

NANOTECHNOLOGY IN MEDICINE = NANOMEDICINE

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RESEARCH PAPER
BASED ON
PATHOLOGY LECTURES
AT MEDLINK 2010

Abstract:

In this research paper based on gedanken experiment I will be investigating into a sub disciplinary field of nanotechnology called nanomedicine. Nanotechnology is defined as the study of manipulating matter on an atomic and molecular scale. It generally deals with structures which are just a few nanometers in size. Professor Norio Taniguchi from Tokyo university described it as "the processing of, separation, consolidation, and deformation of materials by one atom or by one molecule" in his paper in 1974.

Nanomedicine being the medical application of nanotechnology is what I will be focusing on in this research paper. I will investigate into the many ways nanomedicine is currently being used and how it is revolutionizing medicine as well as well as realistic future developments based on current level of knowledge and technology. Some issues associated with nanotechnology will also be discussed along with the analysis of its benefits and risks.

Introduction:

Since Richard Feynman's talk at the American physical society in 1959 titled "There's plenty of room at the bottom" many advancements have been made in nanotechnology.

In the 1980s Drexler looked at the deterministic idea of nanomedicine and promoted its importance through books such as 'Engines of creation: the coming era of nanotechnology' and his vision called "molecular nanotechnology". Since than importance of nanotechnology for medical applications has grown. One of the priorities of the National institutes of health (NIH) is to develop nanotechnologies for medical applications. Eight nanomedicine development centers have been established as a result which are investigating into new ways in which nanotechnology can be used in medical operations.

Processes in the body take place due to specific interactions within molecules and because nanotechnology is focused towards molecular precision, it could be very helpful when it comes to treating illnesses. Although devices on a molecular scale used to treat patients (nanorobots) are still a vision but nanomedicine involving engineered molecules has emerged. One advancement is the smart drug developed by Yoshihisa Suzuki of Tokyo University in Japan which only releases antibiotics in the presence of an infection.

The table below shows a list of companies which are currently using nanotechnology for several medical applications.

Company name	Type of medical application	Description of the product in development
Eiffel Technologies	Drug delivery	The company is aiming to reduce size of drugs to 50-100nm.
NanoCarrier Co.Ltd	Drug delivery	The company is developing miceller nanoparticles in which drugs and proteins can be encapsulated for delivery.
Advectus life sciences Inc.	Drug delivery	Polymeric nanoparticles engineered to carry anti-tumor drug across the blood-brain barrier
BASF	Toothpaste	Producing hydroxyapatite nanoparticles which have the potential to improve dental surface. This could reduce chances of tooth related problems such as tooth decay and acid erosion.
Oxonica	Sunscreens	Transparent nanoparticles which can absorb UV radiation preventing risk of skin cancers and tumors.
NanoBio Corporation	Pharmaceutical	The company is developing antimicrobial nano-emulsions which will have the potential to be used as disinfectants and also in skincare products.
KES Science and Technology Inc.	'AiroCide' filters	These filters will have nano-TiO ₂ which can destroy pathogens in the air. Hence this will reduce the chances of airborne diseases such as influenza, chicken pox and common cold or throat infection in public places such as hospitals.

Salata *Journal of Nanobiotechnology* 2004

There are several applications of nanotechnology in medicine. Both recent, current and future developments will be discussed in this paper

Discussion:

As it stands now several developments in nanomedicine can be seen. There are several types of nanomaterials being used in medical applications and more are being developed.

In early 1980s the development of scanning tunneling microscope (STM) led to the discovery of two very important nanomaterials: carbon nano-tubes and fullerenes which are also known as Buckyballs. Carbon nanotubes are currently being tested in Kanzius therapy. Unlike chemotherapy where normal body cells can also be damaged along with cancerous cells Kanzius RF therapy uses single-walled carbon nanotubes (SWNT). These can direct radiation only at cancer cells preventing damage done to normal functioning body cells. Kanzius therapy aims to induce apoptosis of cancerous cells using heat transmitted to a site by nanoparticles using radio waves produced by the Kanzius Machine. Similar to single carbon nanotubes 'gold nanoshells' can also destroy cancer cells especially soft-tissue tumors. This is because of their ability to absorb infrared radiation. After being administered these nanoshells enter tumor cells and radiation is applied. The nanoshells absorb the energy from radiation and heat up to kill the cancerous cells. Some nanoparticles release electrons at tumor sites they have bonded to when activated by X-rays. Nanobiotix has already released preclinical results for this technique. Its product Nbtxr3 has been demonstrated to be uptaken by mammalian cancer cells with good dispersion at tumor sites leading to a total regression of tumor on all animals tested.

Nanomaterials can also be used in drug delivery. This application of nanotechnology in medicine is still in development by companies highlighted in the table earlier. Doctors will be able to administer drugs in nanoparticles into patients. This can reduce the overall drug consumption and reduce its side effects because the drug will only be delivered to the region where needed. As suggested by Dan Luo, Cornell assistant professor of biological and environmental engineering drugs could be encapsulated in Buckyballs to be carried into cells, where natural enzymes would break down the DNA, releasing the drug. Buckyballs also known as fullerenes are 70% hollow from the inside so making them excellent for encapsulating drugs in. Because of their size drugs encapsulated in Buckyballs can pass from the stomach into the bloodstream so they can be given orally. Encapsulating drugs in nanoparticles also prolongs their life instead of for example directly injecting them into a tumor often since often causes them to diffuse away before effectively killing the tumor cells. Another use of Buckyballs is to trap free radical products in an allergic reaction and block inflammation that is caused by an allergic reaction.

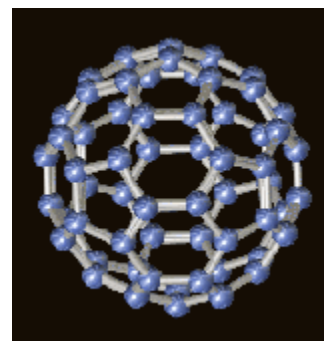


Fig 1 Copyright Dr. Roger C.

In certain medical applications such as Photodynamic cancer therapy nanoparticles can be used for drug delivery. In this therapy a greater quantity of a special dye that is used to generate the cytotoxic atomic oxygen is taken in by the cancer cells in contrast to healthy cells. Due to this, only the cancer cells are destroyed when exposed to a laser radiation. However some of dye molecules can migrate to the skin and the eyes causing harm. The patient can get sensitive to daylight exposure for weeks. According to the American journal of chemical society, test carried out at state university in New York researchers

used the hydrophobic version of the dye molecule can encapsulated in a nanoparticle. The results were that the dye stayed trapped inside the Ormosil nanoparticle which also prevented it from spreading to other parts of the body hence avoiding side effects highlighted earlier. At the same time, its oxygen generating ability was not compromised.

Another recent application of nanotechnology is tissue engineering. Natural bone surface has features on its surface which are around 100nm across. If artificial bone transplants were left smooth it will lead to the production of a fibrous tissue covering the surface of the implant. This will loosen the implant as the layer reduces the contact between bone and implant and will lead to inflammation. Nanosized features on bone surfaces can reduce chances of rejection as they stimulate osteoblasts responsible for bone development and growth. As shown by work of Dr. Wang of the Department Biomedical Engineering at Stevens Institute of Technology, principles of nanotechnology like the 'bottom-up' approach can enable bones to be regrown on carbon nanotubes scaffolds. Research at University of California has also shown that carbon nanotubes are suitable scaffold materials for osteoblasts proliferation and bone formation.

Nanoparticles are also useful in oncology, especially in imaging. Quantum dots are fluorophores. They absorb photons of light and then re-emit the photons at different wavelengths. When Quantum dots are used in conjunction MRI detailed images of tumor sites can be produced. Quantum dots are brighter than organic dyes and therefore give better contrast in images. Whereas other dyes deteriorate quantum dots have also. Long-term photostability so they can be used for live-cell imaging and tracing. This property also makes quantum dots helpful in tracking drugs or a group of cells in the body. Quantum Dots may be used in the future for locating cancer tumors in patients as well as performing diagnostic tests in samples. Invitrogen's website provides information about quantum dots that are available for dual purposes although currently in vivo tests are only being done on animals. Iron oxide nanoparticles can also be used in medical imaging. These are coated with peptide bonds which enable them to attach to tumors. The magnetic property of iron oxide nanoparticles gives better quality images in a magnetic resonance imaging (MRI) scan.

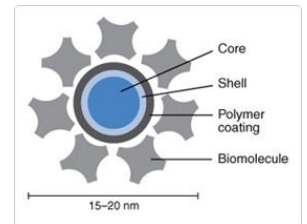


Fig 2 Schematic of the overall structure of a Qdot®

Nanoemulsions are also being developed by some companies. These are as oil-in-water emulsions with mean droplet diameters as small as 50nm. They are prepared by high pressure homogenization. This produces particles with a lipophilic core surrounded by a layer of phospholipids. Due to their lipophilic interior nanoemulsions are more suitable for transporting lipophilic compounds than liposome's making them better for skin care products. They

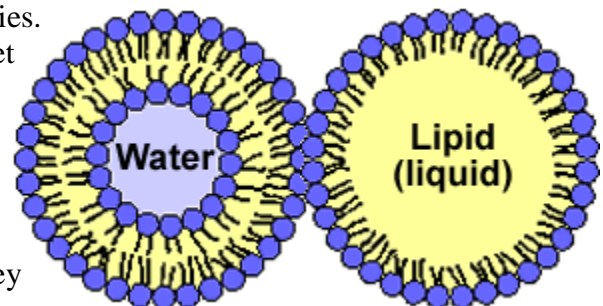


Fig 3. On the right is an illustration of a nanoemulsions compared to a liposome on the left. <http://www.azonano.com/Details.asp?ArticleID=1244>

are able to transport suitable lipids to skin and can reduce the transepidermal water loss from skin. This indicates that the barrier function of skin is strengthened by using nanoemulsions. These nanoemulsions also do not cream which allows pharmaceuticals to formulate liquid products that can be sprayed. These also don't show phase separation when stored so a better product quality is ensured.

Nanoparticles can also be used in surgery. This has been demonstrated by experiments at the Rice University where in an experiment two pieces of chicken meat were fused into one using a flesh welder. To do this the two pieces were placed side by side and gold nano shells were applied at required place of fusion. An infrared laser was then traced along the seam which welded the two pieces of meat together. This could solve the difficulties and blood leaks caused when the surgeon tries to restitch the arteries that have been cut during an operation such as a heart transplant. Arteries can be welded to stop blood loss. Another way to reduce bleeding is by using Aluminosilicate nanoparticles. These can quickly reduce bleeding by absorbing water from the can more quickly reduce bleeding in trauma patients by absorbing water from the blood causing it to clot at the site of wound quickly. Currently a company called 'Z-Medica' is producing medical gauze that uses aluminosilicate nanoparticles.

As it stands now companies are focused on applying nanotechnology in drug delivery and therapies. However in the future we may be able to produce nanorobots. This could be a possible future application based on current technology and understanding. Designs of such nanorobots have already been developed and are many are still in development. Two of the main labs working on nanorobot designs are the 'Instituted of robotics and intelligent systems' and 'Nanomedicine center doe nucleoprotein machines'. According to current designs these nanorobotic devices will be able to carry out different functions and will be ranging from 1-100nm in size. The material these dives could be made out of could be carbon in the form of diamond or fullerenes can be used too. These both materials provide a good strength to weight ratio. Nanorobot designs highlight their smooth exterior coating. This is to avoid causing an immune response from the body's immune system. Diamond coating can be used. Although such designs have been developed by research labs but no working model has yet been developed so far. Nanorobots can derive power by metabolizing local glycogen and oxygen. Externally supplied acoustic energy could also be another option. Communication with the nanorobots can also be achieved by acoustic signaling.

The medical nanorobots of the future could take various forms. Recently a design for a nanorobotic device named the 'Respirocyte' was made by Robert A. Freitas Jr. who is a research scientist at Zyvex LLC, a nanotechnology research and development company in Texas. This was a spherical nanorobot made up of around 18 billion atoms yet no bigger than a bacterium. The atoms were precisely structured in a crystalline manner to form a pressure tank which could hold up to nine billion oxygen and carbon dioxide molecules. This makes them a lot more efficient than red blood cells as 'Respirocytes' can hold and transport 200 times more gas per unit volume. Respirocytes would have sensors to signal them on when to load oxygen and disassociate carbon dioxide. Molecular pumps could be used on the Respirocytes to control the flow of gases. Due to a high carrying capacity of oxygen molecules respirocytes can be remarkably beneficial. They could keep tissue oxygenated for up to four hours after a heart attack.

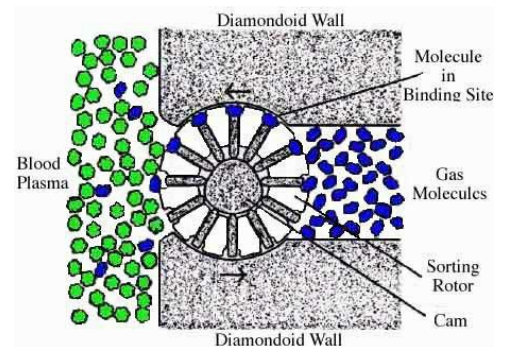


Fig 4 Respirocyte delivering oxygen molecules to tissue.
(<http://dev.nsta.org/evwebs/10955/page4.html>)

Another future possibility of nanorobots is their application in terminating pathogens in the body. Designs of a mechanical phagocyte called the 'microbivore' have been created by Robert A. Freitas Jr. The microbivore measuring 3.4 microns has a spherical shape and consists of 610 billion structured particles. As it measures just 3.4 microns it is able to pass even through the narrowest capillaries in the human body which are 4 microns in diameter. According to the designs the microbivore will be able to digest pathogens in one gulp. Microbivores will follow a digest and discharge protocol and are estimated to be a thousand times more faster-acting than the body's own phagocytes. They will be able to give significant help to the immune system and could eliminate an infection within minutes. Microbivore if developed can reduce mortality caused by illnesses in our society.

There are several other theoretical possibilities relating towards the uses of nanorobots for example nanorobots can also be used to cure skin diseases. A cream with nanorobots can be applied. The nanorobots can remove appropriate amounts of dead skin, remove excess oil and apply moisturizing compounds. This can prevent skin from getting dry and damaged. Nanorobots can also carry out pore cleaning tasks by cleaning out pores. This can prevent them from clogging up and reduce the chances of a patient developing acne. Nanorobotic devices can be injected into the blood stream which can eliminate atheromas in the arteries and reduce atherosclerosis. This can restore arteries to their health. Cell herding devices could restore artery walls. This would prevent the chances of coronary heart disease. Nanoparticles in mouthwashes can be used to destroy pathogenic organisms in the mouth. This could decrease chances of tooth decay and mouth diseases.

Conclusion:

Nanomedicine and nanorobotics are relatively new areas of science but they offer much technological advancement for humanity. Many forms of nanomedicine have begun to appear and may yet to be explored by researchers. It is assumed that in 20 years time several applications of nanotechnology in medicine such as drug delivery, tissue engineering and Krazius therapy will be common. If nanorobotics becomes a reality and nanorobots are successfully developed they will not only eliminate disease; they will actually improve on the gifts of nature. Bones would become stronger with the addition of diamond scaffolding. Nanometers could be implanted in muscles to make them more powerful. Nanorobotic devices can reduce aging. According to many scientists aging is a result of several molecular processes and malfunction in cells. If nanomedicine can learn to reverse most cellular malfunctions this could mean that elderly people could be able to recover health, strength and beauty, and enjoy a significant extension in life.

Nanorobotics may seem like science fiction at present to many but futurists believe that it will be a part of our lives by 2030. Considering how much medicine has evolved over the past 100 years it is realistic to say that nanorobotics will be a reality in a few decades. Medical advances took place at a stunning rate in the twentieth century. We now have cures to numerous diseases which were not even named before. Application of nanotechnology in medicine will become widely available by the middle of the 21st century as estimated by many scientists. This could help reduce human suffering such as a chemotherapy which could be replaced by Krazius therapy. Microbivores could end suffering caused by an infection within minutes. Respirocyte could prevent deaths caused by heart attacks by keeping tissue oxygenated for hours even after the heart stops.

Although the possibilities of how nanorobotic devices and nanomedicine procedures can help us are vast, there are however some conditions that may remain incurable. An example of such illness is memory loss which can be an advanced case of Alzheimer's disease or a head trauma. Restoring information that has been erased from the brain is far more complicated than eliminating pathogens and tumors. There are certain issues with nanomaterials such as nanotoxicology. Some nanomaterials have been identified as being toxic however further research is being carried out in nanotoxicology.

In conclusion to my gedankeen experiment at the application of nanotechnology in medicine I believe the benefits of nanomedicine outweigh its risks and issues associated with it. Nanomedicine is a large industry with nanomedicine sales reaching 6.8 billion dollars in 2004. There are over 38 products related to nanomedicine worldwide and 200 companies researching on new applications and drugs. Due to this it can be said that the world of nanomedicine is rising and soon I believe that nanomedicine and nanorobots will be as common as the drug aspirin is today.

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