems and fuel cells and high performance polymer composites. Several authors have also addressed potential medical applications, although perhaps inevitably at this stage, little has reached routine clinical practice. An excellent review paper by Harrison and Atala put some of these putative opportunities into perspective.[3] Among the possibilities are cell tracking, cell labelling, sensing cellular behavior, drug and biomolecule delivery, and enhancement of tissue regeneration.

For example, a number of procedures in cell therapy and tissue engineering suffer from a difficulty of monitoring the progress of tissue regeneration or cell performance, and non-invasive methods to do this would be extremely helpful. Observations on the movement of cells could be conducted using optical imaging in the infrared or near-infrared region by following the movement of injected agents that are targeted to these cells. Carbon nanotubes provide many characteristics that are suitable for detection in these regions. A number of scattering and spectroscopic techniques have confirmed that these nanotubes can be followed once they have been targeted to a cell. Carbon itself gives poor contrast in magnetic resonance imaging, but it can be chemically functionalized to make it more readily detectable. Indeed, it appears that gadolinium attached to the surface could provide for considerably better contrast than any currently used substance. With respect to cell and tissue behavior, the potential exists to use the unique electronic properties of carbon nanotubes in electrochemical sensors, possibly giving real-time data of parameters with good spatial resolution. MWNT have already been shown to be able to monitor insulin levels with the possibility of evaluating pancreatic islet cells before implantation into a diabetic patient.

The high surface area to volume ratio of the carbon nanotubes and the ease with which they may be chemically functionalized suggest potential applications in targeted drug delivery and gene transfection. One particularly useful aspect is the difference in chemical reactivity of the surface of the walls of the nanotubes and of their ends, because different molecules may be attached to each part. The ends of the tubes could be functionalized with an antibody to target the nanotube to a particular receptor on a cell. The sidewalls could be functionalized with a drug attached via a biodegradable linker. Similarly, carbon nanotubes have been reacted with deoxyribonucleic acid and ribonucleic acid, again with cleavable linking molecules being delivered to target cells for their gene transfection.

Proceeding with caution

At this stage, a large number of potential medical applications for these minute, reactive, traceable nanoparticles have been identified. These have to be addressed, of course, in a cautious manner because those features of chemical reactivity, mobility and size could also be associated with toxic effects. There have already been studies published that show that carbon nanotubes can exert cytotoxicity in vitro, with significant and serious effects on processes such as cell growth, metabolism and proliferation. As with all aspects of nanomaterial toxicity,[4] it is difficult to determine mechanisms of in vivo toxicity and adverse events, and to relate any observed effects with the characteristics of the materials. Nanoparticles are notoriously difficult to administer to animals in toxicological tests and simple phenomena such as tube aggregation may produce spurious results.

There are clearly some exciting opportunities here, but equally, all of the attendant risks of toxicity will have to be identified and minimized if these putative applications ever see the light of day.

References

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