

# Nanotechnology in Drug Delivery



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PASS

## *Abstract*

*This paper reviews the biological chemical apparatus of nanotechnology in the aspect of Drug Delivery. It will consolidate the progress of the applications and the positive and negative effects nanotechnology in medicine may have. Later in the paper we will review the technology used and its design and conclude with how nanotechnology could help the patients of tomorrow.*

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# The use of Nanotechnology in Drug Delivery

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## Introduction

Many drugs used in medicine can have a detrimental effect on the patient's health. For instance chemical therapy on cancer cells has shown effectiveness in a number of cases. But this can also have disastrous effects on the patient's health such as hair loss or damage to the immune system. Since the 1990's when the fullerenes were discovered buckminsterfullerene has been a pioneer for many research products, from a fuel lubricant to a key component to nanotechnology.

## So How Big is The Box

In 1959 Richard Feynman led a memorable speech of "there's plenty of room at the bottom." In this he challenged physicists around the globe to work on building devices that could work on the microscopic scale. Feynman offered \$1000 to anyone who could build a motor 1/64 of an inch. (1)(Approximately 0.4mm) Many people tried to claim such a prize but it was only until William McLellan had made this motor. Working with experience from watchmakers he made the parts of his machine smaller and smaller thinning the wires to the width of a hair. When McLellan presented the motor to Feynman, Feynman offered up the prize money. (2)



Figure 1: Feynman viewing McLellan's mini motor (A)

Since then Nanotechnology has moved on from the miniaturisation stage to manipulate uses for nanotechnology (building from atoms). In the early 1970's a group of the University of Sussex led by Harry Kroto and David Walton, had studied the chemistry of unsaturated carbon configurations. They were observing dense clouds in the Inter stellar medium (the matter that exists in the space between the star systems in a galaxy) and studying the long chained polyynylcyanides. In the 1980's The Rice University had developed a technique led by Richard Smalley and Bob Curl on using laser vaporisation of a suitable target to produce clusters of atoms. Kroto realised that by using a graphite target the cluster apparatus could be used to probe the long carbon chains, so he planned a collaboration of the two universities. The Sussex/Rice experiment took place in September 1985 this experiment confirmed that when graphite was vaporised by the laser, large carbon structures such as C<sub>60</sub> and to some less extent C<sub>70</sub> had been formed. (3)

## Buckminsterfullerene: The new Frontier of Medicine

$C_{60}$  is the roundest and most symmetrical large molecule known to man. Mostly known as buckminsterfullerene (or commonly as Bucky Balls) these large carbon molecules develop new properties almost every day. Named after American architect R. Buckminster Fuller who designed a geodesic dome with the same fundamental symmetry, buckminsterfullerene is one of the major forms of pure carbon including graphite and diamond. (3)

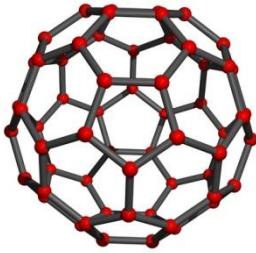


Figure 2: Buckminsterfullerene is shaped like a ball made of a pentagon surrounded by hexagons this is a large however simple covalent carbon molecule (B)

One novel use is the casing for most drug delivery chemicals as  $C_{60}$  is so strong it can withstand most forces and processes carried out by the human body. Because of this molecule's large spheroid buckminsterfullerene has the potential to be filled with any medicine needed. If manipulated correctly many procedures in drug delivery could be more effective with the use of nanotechnology. The main problem that can be faced is delivering the drug through the body; approximately 99% of medical molecules don't reach their target and subsequently stay in the patient. For the molecule to successfully pass through the body it must not be recognised by the body's immune system; therefore hair or cell-like features may be added to the buckminsterfullerene to generate this natural camouflage. Buckminsterfullerene strength is also a key factor in this process; many medicines such as cancer treatment drugs are very toxic to the body and only want to be exposed once contact with a target such as a tumour. A specific example is in the process of chemotherapy (chemical therapy). Using nanotechnology we can implant the chemical drug inside buckminsterfullerene, the molecule is then coated with this organic camouflage as stated above. This apparatus is implanted into the patient, this may be done orally or intravenously (because this method is still in trial stage at this stage no specific methods had been identified). The drug will then travel to the affected area; in this case the tumour, the chemical will latch onto the cancer cells and disperse the drug (this could be triggered by a light sensor and illuminating the growth or a heat sensor as most tumours are slightly hotter than the surrounding tissue (4)) and cause apoptosis (programmed cell death) which is normally the function cancer cells cannot do, which is why they multiply so rapidly. Rather than trying to kill the tumour, this process allows the tumour to kill itself, minimising the affect to the body and therefore the patient. (4)



Figure 3: Shows a cancer cell undergoing apoptosis, this is a false coloured SEM image (C)

Current research is being undertaken in this process and more externally how to safely deliver drugs. A challenge for nanotechnology in this research is to manipulate a device that can carry the drug to its target. This device must be able to be monitored but the structure must be strong and made of organic substances such as carbon so the adverse side-effects can be minimised or eliminated and the immune system will not attack the molecule.

## The Discussion

Although most aspects of nanotechnology such as drug delivery have not reached their full capabilities yet using the basics we know on the Human body's processes we can build our structure based on this. Although this paper is specified to drug delivery an appreciation must go the recent work in Alzheimer's research in which Early detection of Alzheimer's is now available.

Alzheimer's disease is the most common cause of dementia; this physical disease affects the brain eventually killing the brain cells. Around 465,000 people are diagnosed with having Alzheimer's disease in the UK alone. (5)

However one of the first examples of nanotechnology is being used for detecting minute amounts of certain disease proteins in bodily fluids. In this disease the marker is known as ADDL (amyloid-beta derived diffusible ligand) this is the sub-unit that groups into the nerve-entangling amyloid plaques that can cause defects to the brain in the further stages of Alzheimer's. These markers are used for detecting Alzheimer's but sadly the evidence is only available in a post-mortem examination. With a new nanotechnology system the BCA (Bar-code amplification) technique can detect the presence of minute ADDL molecules even at minimal levels; therefore detection can be earlier and sometimes even before symptoms can occur. This will allow more time to begin the process of eliminating the disease (if applicable) or at least delaying future symptoms. (6)

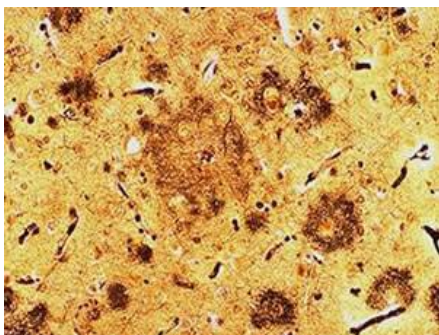


Figure 4: Shows an amyloid plaque built up from peptides on the brain, this is affected by Alzheimer's disease (D)

From these events we can gather that nanotechnology is no longer a “Star Trek Science” but moreover a current research that with a few adjustments could be a common medium between effective medicine and patient care.

## Financial Restraints

One of the main setbacks for nanotechnology is funding, although using a minute amount of material the apparatus needed to assemble these structures is very expensive. In a financially receding economy nanotechnology may not be viable for the future as cheaper alternatives may have to be used. As specified before Buckminsterfullerene can only be assembled using laser vaporisation and for this method to have effectiveness production of buckminsterfullerene would need mass production but would need to reduce defects as the drugs implanted into them may be harmful to healthy cells. With the UK GDP suffering shock contractions of up to 0.6% how do we know nanotechnology is still viable in medicine today? (7)

## Ethical Judgement

Many people consider the idea of arranging individual atoms (the definition of nanotechnology) as playing with fire. As a global research we only know a fringe of the capabilities nanotechnology has. With most of the scientific basis we know being based on theory such as Evolution and the atomic structure how do we know that the effects of nanotechnology will not perhaps be suicide for patients rather than a cure?

However many people consider the applications of nanotechnology, although in drug delivery this could save lives, once a design is made it can be altered for a specific purpose, a simple explanation would be the invention of the nuclear reactor which was soon manipulated for military purposes into the nuclear bomb. In a world of peace maybe nanotechnology could stand as a cure but in practical aspects, hypothetically how do we know if a private company sells nanotechnology to the NHS as well as Al Qaeda?

Considering these aspects the biggest influence to nanotechnology is the patient itself. A doctor will choose nanotechnology if it is safer for the patient reduces pain or is effective in its role. Going back to our chemotherapy Nano-drug, a doctor would use this if it meant less affects to the host cells and more effect to the tumour. If this drug had a greater effect than some other cancer treatments (chemo, radio therapy and surgery) the Nano-drug would be favoured, if not it may be dismissed. A common dismissed drug is thalidomide for the disease Leprosy. In the 1960's the pill was also given to pregnant mothers as a sleeping-pill-tranquilizer, which once the children were born suffered deformations in their body. In America close to 8,000 babies were deformed by this drug and the company who made this drug only escaped lawsuit as the drug was never licensed for general use. (8)



Figure 5: Thalidomide Sufferer shows limb Deformities; this was caused by the mother taking thalidomide as a prescribed drug (E)

To minimise these effects trials should be taken using the modern day methods such as a test on tissue cultures and then animal testing (although animal testing may be considered ethically wrong it is a government policy made by MHRA) This is known as pre-clinical testing and thousands of drugs go through this but only a handful pass. Most drugs then go through three clinical trials (I, II, III) this is where the drug is tested from healthy men to an average sample of the population and compared with the effect of a placebo. After Licensing further tests can still be taken. In Nano-technological drug delivery further tests may be needed to assure the safety to patients. (9)

## How can we tackle these Problems

Financially Research in Nanotechnology is very expensive and with the current cost to bring a drug to market costing \$802 million (10) research needs to be low cost for a pharmaceutical company to succeed. Although the NHS funds a lot of research in this field and so do a number of charities it is most of the time pharmaceutical companies that produce more or better drugs as they face a higher rate of competition such as the constant battle of GlaxoSmithKline vs. Pfizer which has been lasting for years. Although the NHS will use research in Nanotechnology, Companies manage to acquire materials at a cheaper rate and will do it for profit rather than a service. Although many may consider some companies go to extreme measures to increase profit (such as Nestle in the baby milk marketing (11)) but for nanotechnology to exceed its potential privately funded research may be a necessary evil.

Ethically though the patient's care and wellbeing must always come first, to prevent another "thalidomide" incident appropriate tests must be conveyed. As there is no evidence to whether Buckminsterfullerene and nanotechnology in drug delivery will be generically effective in all areas of the body or alterations will have to be made to compensate other tissues (group of cells working together) of the body specific research in this area is needed. Side effects would have to be evaluated on a basis of risk to patient with respect to curing the disease. This would be some of the necessary measurements to make this process effective to the wellbeing of the patient. Although as said earlier once nanotechnology is developed enough it could be manipulated the benefits nanotechnology has on our economy such as Sunscreens, Consumer goods and low energy electronics or efficiency in agriculture by ultra-chemical filtration (a possible solution to world hunger) far outweigh the risk of nanotechnology being "weaponized". (Converted to a weapon)

## Future Developments in Medicine

With the constant evolutionary process the world of medicine undergoes the mass production of nanotechnology is approaching. When William McLellan made his motor he was without the technological advancements we have today. You can observe this by the timeline of consumer electronics from the LP to the tape, compact disc to the mp3 player then now the multimedia player. The minimization of electronics is a fast movement.

In drug delivery Buckminster Fullerene is assembled using the laser vaporisation method (Sussex/Rice Experiment) to disassemble clusters of carbon to large molecules such as the fullerenes. If the laser uses less energy and more efficient (produced more buckminsterfullerene) the “Bucky ball Cost” would be considerably less.

In 1985 Binnig, Quate and Gerber invented the AFM (atomic force microscope.) The AFM was originally invented to overcome the disadvantage of a SEM (scanning electron microscope) which needed a semi-conductive surface for the specimen to be seen. The AFM can view almost any surface with nowadays using a laser beam deflection system (introduced by Meyer and Armer) with a tip radius of about 0.1 nm (Nano-metre.) This microscope has a specific use in nanotechnology as it allows us to manipulate the position of individual atoms with a laser tweezers and unlike an SEM the sample does not need to be covered with a conductor to be seen which could damage the fullerene or the drug itself. (12)

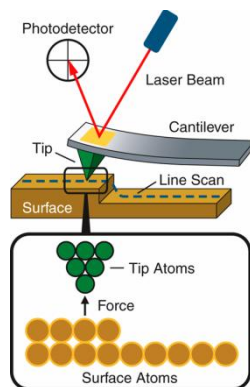


Figure 6: Diagram of an Atomic Force Microscope (how it Works) (F)

## In Summary: How can Nanotechnology help Tomorrow's Patients

We have evaluated the effects of nanotechnology and seen the uses in drug Delivery. As stated earlier 99% of drugs don't reach the targeted area and with some drug-immune diseases Nanotechnology in the drug allows the cell to undergo apoptosis so the cell will hydrolyse itself. (Break down)

Nanotechnology can also make the wellbeing of the patient easier; with the Drug Delivery host cells will be unaffected which means the patient's physical condition will not be getting worse than originally. Less dosage of the drug can be inserted into the molecule (e.g. Buckminsterfullerene) as impact site would only be a concentrated area.

We have considered the ethics of research in nanotechnology, although there are some views why private research may produce a faster paced and better product of nanotechnology, a publically

funded research programme will have less chance of being sold to a black market. Although Nanotechnology in Drug Delivery should be tested rigorously once licenced as a drug Doctors will have better control for the drug itself.

## Where Does Nanotechnology Stand Now

In America the first nanotechnology based cancer drugs have already passed the regulatory testing from the FDA (Food and drug administration) which is the American version of the MHRA in the UK. Drugs such as Doxil® and Abraxane® are already on the US Market. (13)



Figure 7: Doxil® and Abraxane® (G)

As for the UK, Nanotechnology is not currently based in any major drug and will probably take some time for this application to be used in drug delivery. But from Feynman's favoured speech of evolutionary steps in miniaturization, Nanotechnology in Drug Delivery is a current research and not the Science Fiction many people observed in comic books.

Many more global drugs based on nanotechnology are passing through the hoops of government testing everyday it is only until some drugs are fully licenced in the UK they may be used as standard practice in the Health Service. However many people believe although the Technology of Drug Delivery is available, it should be perfected before using as a general practice in drug delivery. Although some people who are victims of diseases which could be assisted with nanotechnology in drug delivery feel that the testing enforced by governments are restricting their access to new products and other beneficial aspects of nanotechnology. (14)

## Conclusion

In viewing these facts I believe that Nanotechnology is a better/improved approach to delivering drugs. I accept that there are other methods that may be more suitable to a specific disease and that there are many risks such as the drug inside the molecule experiencing damage or a premature dispersal which could cause detrimental effects to the patient, but if all the possible defects were evaluated and the risk of occurrence was minimised, it would be a stable delivery system.

Nanotechnology in Drug delivery could be used in such methods as Cancer Therapy and Disease which are immune to basic drugs such as strains of Drug-Resistant Influenza strands which can be deadly to the young or the elderly. Although Ethical problems could occur from this application of nanotechnology it is almost certain restrictions or regulations will be set in place by legal governing bodies such as the MHRA and FDA to increase the safety of nanotechnology based drugs.

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- E. Image from BBC Inside out: Thalidomide 50 years on  
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F. Diagram of AFM

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G. Abraxane and Doxil

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