Exploring the Potential Use of Nanotechnology to Produce Nano Sized Transport Capsules to Overcome the Current Challenges of Conventional Drug Delivery Systems

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ABSTRACT

This report outlines the current work in nanotechnology and drug delivery systems as two different areas and explores the potential for carbon nanostructures to encapsulate a pharmaceutical compound to increase its safety and efficiency in the body. It looks at the uses, creation and safety issues of fullerenes and nanotubes. This technology would overall once produced reduce costs of the administration of drugs as well as making the drugs more available to everyone around the world.

INTRODUCTION

The History of Nanotechnology

Nanotechnology is essentially the manipulation and use of technologies at the size one-billionth of a metre. This means anything in the range of one to a hundred nanometres (10^{-9}). Figure 1 shows the relative dimensions of various objects in nanometres. At these sizes the physical properties of structures change, mainly because of dramatic changes in the surface area to volume ratio. Materials at the nano-scale will have different "mechanical, thermal and catalytic properties" [1]. Examples of this are; platinum, which is very un-reactive at the macroscale, but a catalyst at the nanoscale (used in such things as vehicle catalytic converters); and aluminium, stable at the macroscale but combustible at the nanoscale[2].

Although almost all of the work into nanotechnology has been done since the twentieth century it is not a newly founded concept. It has been used around the world for thousands of years, with nanoparticles being found present in cave paintings[2], and it is only recently since the physicist Richard Feynman's famous after dinner-speech "There is plenty of room at the bottom" that major advances have been made in this area. Feynman suggested a way of being able to manipulate molecules at such small scales by using "one set of precise tools to build and operate another smaller set, and so on"[1] until the required size is reached and by using this method, new materials and processes similar to those in organisms, such as the proteins in cells, could be produced.

Methods of Creation

There are two main ways of synthesising structures at the nanoscale. Firstly there is the "bottom up" approach where each individual atom or molecule in the structure is chemically manipulated into position, and secondly there is the "top down" approach where larger structures are broken or cut down to construct these nanostructures.

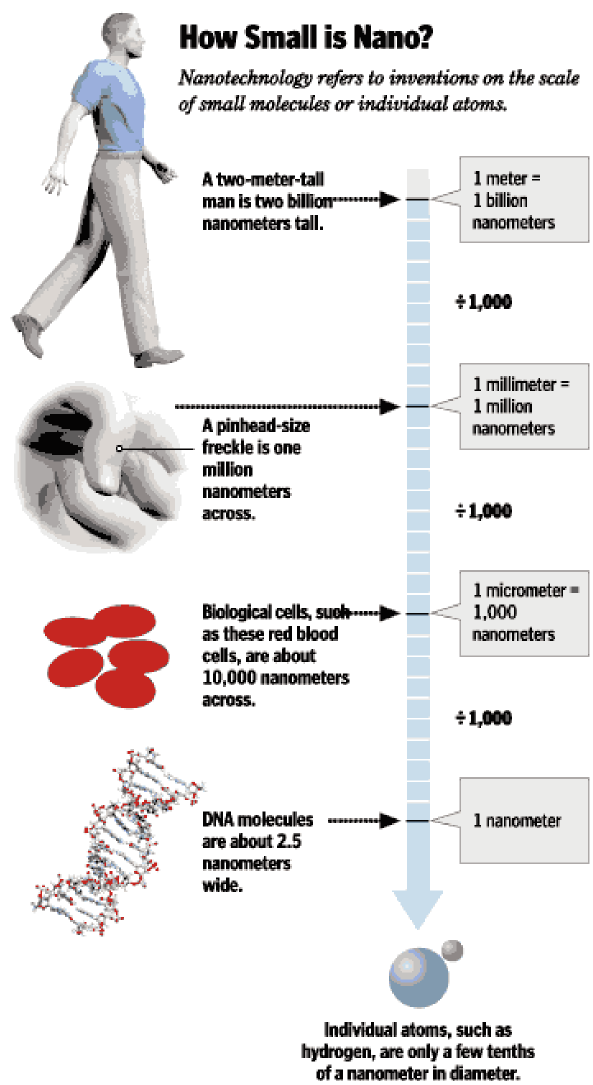

Figure 1

Nanotechnology in Medicine

There are currently many wide-ranging uses of nanotechnology in medicine, such as in drugs for appetite boosting, cholesterol lowering and hormone therapy[3]. Looking ahead there are lots of potential uses for it. It could be used in diagnostic and imaging techniques[4] for example iron oxide nanoparticles have a peptide coating which can bind to cancer tumour cells making MRI results clearer and allow the tumour to be caught earlier on, and similarly other nanoparticles could bind to proteins and other molecules to show diseases in patients at earlier stages of infection. It could be used for cell repair[4] by producing nanorobots that can repair damaged or diseased cells just like our own bodies antibodies. And it could be used to increase the efficiency and safety of drug administration and this is what I am going to explore in my paper.

Current Problems with Drug Delivery Systems

Drug delivery is "the process by which a formulated drug is administered to the patient"[5] and this is achieved by a number of different ways[6];

Orally- This is most often taken as a pill which passes through the bodies' digestive system and is absorbed through the mouth, stomach and mainly the small intestine into the liver, which then sends it round the body. Although this is the most commonly used way of administering drugs, because it's usually the safest, most convenient and cheapest method, it is not usually the most effective and has many drawbacks. The main challenge facing drug delivery systems at present is their poor bioavailability ("the degree of activity or amount of an administered drug or other substance that becomes available for activity in the target tissue"[7]) This could be because of; metabolism of the drugs in the small intestine and liver before reaching the required target; food in the digestive tract effecting the rate and quantities of drug absorption; other drugs in the digestive tract being taken at the same time effecting the rate and quantities of absorption and causing other more harmful and unpredictable side effects; acids and enzymes in the stomach destroying the drugs before they're absorbed; smaller doses having to be taken than in other methods to avoid damaging healthy cells; plasma fluctuations where either too much of the drug or too little are in the blood.

Other ways are then used if the drugs doses need to be too big to be taken orally or if they need to reach a certain area of the body that wouldn't be reached otherwise such as the eyes (Ocular), the vagina (Vaginal), the rectum (Rectal) or by injection (Parental administration) to the veins, the muscles or the skin. These are all usually more expensive, more invasive and require a qualified person to administer. This opens up the need for the creation of new oral drug delivery systems by nanotechnology which work more efficiently and safely than any other current methods of drug delivery to reduce the need for the use of these alternative methods.

DISCUSSION

Nanostructures have the ability to encapsulate drugs to increase their bioavailability by protecting them from all the problems involved in digestion and only releasing for use at the area in the body required.

This has the potential for not just drug transportation but for the transport of proteins and genes as well as for a more sustained and continuous drug delivery by remaining in the body's blood circulation for longer. This could reduce plasma fluctuations in the blood, therefore reducing a drugs side effects whilst simultaneously increasing effectiveness. The size of the nanoparticles could allow them to be absorbed into body tissues around 15 to 250 times faster than similar drug delivery devices in the micro (10^{-6}) scale. Figure 2 shows a simplified computer generated model of molecular encapsulation.

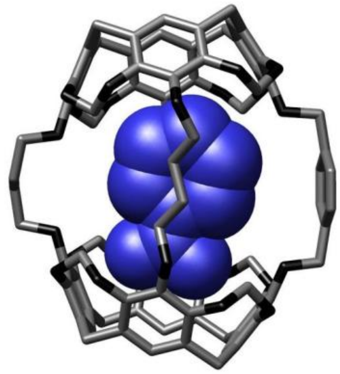

Figure 2

Carbon Nanomaterials

There are two types of carbon nanostructures which could be used for creating new, more efficient drug delivery systems. These are nanotubes/buckytubes (shown in Figure 3) and fullerenes/buckyballs (shown in Figure 4).

Fullerenes

Fullerenes are spherical, hollow molecules that are made entirely of carbon atoms arranged by mixtures of hexagonal, pentagonal or heptagonal rings of atoms bonded together. They are similar in structure to graphite with the hexagonal rings of carbons. The first fullerene to be discovered was the Buckminsterfullerene (buckyball), shown in figure 4 which is one of the molecules that can potentially be used for a new drug delivery system.

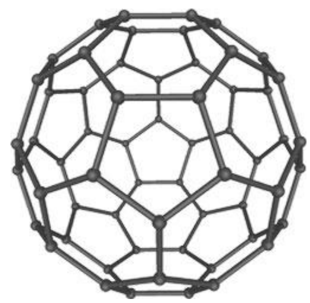

Figure 4

How It Would Be Used For Drug Delivery

"Fullerenes can be functionalised for delivery of drugs and biomolecules across cell membranes"[10]. New research being conducted at Virginia Tech[8] is showing the ability to insert other elements and molecules into the centre of carbon buckyballs (testing specifically on C_{68}) which will not only have the desired effect of that molecule being protected by the buckyball, but also that molecule helps stabilise the buckyball. This means that when the molecule is extracted from the buckyball by hydrolysis in the cell then the buckyball becomes unstable and is therefore more easily broken down by the body. This would be useful as certain buckyball configurations have been found to put human cells into a sort of "suspended animation where they don't die, divide or grow"[9] which is toxic to healthy human cells, so if the buckyball is unstable then it could be broken into harmless carbon atoms which can then leave the body as $C0_2$ leaving behind the useful drug in the cells.

These new buckyballs would be able to be taken orally because of the carbon coating to the drug, protecting them from prematurely being broken down in the digestive system. They would then be absorbed into the blood, taken to the liver and then circulated around the body until the required destination of their load is found, and this could either be triggered by heat, light or radiation from sources (e.g. lasers) outside the body. They will then leave the blood by diffusion going down a concentration gradient into the required tissues to be broken down by enzymes releasing the pharmaceutical compound in the cells. The biologically safe carbon waste products will then leave the body.

This will provide a much more specialised way of delivering drugs to certain areas of the body with the same or more accuracy of an injection simply through a pill. And this pill can hold a higher concentration and volume of the drug because of the lack of interaction with other, already healthy cells.

Nanotubes

Nanotubes (Figure 3) are compounds of carbon with a cylindrical structure that can be extremely long relative to their diameter and are usually ended with structures similar to those of half buckyballs. Because they consist entirely of sp2 bonds (formed by 2 P and 1 S orbitals), similar to those in graphite, they are extremely strong, making them ideal for protecting pharmaceutical compounds through the digestive tract. They have unique properties such as; low cytotoxicity, meaning that they're not very toxic to the cell, making them preferable to fullerenes; and good biocompatibility, meaning that they are very unlikely to trigger an immune response from the body, even though they are a foreign body.

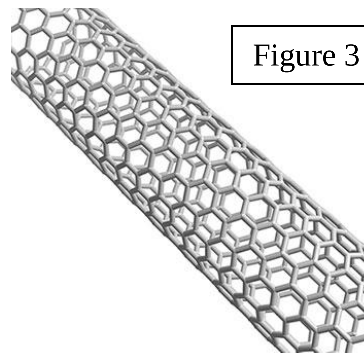

Figure 3

Again these would be taken as a pill and absorbed through the same processes as with fullerenes.

How They Would Be Made

Currently, "carbon nanomaterials are prepared by template synthesis, the carbon-arc discharge technique, catalytic chemical vapour deposition and laser ablation"[10] .All of the structures formed by these will be the same and these can then be manipulated using nitrogen and other atoms or molecules required to put the pharmaceutical compound inside for transport. To accurately make the drugs a 'bottom up' approach would have to be made because of the intricate and specific nature of the cells being made.

Safety Issues Around Carbon Nanomaterials

Fullerenes can be toxic inside the body if they are not broken down into their biologically safe element carbon. Nanotubes can cause inflammatory reactions from the tissues which could cause more harm than has been achieved. Unfortunately new research[11] is pointing towards carbon nanotubes being similar to asbestos if inhaled in their cancer causing properties. Asbestos is a problem because it is small enough to penetrate the lungs but too long to be broken down by the body's defences just like carbon nanotubes which will only be a few nanometres in diameter but can get up to being whole centimetres long. This could be a serious problem if trying to use carbon nanotubes as an alternative drug delivery system, and rigorous clinical trials would have to be carried out before any new drugs using these devices are made available meaning that these types of technologies might not be available for a few years to come.

CONCLUSION

I think that in terms of future developments of drug delivery systems to be researched, the use of carbon nanoparticles to encapsulate the pharmaceutical compounds for the use in a pill would be a highly useful path to go down. It would revolutionise drug administration, making it safer, less invasive, less expensive and more effective and it would also drastically improve the lives of those in third world countries. This would be because so many more drugs would be available to be taken orally, taking away the other complications previously outlined about administering drugs using alternative routes that have restricted medical standards in these countries up to now.

Unfortunately it does have its draw backs; the cost once developed is likely to be higher than a normal pill because of the new technology required; the process of administration might not be as simple as current pills because of external triggers that might be required to break open the nanostructures to release the drugs in the right places; and each drug already on the market would most likely have to be re-tested once it was encapsulated in the nanostructure to monitor the effects, and any new effects this could have on the body.

These problems could be combated in the future; the cost of development is likely to drop as these techniques become more familiar without much research needed to help with this; the most likely requirement of external triggers could be solved by researching possible enzymes specific to the areas of the body that the drug is targeted at which will break down the carbon nanostructers without the need for external interference; the re-testing of drugs is most likely unavoidable but by testing these carbon nanostructures and looking at their general interactions with the body, the tests of other drugs wouldn’t have to be that extensive.

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