

# Nanotechnology – The next step in drug delivery

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### **Abstract:**

The recent developments in nanotechnology allow us to construct specific atomic structures, from the atoms that they consist of. The applications of this specificity and control over molecular structures have great potential, but this paper will focus on the medical applications, specifically the potential that these structures and purpose-built molecules have for controlled drug delivery and release. The theory which this idea uses, could allow us to very specifically target the drugs, without affecting their chemical makeup, to a precise part of an organism, allowing us to potentially target toxic drugs at cancerous cells, resulting in a way to prevent damage to other body cells whilst affecting cancerous cells. The release mechanism for these drugs into the targeted area would use a form of electromagnetic radiation to vibrate the molecules and break apart bonds in the nanostructure, releasing the encased drug into a specific area of the body. This precise technique has not been used before but it is based upon existing theory to do with resonant frequencies on a larger scale. The advantage of this is that it would allow an extremely concentrated and strong drug to be used.

### **Introduction:**

The ability to manipulate a compound or complex molecule at a molecular scale is a massive advancement in the development of specific and targeted substances. REF<sub>0,0</sub> It reduces and almost eliminates the need for compromise in technological and chemical applications. This is because the problems that currently arise with modern drugs often originate from parts of the drug which are not active in carrying out the function for which the drug was designed. The theory of atomic manipulation REF<sub>0,1</sub> which is the basis for nanoscience suggests that the drugs and chemicals which are needed for a certain purpose must merely be designed and can then be created, rather than having to be themselves discovered, or formed from a reaction. This in turn means that not only the active part of the molecule can be created or used, but the macrostructure of the molecule itself can be designed to reduce any interference or effects with other biological structures or chemical compounds. Eric Drexler was the first to begin to link the original nanotechnology ideas put forward by Feynman to real life macrostructures, and so developed a theoretical link between the concept of specific atomic theory to its realisation as a modern technology. The work of Drexler, however was only conceptual, and was a stepping stone from the original 'idea' of atomic manipulation to the actual atomic manipulation that is now possible. This allowed the field of nanotechnology to jump from the theoretical and conceptual to the experimental and testable.

There are many uses of such specificity in molecule creation and it has opened up a new branch of chemical science. Modern advances have resulted in the creation of nanowires REF<sub>1</sub>, which allow us to produce extremely small electronics and computer chips, such as the germanium/silicon chips produced at Harvard, which is one advancement which nanotechnology allows. The ability to manipulate matter on such a minute scale improves greatly our control of substances and this control over the interaction of molecules with other molecules is a key aspect in the science of medicine. This means that the size and creation of these nanowires, even though used in a totally separate field, suggest great potential for similar high-control applications in medicine. One such application is nanowire sensors which are used in medicine in order to identify and label specific cells or parts on

the body which are infected or diseased. This allows the disease to be specifically treated, meaning that there is great specificity and control over the treatment. As well as this, optical imaging can be aided by such particles, and magnetic nanoparticles, which behave differently to larger versions made from the same material, which is a property solely due to their small size. These particles can be injected and their resonance and magnetic properties used to aid the imaging of that part of the body.

Fullerenes were the first creations using the new nanotechnology. They are a naturally occurring form of carbon, with each molecule containing around 60-80, and form a spherical shape composed of pentagons and hexagons, similar to the construction of a football. REF<sub>2</sub> These are a good basis for other molecules to be created around or to be developed from. They also provide an obvious base shape for a transport vessel, which can be used in medicine for applications such as drug targeting and carrying the drug through areas of the body like the stomach, where the fullerene is protecting the drug. They are based on carbon, and so integrate well in the organic environment of a person or animal, and so are very compatible with medicine.

The main use that will be focussed on for these specific structures would be in the creation of transport molecules, to encase current cancer drugs, that bond to the specific glycoproteins or glycolipids found on the outside of certain cancer cells, which could be identified using an autopsy of the cancerous tumour. REF<sub>3,0</sub> This could then be used to target the cancerous cells. REF<sub>3,1</sub> Further information about this idea will be discussed later on in this paper.

The drug delivery system would rely on molecules such as fullerenes and carbon nanotubes, which are a simple carbon structure formed by folding over a layer of graphene into a cylindrical shape. These could be developed into a very specific casing structure for the application it is created for. These molecules would allow us to store and transport another smaller molecule such as cisplatin – the chemotherapy drug – inside them. The fullerene is unreactive and won't cause any harm to a patient's veins and arteries. When these fullerenes reach the cancerous area, however, they could be broken apart by electromagnetic waves which would then release the drug into the cancerous region. The details of how this release would be carried out will be discussed later on in the paper.

## **Discussion:**

This section will be divided into 2 main sections the first section will discuss the creation of the new drugs themselves and the nanotechnology required for their creation. The second section will discuss the drug delivery system that will be used to more specifically target the affected area.

Cancerous cells are in many ways self-originating, being produced from your own cells, with no control of this replication by another separate organism. This means that in many ways, they are similar to normal cells, but there are a few ways in which they can be identified. The identification of these cells as different from normal is a key part of cancer development and research, and so would improve greatly the effectiveness and potential of current drug systems. Nanotechnology could have the potential to improve our identification systems greatly, and future development of our ability to manipulate these atoms with improved ease would make these theoretical solutions to a problem such as identifying cancer cells even more viable. The manipulation of structures on an atomic level is already possible, and after the production of a molecular 'IBM' label, made from Xenon atoms, the potential for this kind of structure and chemical manipulation has become even more obvious.

As cancer cells are very difficult to identify, targeting them is hard when the exact composition of a chemical compound or drug is not entirely controllable, but when the manipulation of the drug on a molecular level is possible, as it is now, to a certain level, production of specialised drugs becomes a realistic solution. Despite being produced by your own cells replicating, there are certain parts of a cancer cell which distinguish it from your other cells. One such thing is the glycoproteins and glycolipids, otherwise known as your cells antigens. Although very similar for many cancer cells and non-malignant cells, in many cases, there are a few glycoproteins common to the cells of the cancerous tumour, and not present on those cells which are not cancerous. To determine these specific glycoproteins, analysis of a tumour biopsy would have to be carried out, and so at first, this does not seem an immediate and common solution to the problem of cancer identification. However, if these antigens can be identified REF<sub>4.0</sub> and REF<sub>4.1</sub> then it would be possible to manufacture, using current techniques, a molecule which has a complementary molecular shape to the antigens present solely on these cancerous cells. The production of this molecule to be complementary in structure to these specific antigens on the cell's membrane would allow very specific identification of the cancerous cell, either by attaching a radioactive or fluorescent marker to the nanostructure, or by integrating the complementary site into a larger transport molecule, used to itself carry the drug to the site of the cancerous tumour. The theory of how this integration of the drug into the nanostructure and its release will be discussed later on in the paper.

Producing a molecule which is specific to this antigen which is identified via biopsy on the cancerous cells would be, in effect, mirroring nature and how viruses and bacteria currently bond to specified cell types and tissues. This means that the theory of producing a molecule

specific enough to be taken out of the blood stream onto one unique cell type is proven to have worked, and once the nanotechnological procedures and equipment have advanced enough to not only be able to create a structure specific to a design, but to be able to make it on a large scale (which is not unrealistic within the next few years), then it will be possible to design, as nature has done through natural selection, a molecule which has an exact complementary fit onto the antigens present on the cancerous cells. This is also similar to enzyme action, and so as an alternative to the release mechanisms mentioned later on in the paper, the act of bonding to the antigens themselves may be enough to disrupt the nanostructure of the transporting vessel, releasing the drug it contains into the targeted area, thus preventing it from affecting other cells. Nano-manipulation, in effect allows us to create our own versions of nature's systems, and allows us to create molecules which are not seen as foreign by our bodies, but are in fact very similar, and integratable with our body's cells and organelles, creating a method by which to prevent cancer drugs from affecting our cells, but allowing them to destroy cancer cells.

The complexity and variation that is present in protein structures in our body suggests that a protein molecule (similar to that of an enzymatic structure) would be a possible start and basis for a specific targeted structure, although if used as a transport molecule as well, the specific protein structure would have to be incorporated into or bonded onto an already existent structure such as a fullerene or nanotube, allowing a drug to also be transported with the molecule, delivering it extremely specifically to the cell itself. Advanced computers and modelling programs REF<sub>5</sub> would allow us to create such structures which are likely to be chemically stable, and the atomic manipulation that nanotechnology is beginning to offer would allow these complex structures to themselves be created.

A likely method for production of such molecules would be to use a carbon layer to create a base for the structure, and then to use atomic manipulation to build up a net-like structure on this carbon layer, creating the 'opened out' version of the molecular drug carrier. This structure could then be rolled or curved into a ball or tube like structure, encasing a drug molecule or group of molecules which would be released when the transport molecule is broken apart. This is a realistic projection of what may be possible within the next few years, as atomic manipulation and creation of nanotubes and fullerenes are already commonplace in the nanotech industry. Structures such as nanowires also show us that it is possible to incorporate other elements and encase them within these structures, and so the use of these molecules as drug transport molecules is achievable and is a logical progression from the current uses of nanotechnology.

The major advantage of this idea is that chemists and pharmaceutical companies would no longer need to 'discover' the molecules that they required for drug delivery (also has potential for construction of drugs without the side effects that some drugs currently cause), they would merely have to design what they needed, and production of this molecule could be carried out using the above processes resulting in an ideal compound or

molecule. This is a similar development to that which is seen in the surface science and material industries, where originally, natural materials were manipulated, but would have to be discovered, however materials are now created from scratch using the elements, and are designed for a purpose. This means that as our ability to control and manipulate matter is getting more and more advanced, and so the progression that has now been seen on a macro scale such as this can be applied to a nano scale, to things such as drugs and delivery molecules, allowing us to use our understanding of the body and its cellular function to control and manipulate them, ultimately allowing us to more effectively treat seemingly uncontrollable conditions such as cancer.

The main problem with chemotherapy is that the drugs that kill off the cancer cells also harm the healthy cells within your body. Although the damage done to the body is less compared to the damage done to the cancer, due to this chemotherapy must be stopped after a few treatments to allow the body to recover. However, during this period the cancer cells also have a chance to multiply again so the cancer can return. To improve this, better drugs could be created that only target the cancerous cells or cause less damage to healthy cells within your body. The other option is to only allow the drugs to act in the area of the cancer. This would mean that only a few cells would be affected by the drug compared to the number of cancerous cells affected. Now the drug could be delivered to the tumour by injection and this idea is being tested in Northwestern University in Chicago REF<sub>6</sub>. However the issue with this delivery system is that expensive equipment and skills are needed to work out exactly where the drug should be injected into the tumour; our method would require less specialists as the drug could be taken into the body through an Intravenous drip. This would reduce the chance of infection from the injection. The drug (mentioned above) would be held inside a fullerene or carbon nanotube. To get the drug inside the carbon shell atomic manipulation would be used (also discussed above) to temporarily open the fullerene and insert the drug into it. There could be problems with the fullerene's structure not wanting to break and if this was the case then a carbon tube could be used due to the open ends of the tube. To prevent the drug from leaving the nanotube, fullerenes could be added to the ends. As this is all theoretical there is the possibility that this method of getting the drugs inside the fullerene wouldn't work. The other option is to have the drug present when the fullerenes are formed so that the fullerene will form with the drug within it. Since it is unknown which molecule the drug will actually be stored in it can be assumed, for the purpose of dealing with the resonant frequency, that the storage molecule will be a fullerene.

With the drug now in a form that won't harm the body as it travels around the veins and arteries it can safely be taken into the body. However the drug won't be able to get out of the fullerene when it gets to the cancerous area. To release the drug electromagnetic waves would be used to break down the fullerene. This would require that the resonant frequency of the fullerene be known so that EM waves could be fired at it with the same frequency so that the fullerene would break apart. This theory is the same as when

microwaves heat up water because they have the same frequency REF<sub>7</sub>. There will be problems with this method depending on what band of the electromagnetic spectrum the frequency lies. If it is in the radio wave area then there is very little problem as radio waves don't cause damage to the human body so the only issue would be targeting the rays effectively (this will be discussed later). If it is in the microwave band then there may be problems as the microwaves could cause the water in your body to heat up and boil. To overcome this problem the microwaves could be fired from several different positions so that they overlap in the same spot in phase. This would cause a high energy spike where the waves overlap causing the fullerene to break down. Meanwhile the rest of the microwaves would be to low energy to cause any significant difference to the body. If it is infra red then the same technique could be used. However, if the infra red rays are fired as a laser (they all have the same frequency) then they would only be absorbed by molecules of a specific resonant frequency and the chances of your body's molecules having the same resonant frequency as a fullerene are quite low. Obviously more research would need to be done in this area if the frequency is within this range. UV rays would cause a problem as they interact with human skin

If the resonant frequency is in the UV part of the EM spectrum, then our delivery system may not be realistic, as it would not be possible as far as is known to apply the UV radiation to a point within the body, without affecting the body cells themselves.

X rays and gamma rays can both be dealt with in the same way. Although both of these types of electromagnetic rays are harmful they are used in radiotherapy. In radiotherapy they are used by firing 2 separate low energy beams at the same spot while moving them in a circle. The beams meet in phase so that the waves amplify each other causing a high energy spike where it's needed but less energy in other locations. This could be used in the same way for our drug delivery system with the beams being targeted together at a single spot so that the fullerenes break apart. Since the drugs would need to be broken down after they have spread throughout the body, the gamma rays would need to be in place for longer. Due to the longer exposure, more beams would be used so that a healthy cell would have less exposure to the radiation.

To make sure that the drug is released into the cancerous area of the body the waves would only be fired at this area. If the waves are relatively biologically safe, such as radio waves and infra red waves, then they could be fired at the whole area. On the other hand, if the waves needed are dangerous, for example gamma or x-rays, then they would have to be targeted at the major arteries and veins in the tumorous region. This is because the majority of the fullerenes would pass through these blood vessels and so most of the drug would be released into the system. Finally, because the drug may not act the instant it is outside of the fullerene, further experimentation would need to be done. This would make sure that the drugs react with the cancerous area of the body and don't just pass through this section without damaging the cancer cells.

## **Conclusion:**

To summarise the ideas in this paper; a method for the creation of new delivery molecules specifically targeted to the cancer cells found in your body through the biopsy of the cancerous tumour has been discussed. This has allowed a better method for the creation of drug delivery molecules to deal with cells that are nearly identical to healthy cells. The possibility of targeting these molecules so that the release of the drugs causes significantly less damage to the non-malignant cells in a patient's body has also been referenced and discussed. This would mean that the treatment could have more courses before the damage done to the normal cells is too high.

The main problems with these ideas as they stand are the mass production of these drugs. As it stands each molecule needs to be individually constructed by specialist equipment in a lab. This would make creating the drug very expensive and not very efficient, thus making this solution not particularly viable. However, as our knowledge and control of molecular manipulation increases, the creation of these drugs will become cheaper and more efficient, making this solution to targeting cancerous cells a more realistic option.

The main problem found with the delivery system is that there is no way of knowing the resonant frequency of a fullerene or nanotube without further experimentation. However, as mentioned in the discussion section there are areas of the electromagnetic spectrum that would make it a lot harder to use this drug than others. Although radio waves and infra red rays are relatively simple to use UV and visible light would be very difficult. However, as knowledge of UV grows it may be possible to get UV rays into the body without causing excessive damage to healthy cells. This is already being done with new technology that is using UV rays to image the body.

Overall we would say that our research does have some issues that need to be addressed. Our research is, however, currently theoretical, and so these problems could all be potentially solved within a few years allowing a greater rate of cancer survival.

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