NANOTECHNOLOGY IN DRUG DEVELOPMENT RESEARCH

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ABSTRACT

Nanotechnology is an area that has been researched by scientists because of the possibilities of momentous discoveries that could occur in the future, such as far more advanced medical apparatus. It is a branch of science and engineering that involves the designing, along with building, of structures and devices smaller than 100 nanometres. In the words of Sakshi Agrawal's work (2009), nanotechnology is a "revolution occurring in science". This paper will examine how drug development is aided and expedited by nanotechnology, for example, the buckminsterfullerene, which will be discussed later in the paper. It will also examine how medical tools such as nanoneedles make it easier to apply drugs. The following discussion will show an understanding of how nanotechnology in drug development has a good future in a safe and cost effective way.

INTRODUCTION

Nanotechnology has been around for the last four decades with scientists dedicated to researching more information about it. Nanotechnology can be closely related to nanoscience because together in the 1980's there were two developments; nanocluster science and the Scanning Tunnelling Microscope which lead to the discovery of Buckminsterfullerene in 1985 and Nanotubes in 1991. According to Darin Y. Fergeson Phd (2008), the demand for "nanotechnology medical products will grow more than 17% annually to reach $52 billion in 2011". Due to the discoveries and developments in nanotechnology, the demand for it has increased vastly, leading to further research.

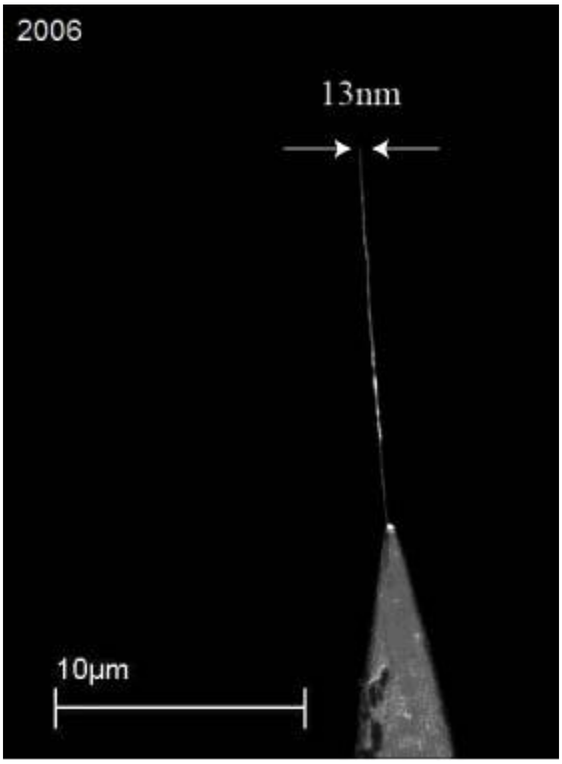
The uses of Nanotechnology are mainly in medicine in order to diagnose someone, prevent a disease or even deliver drugs to a specific target in the body. Nanomedicines have also been used; re-engineering the human body to improve the natural biological systems, Sakshi Agrawal (2009) calls this "augmentation". According to the work of Darin Y. Fergeson (2008), "12 nanomedicines have already been approved/The most active area of medical Nanotechnology is drug delivery". With the use of addition technologies such as Nanotools, Drug Design, Computational Biology, e.g Nanoneedles and Buckyballs; a whole new world can be discovered in the world of drug delivery and development.

Buckminsterfullerene

Figure 1 – Structure Of a Buckyball

Buckyballs were discovered in 1985, consisting of 60 carbons atoms ($C60$) that are arranged in such a way that they interlock with each other, creating a structure that is similar to the shape of a football (see figure 1). According to the work of Nanotech-Now , "buckyballs are the only molecules composed of a single element to form a hollow spheroid"; showing how it has the potential to carry molecules or drugs within its shell. Scientists have now developed Buckyballs with branched DNA-polystyrene hybrids rather than carbon atoms still with the same structure and properties as figure 1 – 70% of it being hollow. Sometimes, there can be difficulty when applying drugs to certain areas of the body, both in the correct place and at the right moment in time. This is why, with the use of the Buckminsterfullerene, drugs can be encapsulated, then migrate into cells, where biological enzymes can digest the DNA, releasing the drug; thus controlling the timing of the drug's release. This could be beneficial for cancer treatment, where only cancer cells could be treated, without the damaging of healthy body cells and vastly reducing a patient's side effects.

Nanoneedles



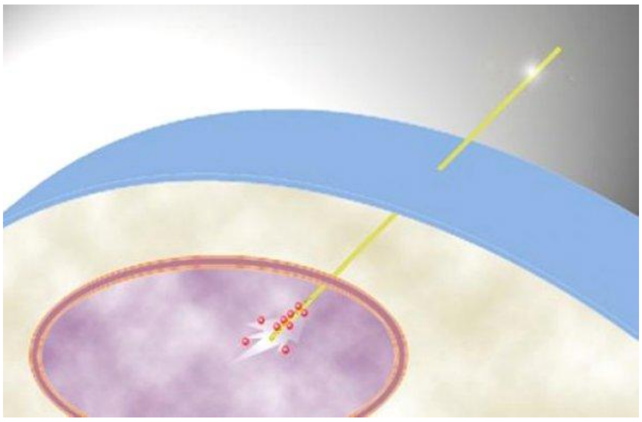


Figure 2 – (diagram) Nanoneedle into a cell

Figure 3 – Nanoneedle

Nanoneedles are an important development in the Nanotechnology world, in the delivery of drugs. The diameter of the needle is 13nm, as seen in figure 3. This device gives itself the ability to deliver different types of drugs, straight through the cell membrane, either into the cytoplasm, or inside the nucleus. This can be seen in figure 2 (the blue representing skin, the purple representing a specific cell, the yellow representing the Nanoneedle). This development in drug delivery gives a more direct and quicker approach to the implementation of the drugs; the ability to manipulate biological molecules such as DNA, and give a better understanding of the processes at Nanoscale.

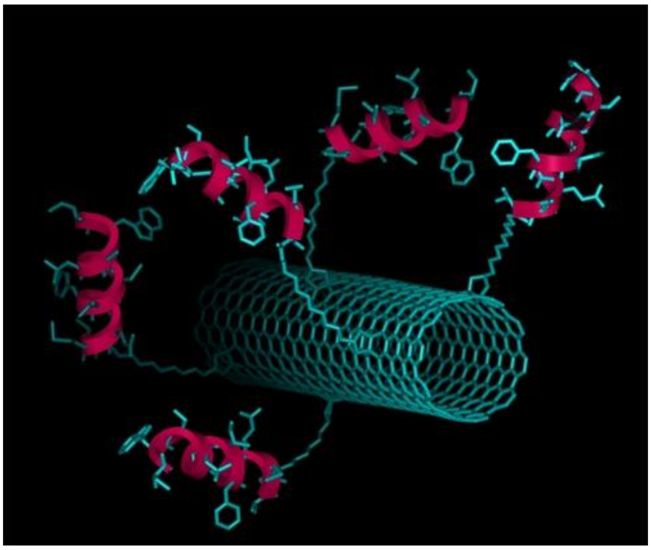
However, even with the present developments in nanotechnology, it is difficult to understand the nature of reactions that are at a Nano level. Nanotechnology is needed to understand these reactions and make appropriate drugs, and for drug delivery; allowing for minimum invasion and side effects.

Healthcare gets better in proportion to the aging of the world's population. The results of this is that the health care services (e.g NHS) are feeling the pressure on spending in order to improve themselves; plus there is also the problem of increasing costs for developing drugs. This leads to increased pressure in trying to making savings by whatever means. Nanotechnology can reverse this problem with product discovery and development costs reduced. Costs can be reduced by the improving efficiency and decreasing the probability of a product failure.

DISCUSSION

Carbon nanotubes are unique because of their ability, which was shown initially in 2004, to cross the phospholipid bilayer membranes of different cellular types using translocation mechanisms termed the *nanoneedle mechanisms*. Thus, Carbon nanotubes will open up immeasurable potential for future discovery of drugs because of their ability to obtain information about, and pierce areas, like the nucleus, which had previously been unreachable. Their use for delivery of drugs is favoured and is to be developed in the future because of their ability to be rapidly eliminated from the body, when they have been used, so Carbon nanotubes are useful in that they can be used with proportionality - they can be destroyed so that their effect is not too great and can be exactly measured; reducing side effects of surplus dosage inside the body. CNTs as vehicles for drug delivery have shown the specific possibility of targeting cancerous cells with a lower dosage than conventionally used, although is just as effectual in killing the cells, conveniently not harming healthy cells and significantly reducing side effects and invasiveness of such procedures. As multipurposed pioneering carriers for drug release and diagnostic application, nanotubes have been anticipated and keenly explored.

Figure 4



The usefulness of Carbon nanotubes derives from their nanoscale size and their ability to be added to and taken from, giving them versatility and the ability to be manipulated in size, and also their strength due to the way their carbon atoms are bonded together in the nanotube structure. Their physicochemical features enable the introduction of several molecules which can be delivered and are attached with covalent and noncovalent bonds; leading to drug design becoming more probable in the future as technology like nanotools, e.g. nanobots and nanoneedles, are more developed. Carbon nanotubes could be changed so that they have different functional groups and varieties of moieties for specific purposes, for example therapy targeting, , and imaging. Ammonium-functionalized nanotubes will be used more prolifically in the future as capable vectors for nucleic acids and tools for delivery of these in cases of genetic disease, where a correct gene or base sequence could be inserted to replace defective or mutated, disease-causing chains. Conversely, when conjugated with peptides and antigens, Carbon nanotubes could develop as synthetic vaccines to provide artificial active immunity by simulating a pathogen with the antigens of that pathogen bonded to the nanotube's surface and stimulating antibody production, withought an attenuated or weak pathogen needed, thus meaning the rate of infection from the vaccine would be 0%. A new and effective system for applications.

Carbon nanotube excretion rates and accumulation in organs and any reactivity with the immune system will determine the Carbon nanotube safety profile and, consequently, any further pharmaceutical development. Caution is advised about the need for systematic data on the long-term fate of these very interesting and versatile nano-objects in correlation with the type of Carbon nanotube material used. Carbon nanotubes are gradually playing a bigger and more important role in the emerging field of nanomedicine; however, we need to guarantee that the great opportunities they offer will be translated into feasible and safe constructs to be included in drug discovery and development pipelines.

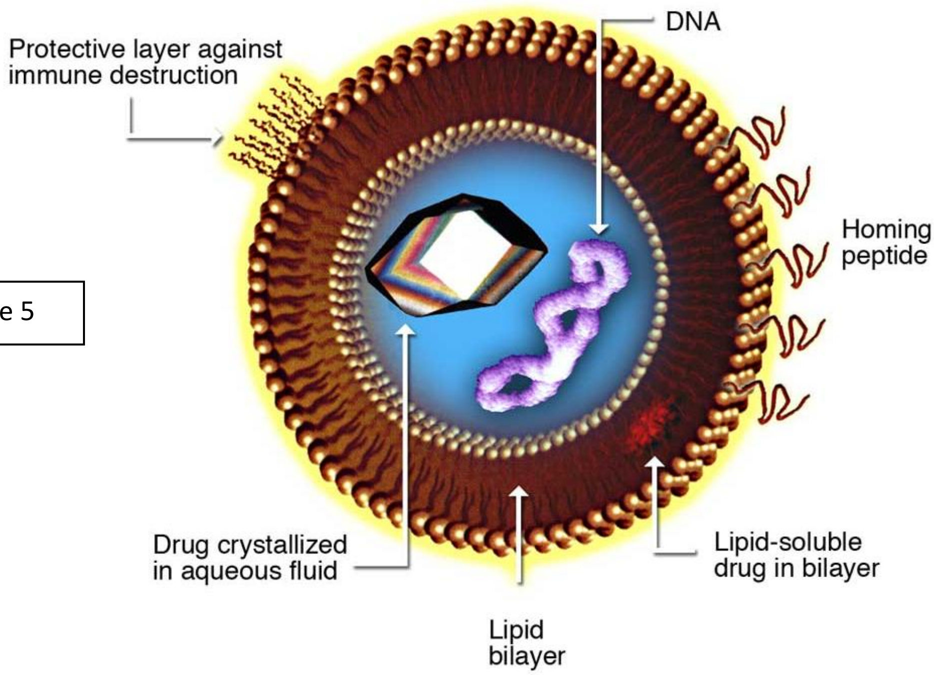


Figure 5

Liposomes are artificially prepared vesicles made of phospholipid bilayer and can be used to deliver drugs by the natural process of exocytosis and were first suggested by Gregoriadis. Liposomes are composed of amphipathic phospholipids and cholesterol molecules for rigidity, which naturally associate into bilayers encapsulating an aqueous interior, with hydrophilic heads on the outside and inside edges and the hydrophobic tails inside the layer. Lipid-soluble drugs can be stored in the bilayer and water-soluble drugs in the internal fluid. Additionally, the liposome surface can be specifically engineered to improve its properties; the newest and most noteworthy surface membrane modification is the amalgamation of the hydrophilic polymer polyethylene glycol (PEG), which acts as a protective layer and a barrier which prevents interactions with the blood, leukocytes and plasma proteins, thus retarding any recognition by the immune system, giving it a greater chance of reaching its target cell and enhancing the circulation lifetime of the liposomes. As a carrier for imaging agents, liposomes have proven to be versatile as well. For example, liposomes could be loaded with fluorochromes (a common imaging agent) and targeted to both T-cell and B-cell lymphocytes for in vitro classification. They could also be used in imaging of lymph nodes and inflammation by loading with radionuclides and radioactive isotopes such as technetium-99 or indium-111, as well as targeted imaging of tumour development and drug delivery to those tumours.

Enhanced Permeability and Retention effect is the property where certain molecules, typically liposomes, tend to accumulate and aggregate in tumour tissues much more than they do in normal tissues because the angiogenic tumour vessels are disorganised and leaky. In order for tumour cells to grow quickly, they must stimulate the production of blood vessels to get a good blood supply. These newly formed tumour vessels are usually abnormal in form and architecture. They are poorly-aligned defective cells with wide gaps to the tissue, lacking a smooth muscle layer. This means that the liposomes could be tracked and, if they were filled with a magnetic compound, for instance, Nickel, they could both be controlled with magnets, and provide clearer contrast in imaging e.g. MRI. Also, this means that liposomes with the drug encased will collect with in tumours; meaning that development should be made in terms of creating the vesicles with cancer drugs inside.

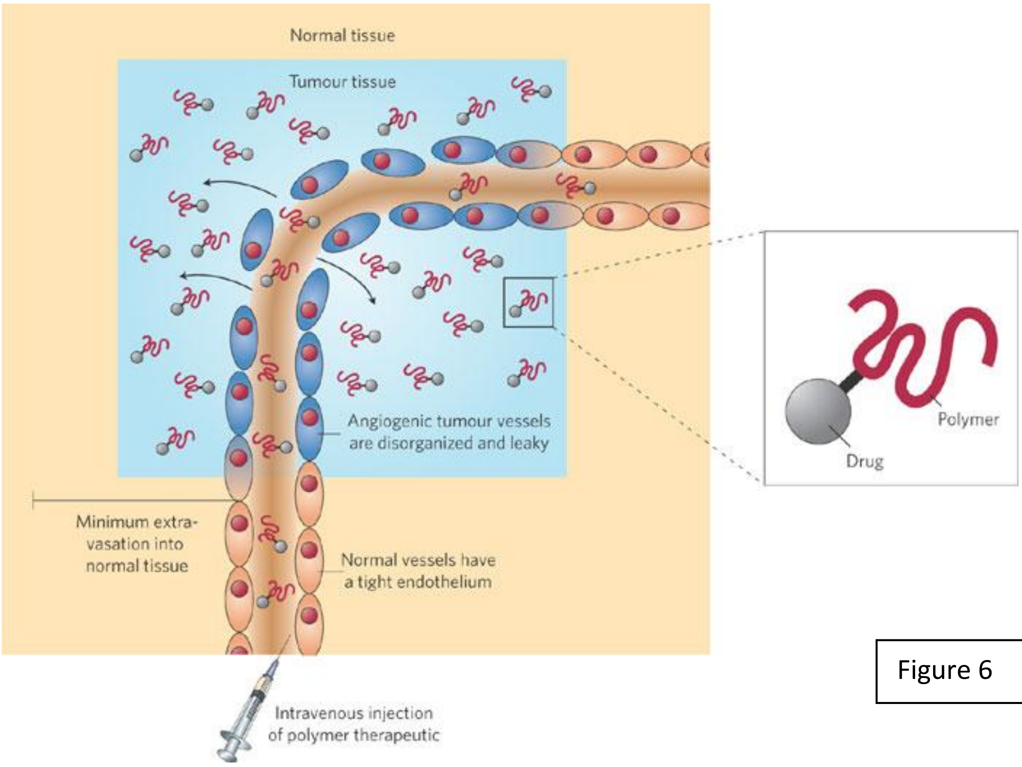


Figure 6

It is the flexibility of engineering and construction that makes liposomal vehicles effective candidates for non-invasive imaging. As targeted drug delivery vehicles, some limitations of liposomes have emerged: most notably, poor control over release of the drug from the liposome (i.e., the potential of leakage of drug into the blood), as well as questions regarding encapsulation efficiency, method scalability, and stability during storage. Perhaps because of these limitations, the use of liposomes as combined contrast agents for T-cell tracking as well drug delivery has not been widely explored.

Some researchers in the United Kingdom and the U. S. received funding from their governments to discern whether carbon nanotubes might be dangerous to health. the long, thin shape of the Carbon nanotubes caused people to question their safety because of its similarity to another poisonous material. It became clear that one of the main reasons that asbestos particles can cause an otherwise rare form of lung cancer named mesothelioma, appears to be that they too, are long and thin which is why asbestos can be woven into sheets from a mineral fibre. Whilst there is not a reason known yet for the correlation between the long thin shaped molecules and cancers, there is abundant confirmation that connects contact with asbestos with mesothelioma. The researchers therefore thought it should be investigated so that they could distinguish whether carbon nanotubes could cause pre-cancerous lesions in mice.

The experiment wasn't continued to the point that the mice actually developed cancer, but they did get inflammation and certain lesions associated with precancerous conditions, therefore proving the chance of contracting cancers from treatment with Carbon nanotubes, and the unethical nature of their use in this way, though used correctly, they could have amazing effects on the world of medicine and ameliorate our society, specifically in the fields of drug development and delivery. It is essential, however, that more research is done to determine any other possible side effects because people's lives could be at risk and if it gets to the point where whole industries are dependent on carbon nanotubes, they would have large vested interests and money in the field and any health sandal or controversy would cause these businesses to fail and a big political battle to break out to keep stability, causing them to implement delays in appropriate regulations, if they become enacted at all; thus putting more lives at risk.

CONCLUSION

Conclusively, my investigation has demonstrated that Liposomes and Carbon nanotubes are new developments which can be used in treatment, therapy and imaging, using a variety of techniques to treat different diseases, though particularly cancers. Not only will they, in the future, be used to specifically target any cell in the human body with a specific drug, but they also can aid in imaging, providing a contrast so that the particles can be tracked non-invasively. Other forms of future treatment do not have this advantage. I have also concluded that if such a form of treatment is to take place in the future the surgery will be minimally invasive, if at all, and many of the procedures needed to be undertaken could be done, more conveniently, out of hospital, and with minimal distress to the patient. However, this dissertation has also shown me that more research will need to be done surrounding prospective nanotechnology for drug development, especially in the dubious and greatly undiscovered area of carbon nanotubes. This is because there is evidence of cancers and ethical concerns about what a controversy could lead to.

I deduce that it would be best to focus on implementing lysosomes to help treat patients, though especially in the area of cancer treatments, as at this present time the benefits of the treatment far out-weigh its negative aspects. Due to populations having increased age and vulnerability to disease, as well as prevalence of cancers, it is essential that scientists have the freedom to implement such treatments for people as they will soon prove to be beneficial all over the world.

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