NANOTECHNOLOGY

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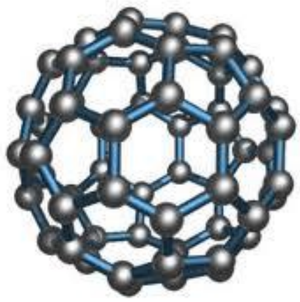
Abstract

This paper suggests nanotechnology has tremendous implications in the development of future both human medicine and veterinary treatment, and finds it to be hugely viable both today and in the future. There are various ethical points to consider against its heavily waged benefits but, taking all into consideration, it is clear that nanotechnology is an exciting prospect with unknown advancements and striking developments potentially at our fingertips. It encompasses the treatment of many of the most common diseases, to include heart failure, the UK's biggest killer affecting over 750,000 people. Severe heart failure has just a 40 - 50% chance of living another five years: worse than most forms of cancer. Cancer itself was responsible for 27% of all deaths in the UK in 2008 - 30% for males and 25% for females. The prospect of enhancing traditional methods and discovering new ways of treating these all-to-common medical problems promise great advantages.

Introduction

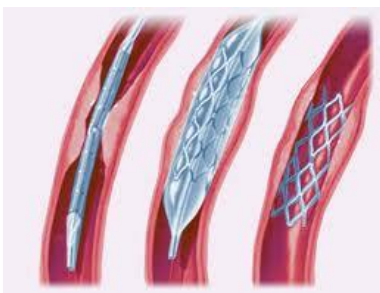
Nanotechnology is an exciting, new, upcoming field that has already has, and will continue to have, vast opportunities for the future of medicine. This results in major breakthroughs in medicine and veterinary science and thus human and animal health. The technology is based on previous findings incorporated with innovative ideas, an example being the use of the physical characteristics and behaviour of the Buckminster Fullerene – C_{60} [figure 1]. 'Buckyballs', as they are more commonly known, have many properties that make them useful in medicine, other than their nanoscale size. These benefits include they fact they are inert, nontoxic and, because of their size, can interact easily with cells, proteins and viruses. Furthermore, it is easy to put pharmacological agents inside them as they are hollow. Diagnostic imaging may also be a field where the C_{60} molecule can be used, as it is feasible to put radioactive agents inside the buckyballs. This will enable them to travel through the bloodstream and emit radiation. From a safety point of view in order to reduce the risk associated to radiation toxicity, the molecules are excreted intact and radiation is removed from the body, making it safer to use than traditional x-rays for unborn babies and mothers especially.



1. 'Buckyball'

Nanomaterials are increasingly used in diagnostics, imaging and several tumour-targeted nanomedicines have been evaluated. For example, the design of multifunctional nanoparticles capable of targeting cancer cells, delivering and releasing drugs in a regulated manner, and detecting cancer cells with enormous specificity and sensitivity. This is only made possible because of the extremely small size of nanoparticles of 500nm which allows them to penetrate cells and interact with cellular molecules. These are just a few of the examples of the potential application of nanotechnology to treatment in oncological diseases, with developments in other areas such as cardiology proving equally as exciting.

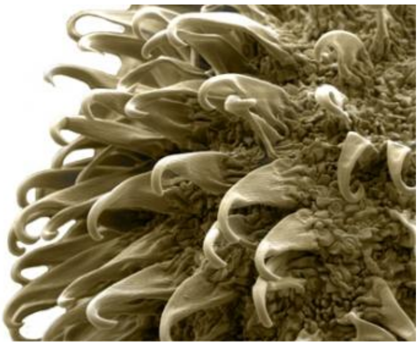
A current trial is with the stent [figure 2] used in the conventional coronary angioplasty procedure, which most commonly treats aneurism (a blood filled bulge in a blood vessel which weakens and can result in haemorrhage) or atheroma (fatty deposits which narrow and can block a blood vessel.) Stents either bypass the aneurism or widen the artery by compressing the plaque of the atheroma, improving blood flow. The nanotechnology is used alongside stents by releasing drugs, as well as in the material used to make the stent, in order to make the material less likely to be rejected by the body, a common risk



2. Stent

of the procedure.

Another current development in the treatment of heart disease are 'nanoburrs', the dubbed term for the nanoparticles that can cling to artery walls and slowly release medicine. The term 'nanoburrs' originates as they are coated with tiny protein fragments that allow them to stick to target proteins, in a similar way to the burrs that stick to pets fur, and have the added advantage of being designed to release the drugs over several days. Furthermore, drug-eluting stents have the disadvantage of a long term course of medicines such as aspirin and plavix, anti-platelet drugs to prevent clots forming in the stent or restenosis (the reoccurrence of stenosis, a narrowing of a blood vessel, leading to restricted blood flow.) The nanotechnology alleviates this, an obvious advantage of the development.



3. Nanoburr

Discussion

In the future, the hope is to use nanoburrs alongside stents — or in lieu of them — to treat damage located in areas not well suited to stents, such as near a fork in the artery (bifurcation lesions), diffuse lesions, larger arteries, and also already-stented arteries which may have more than one lesion. There are also conditions which do not allow for drug-eluting stent placement, such as in patients with renal failure, diabetes and hypertension, or patients who cannot take the dual drug regimen of clopidogrel (antiplatelet agent used to inhibit blood clots in coronary artery disease) and aspirin that is required with this treatment. It has to be exaggerated this is not 'Star Trek' science – researchers at Harvard Medical School and the California Institute of Technology (Caltech) have already expressed significant hope in this as a new form of treatment for one of the most common procedures; as many as one million Americans a year under angioplasties. For instance, Massachusetts Institute of Technology (MIT) Institute Professor Langer said "This is a very exciting example of nanotechnology and cell targeting in action that I hope will have broad ramifications." The nanoburrs consist of spheres 60 nanometres across, more than 100 times smaller than a red blood cell, and at its core the particle has a drug designed to combat narrowing of blood vessels bound to a chain-like polymer molecule. The time it takes for the drug to be released is controlled by varying the length of the polymer; the longer the chain, the longer the duration of the release, which occurs through a reaction called ester hydrolysis whereby the drug becomes detached from the polymer. Controlling drug release is already promising to be a very important development; as of today, drug release has been a maximum of 12 days. The hope is to be able to control it more easily, and with the speed of development currently, the wait promises to be short.

It is hoped nanotechnology will also aid in the alteration of stents themselves. They are currently made of a wire mesh of surgical-grade stainless steel or other types of metallic alloys, but blood vessels cannot recover full function with this. The nanomatrix coating, however, does allow for full recovery as it mimics natural endothelium, the substance that lines blood vessels. This will inevitably increase the long-term success of stents, in particular for elderly patients who are more at risk of a secondary episode at the stent insertion point. It should also reduce post-operative tissue scaring along the blood vessel wall which in turn should greatly reduce the possibility of future thrombosis (the formation of a blood clot inside a blood vessel) or blockage at the stent site.

Another advantage of the nanoburrs is that they can be injected intravenously - directly into a vein - at a site distant from the damaged tissue. It is currently in its trial stages but with the hope of progression, proving it is not ‘Star Trek’ science but based on current developments. For instance Mark Davis, professor of chemical engineering at Caltech, says the work is a promising step towards new treatments for cardiovascular and other diseases. “If they could do this in patients — target particles to injured areas — that could open up all kinds of new opportunities.” Trials in rats have shown that nanoburrs injected near the tail are able to reach their intended target — walls of the injured carotid artery but not normal carotid artery. Furthermore, the burrs bound to the damaged walls at twice the rate of nontargeted nanoparticles. The advantage of this is, because the particles can deliver drugs over a longer period of time and can also be injected intravenously, patients would not have to endure repeated and surgically invasive injections directly into the area that requires treatment. This would not only increase patient comfort and satisfaction but reduce the time in hospital for recovery, producing only benefits for those involved.

There is now testing in rats over a two-week period to determine the most effective dose for treating damaged vascular tissue. There are hopes that the particles may also prove useful in delivering drugs to tumours and could have broad applications across other diseases including cancer. This highlights the truly promising hopes for the nanoburrs, and the changes they could provide for medicine.

The development in drug delivery also proves to be a great advancement for medicine, and have enabled some of the predicaments of delivery in cancer to be overcome. Nanoparticles can be used as drug carriers for chemotherapeutics to deliver medication directly to the tumour while sparing healthy tissue. This is because particles are engineered so that they are attracted to diseased cells. This is a great advance because conventional chemotherapy uses cytotoxic drugs that not only kills cancer cells effectively but also kill healthy cells, leading to adverse side effects such as nausea, neuropathy, hair-loss, fatigue and compromised immune function. Not only could the use of nanoparticles in this area of cancer treatment potentially be more effective but the result of fewer side effects from this traumatic treatment would have great implications for the individual patient, as treatment could be less painful physically as well as psychologically. In addition to this nanocarriers have several other advantages over conventional chemotherapy. For example they could enhance the absorption of drugs into tumours and into the cancerous cells themselves because of the nanoparticles high surface area to volume ratio which allows many functional groups to be attached to a nanoparticle, which can seek out and bind to certain tumour cells. Again this is because of the small size of nanoparticles (10 to 100 nanometres’), which allows them to preferentially accumulate at tumour sites. This use of nanotechnology could make drug treatments more effective and efficient, reducing the cost of treatment as less drugs will be wasted as ineffective treatments. This allows more money to be concentrated into nanotechnology research, thus resulting in more developments. Alternatively it could be used in other areas of medicine, creating a vast range of indirect benefits for the health service.

In addition, nanoparticles allow for better control over the timing and distribution of drugs to the tissue, making it easier for oncologists to assess how well they work. Again this would not only directly improve the treatment of the patient, but also indirectly improve research and other areas by having this greater control of treatment.

Also with relation to cancer is an advancement entitled ‘quantum dots’ (semiconductor structures typically 2-10nm that can be made to fluoresce in different colours depending on their size and last much longer than conventional dyes used to tag molecules), which may be used in the future for locating cancer tumours, and would have an immense impact in treating cancer. This works as the nanoparticle is coated with a peptide that binds to a cancer tumour; once the nanoparticles are attached to the tumour the magnetic property of the iron oxide enhances the images from the MRI (magnetic resonance imaging scan). Using this MR technology the presence of specific substances in low concentrations can be detected not only more clearly but more rapidly and effectively. The implications this could have on medicine in future years is that cancerous cells could be detected in much early stages of development, helping prevent malignant tumours forming, thus greatly increasing survival rates.

Nanoparticles may, in the future, be capable of detecting malignant cells, pinpointing, visualizing their location in the body and killing cancer cells with minimal side effects by sparing normal cells and monitoring treatment effects in real time. The advantages for this would be great as it would treat the cancer before it begins as opposed to battling it once it has already formed, as is the most case currently. Again, this hypothesis is based on current information. For instance, a paper online entitled 'Nanomedicine: Nanotechnology, Biology and Medicine' describes specific delivery of a chemotherapeutic drug to specific cells in the lung. The author says "The technology is still in its infancy, but being able to conduct these experiments in the whole animal makes it more promising as a clinical application. The long-term goal would be to do targeted drug delivery through aerosolized techniques, making it suitable for clinical use." This proves the technology is there, ready to be developed and potentially utilised to a great extent.

'Nanotubes' are also a possible application as pharmacological agents that scientists have begun to look into. Currently the antibacterial properties of nanotubes are being considered, specifically those designed by chemistry professor M. Reza Ghadiri and co-workers at Scripps Research Institute. These nanotubes are formed by self-assembled stacking of cyclic peptides having an even number of alternating D- and L-amino acids. From examining cell cultures and studies on mice, it has been seen that the nanotubes have the ability to insert themselves into bacterial cell membranes, acting as potent and selective antibacterial agents.

One area of interest to scientists concerning bacterial and viral infections is the use of nanoemulsions. These can be defined as oil-in-water emulsions with mean droplet diameters ranging from 50 to 1000 nm. One current example is the utilization of soybean oil when it is emulsified with detergents to form 'nanodrops'. When the oil nanodrops contact the membranes of bacteria or the envelope viruses, the drops surface tension forces a merger with the membrane, blowing it apart and killing the pathogen. One very important characteristic of the nanoemulsion is that they don't affect cell structures of higher organisms, which makes it ideal to use in animals and humans. Whilst the nanoemulsion is safe when applied externally, unfortunately it has been discovered that the oil droplets can also destroy erythrocytes (red blood cells) and sperm cells. The reason seems to be that both types of cells lack the support structures that make other cells invulnerable to the effects of the nanodrops, meaning the nanoemulsion can't be used intravenously. This disadvantage will hopefully, with future research and trials, be extinguished, allowing for the utilisation of these promising molecules.

Current research is investigating the use of the tiny carbon based molecules for tissue engineering, with a recent breakthrough being the engineering of spinal cord receptor tissue. This receptor tissue, containing nerve cells, is responsible for carrying electrical impulses from the brain to give instructions on movement to other parts of the body. During a spinal cord injury this tissue is damaged and if broken permanently can lead to disability and the loss of control limbs. It is believed that through the use nanotechnology this tissue can be fined tuned and injected into a spinal cord victim at the area of injury. This tissue may then be capable to grow and link with the undamaged receptors thus completing the link. With the receptor tissue intact it will enable those with spinal cord injuries to transmit the messages from their brain to their legs to walk.

Projects for other uses for tissue engineering are now being tested to try and improve the medicine world. The growing and developing of lung and heart tissue is one major project in that in the future people may be able to have a heart/lungs grown and stored at a tissue farm. Therefore, when there is a need for transplantation, there will be an available and ready source, and would be hugely beneficial as one-fifth of those waiting for heart transplants die while waiting. The links with the use of carbon nanotechnology for the growth and development of the transplants as this is the basis of the engineering.

Within veterinary medicine, nanotechnology is able to create devices that are so small they are able to slip inside cells without being recognized by the immune system. The materials can provide scientists with opportunities to address specific problems and to tailor therapies in order to restore normal cellular function. As the need for different solutions in veterinary becomes increasingly urgent, due to the aging pet population, and the higher costs for veterinary care and medications, nanotechnology will allow the production of new therapeutical compounds to treat diseases. These new compounds - for example - would protect pets from viral or bacterial infections and accelerate wound healing. Also these new compounds could carry drugs and genes into cells, making treatment of diseases more effective.

<u>Ethical issues related to the development and application of nanotechnology</u>

One of the most problematic issues currently, and applies to all fields of research, is that reducing the size of structures to nanolevel results in distinctly different properties of particles. This very small size appears to be a dominant indicator for toxic effects of particles. Therefore, nanoparticles possess a separate problem with the issue of its toxicity. And so chemicals and materials in nanoformation need to be evaluated for their activity and toxicity as nanoparticles. This is because one problem found is that some nanoparticles are non-biodegradable and could accumulate in certain organs e.g. the liver. Further investigation is underway to define the potential harm this could cause.

The general future of nanotechnology is vast and varied: it will affect many areas of day to day life other than human and veterinary medicine. However due to the number of considerable developments it proposes nanotechnology raises a large number of ethical concerns. With the ability to engineer the tissue of hearts, lungs and other organs, will this prompt scientists to create a super race of humans? One with advantages like being able to run faster and farther, jump higher, and hit or throw a ball farther than before? The use of nanotechnology in sport pressures the moral apprehensions; will athletes be tested for engineered parts, like they are now being tested for steroids?

As the industry for scientists being able work at molecular level grows there will be numerous benefits worldwide, in a number of different areas including those of:

- Manufacturing; Precision Manufacturing, Material Reuse, Miniaturization
- Medicine; Pharmaceutical Creation, Disease Treatment, Nanomachine-assisted Surgery

- Environment; Toxin Clean up, Recycling, Resource Consumption Reduction

All of these advantages will help to improve the lives of people not just medically but indirectly also, as the technology could protect the Earth if it is used to reduce our natural resource consumption and the production of toxic gases. If people are able to incorporate this potential technology in an array of fields, what is to stop them using it in, for instance, war? The new technology could see the production of more powerful and destructive weapons, which can then be used to exert a person's/ group's authority and strike fear into a population. This is currently happening in Libya where the armed forces are used to attack the rebels, and as the death of civilians' increases prompting other countries to take action. Additionally, nanotechnology could also be used to create biological weapons, or a 'super' army, genetically better than the opposition. This then raises the issue of perfectionism of the human race and, in a similar way to the mid-20th century Holocaust and the Germans aim to create a racially pure Aryan nation, nanotechnology could be used to create a genetically superior human. Although many of these threats may seem far-fetched or 'Star Trek' science, these may be dilemma's faced by future generations as the technology becomes more advanced, and need to be considered in the present. A closer danger of nanotechnology, although may be less obvious, nonetheless equally concerning, is the use of nanotechnology in electronic surveillance. It could be used to oppress our freedom and privacy; people could use molecular sized microphones, cameras, and homing beacons to monitor and track others.

Another potential problem is that, because of the invisible nature of nanotechnology, it easier to 'disguise' products containing it which could lead to invasion of privacy or the carrying out of procedures that require consent, even without the patient's knowledge. This may be particularly pertinent with regards to clinical trials of nanodrugs in developing countries and needs to be addressed and disassociated with the name of nanotechnology as it is unethical. In the future, consent must be given and proven that all those involved in trials are fully briefed before they are put at potential risk to eliminate this. Overall the paper supports the idea that nanotechnology is an invaluable new resource which we should make full use of to extend our current medical abilities and set a stage for future abilities, whilst maintaining high standards with relation to ethical issues.

While nanotechnology may never become as powerful and prolific as envisioned by scientists it will, as with any potential technology, raise ethical issues both religious and scientific. These moral problems need to be found and solved however, before the technology is irreversibly adopted by society. Scientists must examine the ethics of developing nanotechnology and create policies that will aid in its development, so as to eliminate, or at least minimize, its damaging effects on society.

Conclusion

Conclusively, the paper highlights some of the key treatments the nanotechnology could be used for, to include heart disease and cancer. Its use in veterinary medicine should not be underestimated either, and developments in either field can potentially overlap to benefit both human and animal health.

With any new technology there are important ethical issues which need to be addressed; a variety included in the paper. With more research and trials there is confidence these will be dealt with in order to fully utilise the truly great potential nanotechnology has. Some developments it could provide are also summarised here; it has to be reiterated they are primarily based upon current technology and any hypotheses based upon sound, scientific research. This only emphasises the great influence nanotechnology has and, we believe, will continue to have, in medicine.

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