NANOTECHNOLOGY

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PASS

RESEARCH PAPER
BASED ON
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ABSTRACT

Nanotechnology simply means 'the study of particles at the atomic level.' It involves research and development in the range of approximately 1-100 nanometers to provide an essential understanding of materials at the nanoscale and to create and use structures that have unique properties because of their minuscule size.

This paper will look at the significant applications of nanotechnology within medicine focusing heavily on the how it is used to treat cancer.

INTRODUCTION

The idea of manipulating matter on an atomic scale was first put forward by Richard Feynman in a speech 'There's Plenty of Room at the Bottom.' Although he did not specifically mention nanotechnology, Feynman suggested the possibility *"of manipulating and controlling things on a small scale"* (i.e. creating microscopic structures and molecules) and how they could *"tell us much of great interest about the strange phenomena that occur in complex situations."* He discussed how it would be possible to write the entire Encyclopaedia Britannica on the head of a pin which lead to the need of a more powerful electron microscope to assist in reading it. This approach was known as the 'top-down approach' to nanotechnology. A top-down approach is the breaking down of a system to gain insight into its composition. In a top-down approach an overview of the system is formulated which is then exposed, by 'manoeuvring things atom by

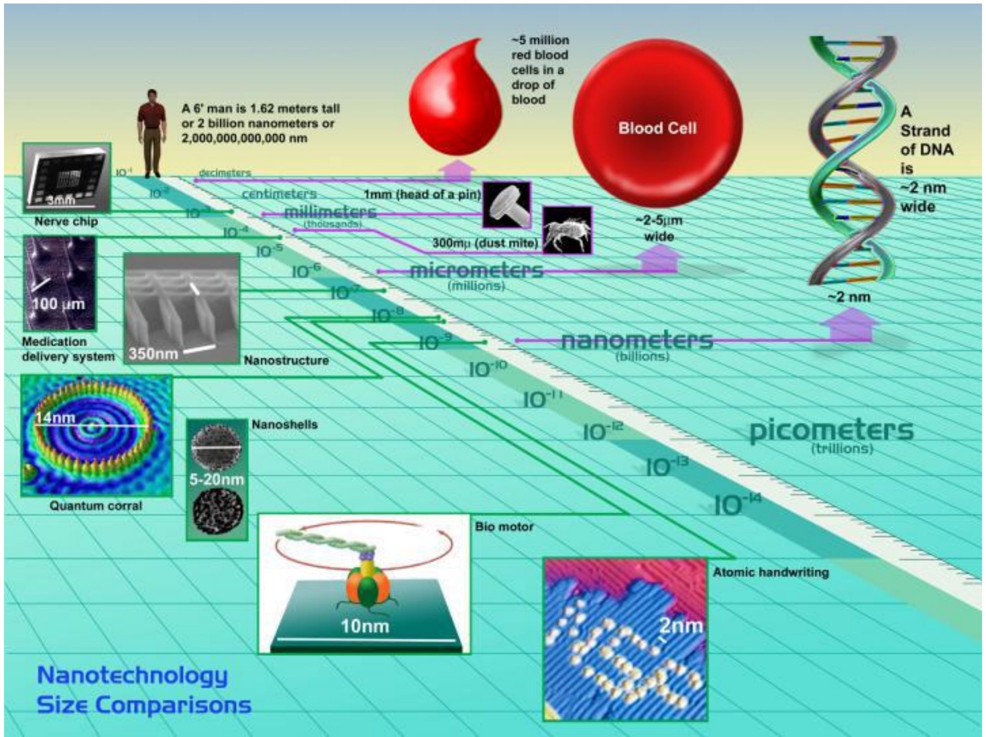
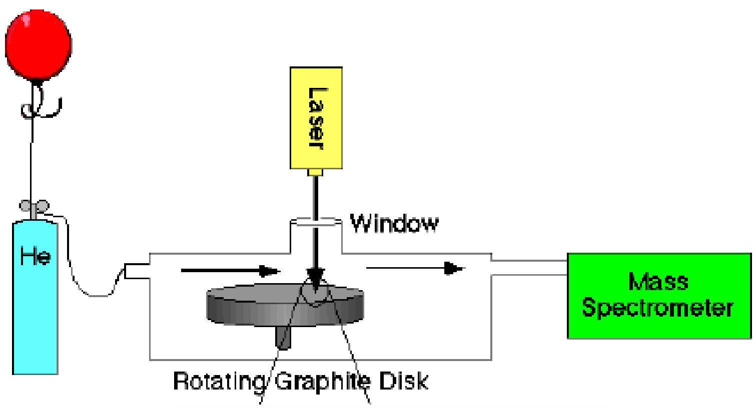


FIGURE 1: Size of nanometer

atom' to reveal the base elements. Materials reduced to the nanoscale can show different properties compared the characteristics demonstrated on a macroscale, enabling unique applications. One example is the increase in surface area to volume ratio as structures are downsized altering thermal and catalytic properties of materials.
After Feynman laid down the foundation of working at a molecular sclae, in 1959, the term 'nanotechnology' was popularised and researchers such as Eric Drexler expanded the idea of molecular manufacturing by integrating modern scientific ideas with Feynman's concept in 1981. The first major breakthrough in nanotechnology can be seen in the work of Richard Smalley along with Robert Curl and Harold W. Kroto in 1986.

Smalley's apparatus, shown, fires a high energy laser beam at a rotating disk of graphite in a helium-filled vacuum chamber. Helium is used because it is an inert gas and therefore does not react with the gaseous carbon. The intense heating of the surface of the graphite breaks the C—C bonds because of the intense energy. Once vaporized, the carbon atoms cool and condense in the high-pressure helium gas, colliding and forming new bond arrangements. Immediately upon cooling several degrees above absolute zero in a chamber, the carbon leads to a mass spectrometer for further analysis. It became evident that the most dominant molecule measured had an atomic mass of 720. By dividing this number by the mass of a single carbon atom (12), it was deduced that the molecule was comprised of 60 carbon atoms. These structures were given the name of 'buckminsterfullerene' otherwise known as 'Bucky-balls.'



Now, scientists have found ways to create Bucky-balls by placing a slab of graphite between two electrodes. The spherical shape of a Bucky-ball makes it a very stable molecule and it therefore is resistant to impact and deformation constantly maintaining its original shape. Bucky-balls are also very chemically stable since each carbon is bonded to another 4 carbons making the structure inert and so they are very

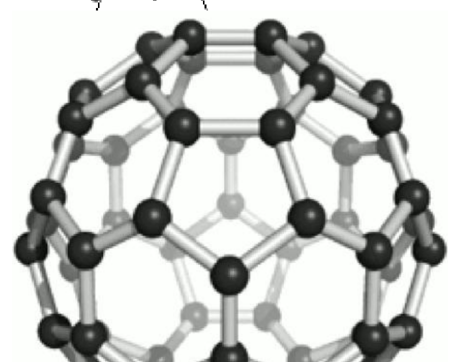


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FIGURE 3:
Buckminsterfullerne

unreactive.

Although the discovery of Bucky-balls is quite recent, they have long been present in nature e.g. in the wax of a burning candle.
The discovery of Bucky balls has also led to the formation of nanotubes also known as carbon tubes. Carbon nanotubes are molecular-scale tubes of graphitic carbon with outstanding properties. They are among the stiffest and strongest fibres known, and have remarkable electronic properties and many other unique characteristics. For these reasons they have attracted huge academic and industrial interest, however commercial applications have been rather slow to develop, however, primarily because of the high production costs of the best quality nanotubes.

The current huge interest in carbon nanotubes is a direct consequence of the synthesis of buckminsterfullerene. The discovery that carbon could form stable, ordered structures other than graphite and diamond stimulated researchers worldwide to search for other new forms of carbon. The search advanced when it was shown in 1990 that C_{60} could be produced in a simple arc-evaporation apparatus readily available in all laboratories. It was using such an evaporator that the Japanese scientist Sumio Iijima discovered fullerene-related carbon nanotubes in 1991.

DISCUSSION

There are many uses for nanotechnology in medicine some of which are:

- to prevent inflammation resulting from an allergic reaction- Buckyballs can be used to trap free radicals generated during an allergic reaction.

Allergic reactions are the 6th leading cause of chronic disease in the United States. Many treatments have been developed to control allergic reactions but so far, no cure has been found. this is where nanoimmunology becomes useful.

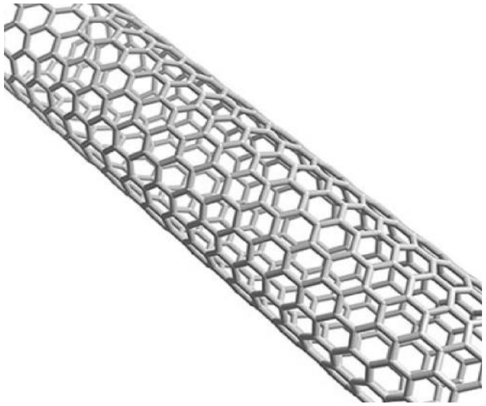

FIGURE 4: Nanotube / Carbon tube

Researchers have found that buckyballs are able to block allergic response in human cell culture experiments. In this study, researchers modified the buckyballs so that they were compatible with

water. Mast cells are responsible for causing allergic response and are packed with granules containing histamine. They are present in nearly all tissues except blood. When mast cells are activated, inflammatory substances such as histamine, heparin and a number of cytokines are rapidly released into the tissues and blood, promoting an allergic response. The buckyballs are able to 'interrupt' the immune response by inhibiting a basic process in the cell that leads to the release of an allergic mediator. Essentially, the buckyballs are able to prevent mast cells from releasing histamine.
The researchers found that the unique structure of the buckyball enables it to bind to free radicals dramatically better than any anti-oxidant currently available, such as vitamin E. Free radicals are molecules that cause oxidative stress, which experts believe may be the basis of aging.

Source: Virginia Commonwealth University 2007

- to quickly reduce bleeding in trauma patients - Z-Medica is producing a medical gauze that uses aluminosilicate nanoparticles. Aluminosilicate nanoparticles can rapidly minimize blood loss by absorbing water causing blot to clot quickly in a wound.

Chemists have introduced cotton gauze with nanoparticles increasing its ability to stop blood loss in all areas of the body including areas where it is difficult to apply pressure e.g. the neck. “Recent tests with Combat Gauze indicate that it decreased blood loss and improved survival," says , head of trauma and resuscitative medicine at the Naval Medical Research Centre in Silver Spring.
After having used both products of Z-Medica's: Combat Gauze and QuikClot the navy found the first product, QuikClot to be the better one; a grainy powder that can be put into wounds to decrease bleeding. This product was then used by the army. However the soldiers did not find this product to be very successful. When QuikClot came into contact with blood or water it became hot and as a result caused burns in some cases.
This problem was solved by Galen Stucky and several graduate students, by replacing QuikClot kaolin clay - a material rich in aluminosilicate nanoparticles -- which trigger blood clotting it has been used in medical tests for more than 50 years

2008

- Nanofibers can stimulate the production of cartilage in damaged joints and therefore can help to relieve the pain of arthritis.

Northwestern University researchers have designed a bioactive nanomaterial that promotes the growth of new cartilage without the use of expensive growth factors. Minimally invasive, the therapy activates the bone marrow stem cells and produces natural cartilage. Damaged cartilage can lead to joint pain and loss of physical function and eventually to osteoarthritis, a disorder with an estimated economic impact approaching $65 billion in the United States. With an aging and increasingly active population, this figure is expected to grow.

Cartilage does not regenerate in adults. Once you are fully grown you have all the cartilage you'll ever have. Type II collagen is the major protein in articular cartilage, the smooth, white connective tissue that covers the ends of bones where they come together to form joints. Our material of nanoscopic fibres stimulates stem cells present in bone marrow to produce cartilage containing type II collagen and repair the damaged joint.

The Northwestern gel is injected as a liquid to the area of the damaged joint, where it then self-assembles and forms a solid. This extra cellular matrix, which mimics what cells usually see, binds by molecular design one of the most important growth factors for the repair and regeneration of cartilage. By keeping the growth factor concentrated and localized, the cartilage cells have the opportunity to regenerate.

Researchers implanted their nanofibre gel in an animal model with cartilage defects. The animals were treated with microfracture, where tiny holes are made in the bone beneath the damaged cartilage to create a new blood supply to stimulate the growth of new cartilage. The researchers tested various combinations. They found their technique produced much better results than the microfracture procedure alone and, more importantly, found that addition of the expensive growth factor was not required to get the best results. Instead, because of the molecular design of the gel material, growth factor already present in the body is enough to regenerate cartilage.

Source: Northwestern University February 2010

CANCER

Another extremely important use of nanotechnology is to treat cancer. Cancer kills 1 in 4 people in USA making it the second leading cause of death after heart attack. Common treatment used by doctors today including radiotherapy and chemotherapy is successful in killing cancer cells but also kills healthy cell surrounding the cancer at the same time, causing damage to other areas of the body and causing many side effects e.g. the loss of hair in cancer sufferers.

National Cancer Institute, which recently announced two waves of funding for nanotech training and research, sees nanotechnology as vital to its stated goal of "eliminating suffering and death from cancer by 2015."
Nanotechnology allows us to treat cancer using techniques such as drug delivery through injections or orally. Nanotubes/rods successfully destroy cancerous cells whilst healthy cells survive. When the rods are exposed to near-infra red light from a laser they heat up, killing the cell, while cells without rods
are left unscathed. thousands of carbon tubes can easily fit into a cell They then placed the tubules inside cells, and found they were quickly destroyed by the heat generated by the laser beam. Researchers introduced nanotubules into cancer cell but not healthy cells by taking advantage of the fact that unlike normal cells, the surface of cancer cells is covered with receptors for a vitamin known as folate. They coated the nanotubules with folate molecules, making it easy for them to pass into cancer cells, but unable to bind with their healthy cousins. Exposure to the laser duly killed off the diseased cells, but left the healthy ones untouched. The researchers believe it should be possible to refine the technique still further, for instance by attaching an antibody to a nanotubule to
target a particular kind of cancer cell.

An experiment on mice has already been carried out to target cancer in mice. The study conducted by scientists at Harvard Medical School and the Massachusetts Institute of Technology, which are pioneering cancer nanotechnology, involved engineering nanoparticles embedded with the cancer drug Taxotere. The particles were then injected directly into human tumours created from prostate cancer cell lines and implanted into the flanks of mice. The mice were watched for 100 days.

The technology being tested involves a nanoparticle made of a hydrogen and carbon polymer with bits of drug bound up in its fabric and attached to a substance that hones in on cancer cells. The polymer gradually dissolves, exposing the nuggets of drug little by little.

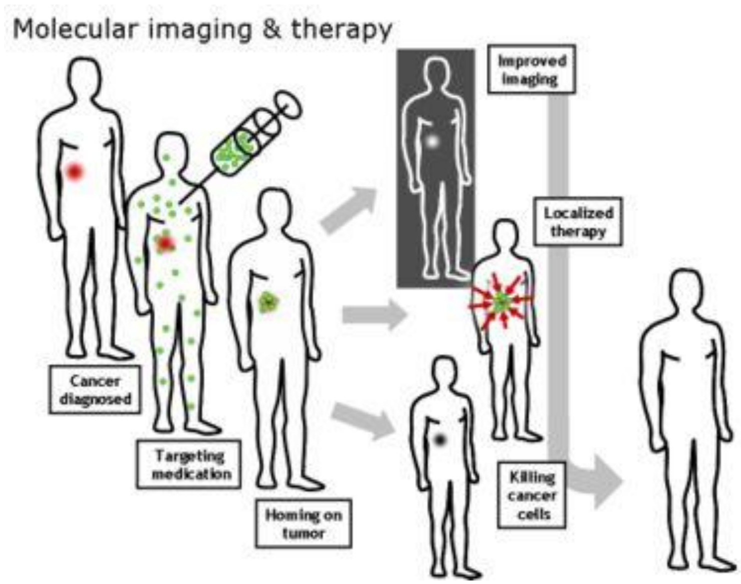

FIGURE 5: How drugs might be used to treat cancer

The mice were divided into five groups, including one that had their tumours injected with ineffective saltwater. A second group died after injections of a nanoparticle containing no drugs.
Another group that were given just one shot of the drug experienced an initial decrease in tumour size and then a strong rebound before they died too.
Other mice were injected with a nanoparticle-encased drug,
but one that was not designed to specifically target cancer cells.
In a final group of mice, scientists injected the targeted nanoparticles containing the drug The tumour completely disappeared.
Injecting targeted nanoparticles into the bloodstream and having them seek out tumours and get inside on their own is still the ultimate goal, but direct injection is also promising for cancers where the tumour is accessible and hasn't spread, such as in early prostate cancer.

One major problem scientists are having in perfecting the blood injections is that the nanoparticles are ending up in the liver and spleen _ an unwanted side effect because once they dissolve in those organs, they release toxic levels of chemotherapy to healthy tissue.

Another problem that cancer patients face is that many of the most potent anticancer therapies can be administered only by injection, which means that cancer patients must travel to receive their medication. A new type of nanoparticle developed by researchers at the Johns Hopkins University School of Medicine, may be used for future cancer patients to enable them to receive their medication in pill form.
A new developed polymeric nanoparticle from three different starting materials that they then linked together in various proportions. The investigators found that the nanoparticles had suitable pharmacological properties. They readily incorporated

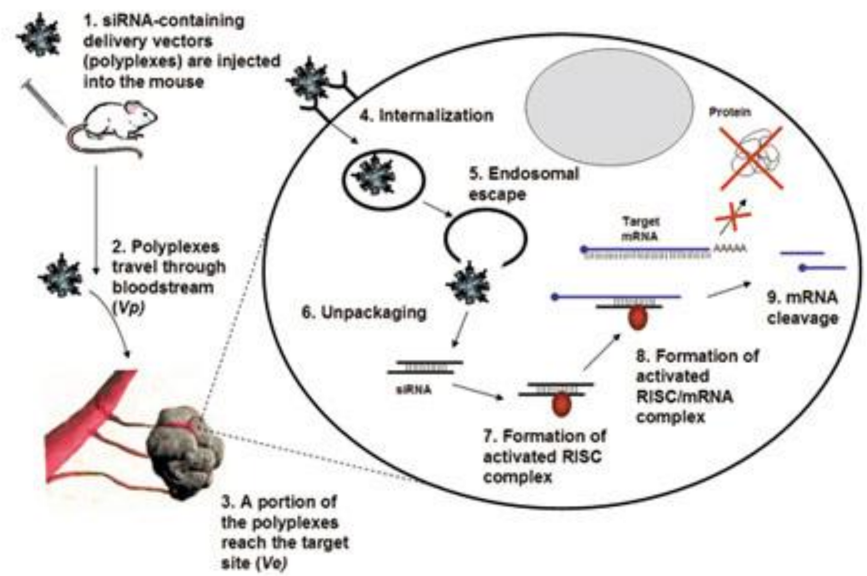

FIGURE 6: Possible method to treat cancer

water-insoluble drugs and were capable of delivering those drugs into the bloodstream after oral administration.
In a paper published in the journal Molecular Cancer Therapeutics, the researchers noted that they chose the three starting materials because they expected that the resulting polymers would stick to the mucosal layer in the gastrointestinal tract (GI). This adhesive property gives cells in the GI tract the opportunity to engulf the nanoparticles and ferry them into the bloodstream.
Tests with the anticancer drug rapamycin showed that this formulation had good pharmacokinetic properties in test animals. More importantly, these nanoparticles were able to deliver rapamycin to human pancreatic tumours implanted in the test animals. In fact, assays showed that oral dosing with this nanoparticle formulation triggered the changes in tumour cell biochemistry expected from rapamycin administration. Additional tests showed that even "mega—doses" of empty nanoparticles administered for 4 weeks caused no apparent toxicities.

CONCLUSION

In conclusion, the integration of modern technology and the theories behind Richard Feynman's speech 'There's Plenty of Room at the Bottom' have led to extremely useful discoveries which have many advantages through our everyday lives especially in medicine as there is no actual cure for cancer. Further inventions in nanotechnology will provide us with essential equipment which will enable doctors to treat cancer in a much better way, leading to healthier patients. The novel properties of Nan particles will enable drug delivery systems to work to ensure that cancer can be detected and treated promptly. As research into nanotechnology increases so will the number of extensive applications leading to greater applications within medicine and maybe even one day to the cure of cancer itself.

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