

A WAY TO END ALL INJECTIONS IN DIABETICS

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Abstract

Our project is about how nanotechnology can be used to improve people's lives and how it can be used to replace conventional medicines, especially in the treatment of diabetes. The paper goes into detail about the different ways in which nanotechnology is used today and how it may be used in the future. Due to the versatility of the particles, in the future it may well replace most modern medicines and allow almost everything to become miniature and will an increased pressure on 'waste' I think it will definitely sway towards that as if nanotechnology is used it does allow less waste as the application of drugs is more specific so less is 'lost' in by other means. At the moment the biggest concerns and the complexity of it and also the cost, once we understand more about the subject, not only will be able to do more with the knowledge in terms of putting nanoparticles to work in more cases but the price of making this specialised equipment will decrease. However, this future thinking is not without complaints. We will also go into the various ethical issues that lots of people are concerned about.

Introduction

Nanotechnology translates to "midget" technology and it truly is, three atoms measure about 1 nanometre which translates to 10⁻⁹m and is in perspective a human hair is approximately 200000nm. Eric Drexler describes nanotechnology as "Engines of Creation" and he was correct. Nanomachines are tiny machines built from individual atoms to manipulate matter at the atomic scale (usually between 1 and 5 nanometres). When working on such a small scale, the building blocks are individual atoms and molecules.

Nanotechnology is used around the World in areas from cancer treatment to suncreams and from battery boosters in mobile phones to tennis racquets. This shows how widely they can be used and what potential they have for the future.

Here are some examples of what nanoparticles can do; nanotubes are folded sheets of carbon atoms and are 100 times stronger than steel and 1/6 of the weight. Due to their size and dramatically increased surface area to volume ratio nanoparticles can consist of van der Waals forces of attraction, atomic bonding (ionic, covalent and hydrogen bonding), electronic charge and quantum effects, which means they often display different properties compared with the same materials on the macroscale. For example gold is solid at room temperature, but as a nanoscale property it is liquid at room temperature. Nanomaterials have very distinct properties and their fabrication is becoming increasingly popular on a practical level.

Applications in medicine

Nanotechnology is often described as biomedical technology or nanomedicine, these terms do mean the same thing which is the use of minute particles in medicine. Due to the size of these particles they can be used in almost every medical application, even though this is the case at the moment it is too expensive and complicated for it to be worthwhile in using them in every situation. The versatility of the particles is due to the fact that they are a similar size to most biological molecules so they can work like them and move around the body in a similar way to them. For example,

nanoparticles can be used as contrasting agents or markers so in images taken of the body certain areas can be shown to be more obvious or easier to see. Also, quantum dots (nanoparticles that use excitations to become coloured and emit different colours depending on different factors) are now used instead of conventional dyes, these have been shown to watch blood flow in the tissue of mice, this means that the images produced were of such a quality that the walls of the blood vessels can be seen to ripple with every heart beat. This is a massive positive step toward the future of medicine. What you can now do is to add antibodies or other molecules to the dots, this means that not only can you see the different types of cells and how they act but also they can target specific cells and use the images to track cells and even identify cancerous cells, this would mean it is a lot easier to treat cancer due to the quick diagnosis and therefore quick treatment. Nanoparticles have many other uses other than to just 'watch' cells, they can be used to encapsulate drugs and release them in very specific areas of the body, these porous nanoparticles are known as buckyballs or dendrimers, this technology has a large effect because they meant that less medicine is used in the body (due to it all going to the specific site it is needed) and therefore the potential side effects to the patient and the costs are minimal.

Another use of nanotechnology is in the replacement of skin grafts. Skin grafts are used where there is not enough skin (usually after an incident where the area affected has no skin and therefore to protection from infections) the extra skin is often taken from the thigh and is literally shaved off the person's leg (if this is where it is taken from) this is acutely painful (they are often said to be more painful than the injury they are covering) and take months of recovery, even then the areas they are taken from are never the same. The skin can often not be extracted from anywhere else or made due to the victim's specific antigens which means that most other skin would be rejected from the body, this means that the patient not only has to go through the ordeal of their first injury but has to deal with the months of pain from where their skin graft was taken, this also leaves them at risk of contracting an infection through unprotected area where the skin has been taken. There is an alternative to this now, you can use tissue engineering to 'help' own skin to grow back, they are artificial materials which act as support to our skin, these materials can be made of nanomaterials which are impregnated with cells which are stimulated to grow. This has been adopted by many hospitals to treat patients such as burn victims who would need to have too much skin than can be produced in a skin graft.

Tissue engineering is extremely helpful in not only skin grafts but with conventional artificial body parts or organ transplantation and can help hundreds of thousands of people but it is not without drawbacks, there is much debate as to whether it is ethical to engineer specific cells to do specific things, and is closely related to the controversial debate over stem cell research, this is because one major way of obtaining the tissues which are used to stimulate the skin to grow is from stem cells.

In vitro there are also many uses for nanotechnology, for example they can be used as tags or labels in biological tests to identify and measure many different substances and not only are the results obtained faster and are more sensitive but it means injections are needed less often which many people would think is a huge positive step in how medicine is administered.

Due to the minute scale of the nano-devices they are perfect for dealing with the human body as these devices fall in to the same scales as many of the building blocks of the human body, such as tissues, enzymes and chemicals such as insulin and glucose. This means that they can be administered in the body and can act as an individual molecule.

Discussion

Diabetes is a common life-long health condition, there are a staggering 2.8 million people diagnosed with diabetes in the UK. It is a condition where the amount of glucose in your blood is too high because your pancreas doesn't produce any insulin, Type 1 diabetes. There is also Type 2 diabetes, the problem is not a lack of insulin output but increasing resistance of your cells to the effects of insulin which means the output of insulin is increased and eventually the pancreas becomes unable to cope. Approximately 30 % of people with Type 2 will eventually require insulin treatment.

Insulin is a hormone produced in the pancreas and removes the glucose from the blood as soon as it enters the gut and helps it enter your body's cells for respiration to occur. Insulin stops the blood sugar levels from getting too high, without an adequate amount of insulin people with Type 1 diabetes blood sugar levels rise and the body will start to burn up its fat stores. In a few days this leads to a condition called diabetic acidosis, which is life threatening. Also too much insulin leads to such low levels of blood sugar that it causes a condition called hypoglycaemia with symptoms include shaking, perspiration, rapid heartbeat, and blurred vision. In some cases it can cause loss of consciousness and convulsions.

The current method is to inject insulin under the skin, normally into the thigh, buttocks, abdomen or upper arm whenever necessary. It cannot be taken orally because the insulin is inactivated by the digestive enzymes in the gut. For all of us that don't have diabetes think of the hassle and unpleasant process patients go through when they are supposed to get numerous injections every day (sometimes before every meal). Even the site that it enters through the skin cannot be overusing because it can cause the fatty tissue there to thicken called lipodystrophy leading to erratic absorption of the insulin, it can even lead to collapse veins.

The long-term side effects of diabetes can include heart attacks, strokes or blindness. The cost of treating diabetes is in excess of £5 billion a year to the NHS. A massive amount of money has been invested into diabetes research over £6 million in 2009. In diabetes the aim is to make the devices more user-friendly and ensure the patient easily accepts the insulin. A few different methods have been researched using nanotechnology to cure diabetes these include implants millions of pancreatic cells that secrete insulin into tiny capsules that can be implanted into

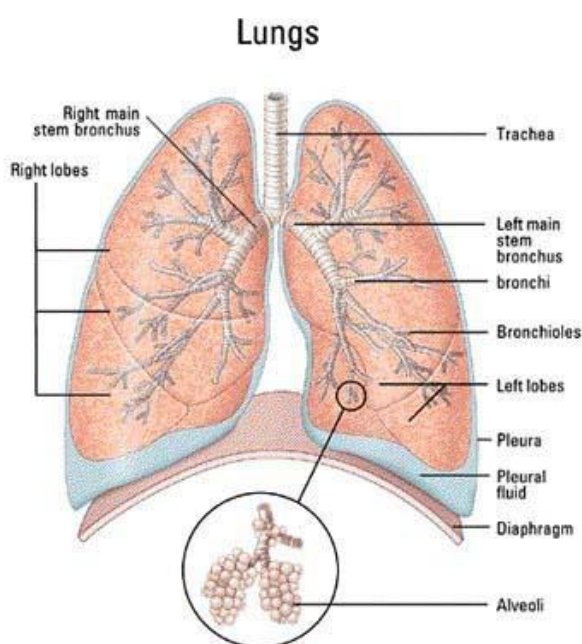
the body in an attempt to create an artificial pancreas. When blood sugar flows inside the capsule, it stimulates the cells to produce insulin to control sugar levels. The device has nano pores, so miniscule that the body's antibodies cannot get in to attack the cells, but large enough that the insulin can flow out and into the body, this is in the early stages of research.

Another suggesting is implanting a nano sized device in the body that can measure the blood glucose level in the body and let the patient know when the insulin is needed and how much to inject. This is a good idea as at the moment every time a diabetic wants to check their blood glucose levels they have to prick their finger and test their blood, with 16 million people in Britain having a phobia of one sort of another (and one of the most common being heamophobia- a fear of blood). However unfortunately this doesn't stop injections being required.

We have focussed out research on a promising method under investigation that would facilitate patients to inhale insulin using an inhaler so it will be transported down to the lungs and then be absorbed to the blood steam though the alveolar walls of the lungs, resulting in no more painful injections. It would also mean that some people who have a phobia (or are even scared) of needles can have an easy alternative which can give them a better quality of life.

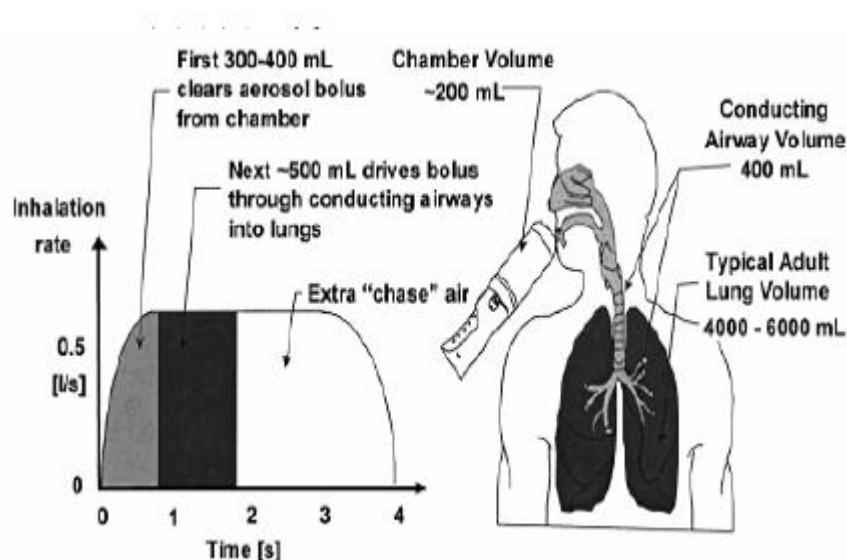
The idea is to inhale powder full of porous nanoparticles that are filled with insulin. The pulmonary route offers many advantages; it has a large surface area for drug absorption ranging from 100-140m squared. Also the alveolar layer of tissue has permeability that allows for rapid absorption of solutes. The human airway is lined with cilia which transport mucus and the clearance of the alveolar lung tissue is slower than that of the bronchiolar tissue which means there is a greater amount of time for the absorption of larger molecules like insulin. This route via the lungs means the insulin acts faster than the regular insulin injections.

The inhalers would use an aerosol (a suspension of solid material and liquid droplets in a gaseous medium) and the drugs would fall because of gravity into the airway as a sediment and then diffuse across the alveoli. A problem is the particle may change size in the high humidity atmosphere respiratory tract. It has been researched that the ideal delivery of particles into the deep lung region is between 1-5 nanometres so nanoparticles are the idea size. During breathing, the nanoparticles pass, along with air, from the larynx to the lower airways that start in the trachea and are followed by the successive junctions into the bronchi and bronchioles within the lungs. The rate of drug absorption is expected to vary at different sites within the lungs due to a variable thickness of the mucus



secreting surface. There is a step increase in the surface area of the lungs within the alveolar region, which is the target site for drug deposition when total drug absorption is desired.

In research they have tested the most effective way of getting the nanoparticles full of insulin into the deep lung. Once inhaled dosing occurs during emptying of the chamber volume (200mL), specifically within the first 300-440mL of the inhalation breath. The following 500mL of inhalation volumes moves the dose through the leading airways into the deep lung into the chamber, and enables inhalation delivery of the powder to the patient. The nanoparticles dissolve across the alveoli easily because of their small size directly into the capillaries that surround the alveoli the blood then travels down the pulmonary vein into the heart and then pumped out through the aorta to the rest of the body where insulin can be distributed out through the porous nanoparticles.



The process is not ideal a major disadvantages with inhalers is that there is a low drug content per inhalation because the particles have to be so small for them to dissolve, so multiple doses might be necessary.

Ethical issues

Nanotechnology as a whole may be a relatively new idea but it has been seen in nature for millions of years (fig 1)

NANOPARTICLES IN NATURE AND OUR ENVIRONMENT		
Natural	Anthropogenic	
	Incidental	Engineered
<ul style="list-style-type: none"> • Volcanic ash • Ocean spray • Magnetostatic bacteria • Forest fire smoke • Clouds • Mineral composites 	<ul style="list-style-type: none"> • Combustion products • Frying, cooking • Sandblasting • Mining • Metal working • Degradation products of biomaterials 	<ul style="list-style-type: none"> • Carbon nanotubes • Quantum dots • Sunscreen pigments • Fullerenes • Semiconductor wires • Metal catalysts

Fig 1

Even though this is the case, at the moment people are exposed to extremely small amounts to nanotechnology and therefore are at a much reduced risk. When they become more financially viable and available they will be used more frequently and will end up being in most consumer products. Will the nanotechnology begin harming people before it's too late?

This is possible, especially as it is the processes that make the nanoparticles that have the possibility of causing harm, so once you have nanoparticle construction on a large scale it is very possible that the health effects begin to be more obvious. It is the processes such as bioaccumulation, biodegradation, fate, and transport which will have more obvious effects on the local community and the way people think of the engineered nanomaterials. Also due to the porous nature of many of them, they are highly reactive and could also harbor unwanted materials.

"Too often, discussions about the social and ethical issues surrounding new technologies are treated as afterthoughts, or worse still, as potential roadblocks to innovation. The ethical discussions are relegated to the end of scientific conferences, outsourced to social scientists, or generally marginalized in the policymaking process," says David Rejeski, the director of PEN (Project on Emerging Nanotechnologies).

Imagine if terrorists got a hold of the technology that has been manufactured to be much smaller than the eye can see and which is designed to either carry materials or attack specific areas in the body, this has the potential to be one of the most powerful weapons in the world, it may seem farfetched but a few years ago the whole idea of nanoparticles being sent into our bodies to do a certain job would have been farfetched! In the future when (and if) nanotechnology is manufactured on an industrial scale the many factories producing them will have the ability to produce many possible life threatening products.

However as the technology is relatively new no-one knows what the associated risks are especially free nanoparticles that are not part of another material that could interact if these are unintentionally inhaled into the body, the release of these materials could also affect specific ecosystems within the environment. As with all new research International bodies are overseeing future applications.

Conclusion

Over the last 50 years we have seen a gradual increase in instances of diabetes and governments and health organizations are now addressing the problem. We are seeing more and more money invested into research and awareness campaigns trying to stem the massive increase in the number of those at risk of developing diabetes, especially diabetes type 2, in later life. Unfortunately there is little likelihood of a short-term breakthrough in the world of medicine which would cure diabetes and lots of the research projects like incorporating insulin into nanoparticles is still in the early research stages. We feel nanotechnology could be the way forward, but we need to invest money for it to go through vigorous trials and tested on animals and humans looking for side effects before it can be used by the public.

The prevention of diabetes is one of the great challenges of the future and one which needs to be addressed sooner rather than later before the situation runs out of control.

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