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Advances of Nanotechnology in Healthcare

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Abstract: The term "nanotechnology" refers to the creation of new objects with nanoscale dimensions between 1.0 and 100.0 nm. The application of nanotechnology to medicine is called nanomedicine. Nanomedicine subsumes three mutually overlapping and progressively more powerful molecular technologies: nanoscale structured materials and devices; and medical nanorobots; genomics, proteomics and artificial engineered microbes. It also holds tremendous potential as an effective drug delivery system. Nanoparticles can be used in targeted drug delivery at the site of disease to improve the uptake of poorly soluble drugs, targeting of drugs to a specific site, and increasing the drug bioavailability. Physicochemical properties of nanoparticles such as their small size, large surface area, surface charge and ability to functionalize them makes them potential delivery systems for effective therapies. The purpose of this review is to throw more light on the recent advances on anesthesiology, where more than million people in this world are undergoing surgery where anesthesia is essential. It also includes the instruments used in the detection of breathing problem which helps in diagnosing asthma patients. It also gives the information of impact on nanotechnology in diagnosing and curing the chronic occurring diseases like diabetes mellitus and renal failure.
Keywords: Nanotechnology, anesthesiology, diabetes mellitus, renal failure.

INTRODUCTION:

A nanometer is one-billionth of a meter, too small to be seen with a conventional lab microscope. It is at this size scale – about 100 nanometers or less – that biological molecules and structures inside living cells operate. Nanoscience can be defined as study of phenomenon and manipulation of materials at atomic and molecular scales (1). Nanotechnology is related to design characterization, production and applications of structures, devices and systems by controlling shape and size at nanometer scale. Nanotechnology involves the creation and use of materials and devices at the level of molecules and atoms. Nanotechnology is the study, design, synthesis, creation, manipulation, and application of materials, devices, and systems at the nanometer scale (One meter consists of 1 billion nanometers). It is becoming increasingly important in fields like agriculture, engineering, construction, micro electronics and health care etc. The application of nanotechnology in the field of health care has become under great attention in recent times. There are many treatments today that take a lot of time and are also very expensive. Using nanotechnology, quicker and much cheaper treatments can be developed (2). Pharmaceutical nanotechnology embraces applications of nanoscience to pharmacy as nanomaterials, and as devices like drug delivery, diagnostic, imaging and biosensor (3). Nanomedicine is defined as submicron size (<1um) modules, used for treatment, diagnosis, monitoring, and control of biological system. Nanomedicine, an offshoot of nanotechnology, refers to highly specific medical intervention at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve (4).

There are two general ways to produce nanomaterials. The first is to start with a bulk material and then break it into smaller pieces using mechanical, chemical or other form of energy -- this is called top-down. Another way is to synthesize the material from atomic or molecular species via chemical reactions, allowing for the precursor particles to grow in size - this is called bottom-up (5).

NANOTECHNOLOGY IN MEDICINE (6)

Nanoscale structured materials are parts of nanomedicine with a rapid evolution, because of the impact of pharmaceutical industry. Pharmaceutical companies are trying today to develop targeted drug delivery using nanotechnology and drugs that already exist. The fact is that we do have useful drugs, but in some cases with pure bioavailability. The problem is how to deliver drugs right where we need it. The possibilities are great. For example, researchers are contemplating the possibility of using magnetic nanoparticles containing drugs to be delivered to specific parts of the body by means of magnetic field. Drugs can also be attached to nano-ligand, the role of which would be to deliver the drug only to target tissue while at the same time reducing its side effects. Some drugs have the problem of poor water solubility. The Nanosystems company, which is part of the Elan Corporation, has developed a process called nanonization to solve this problem. First, drug crystals are reduced until they become particles of less than 400 nm in diameter. To stabilize the particles and prevent aggregation, a thin layer of polymeric surface modifiers is adsorbed onto crystal surfaces. The outcome is a suspension that functions like a solution, which can be used in various dosage forms, like pills, sprays or creams.

Medical nanomaterials may also include smart drugs that become active only in specific circumstances. Yoshihisa Suzuki from Kyoto University has designed a novel drug molecule that releases antibiotic only in the presence of an infection. Suzuki bound the molecule of gentamicin to a hydrogel using a newly developed peptide linker. The linker can be cleaved by a proteinase enzyme produced by *Pseudomonas aeruginosa*. Tests on rats have shown that the antibiotic is not released if no *Pseudomonas aeruginosa* bacteria are present. If any bacteria of this type are present, the enzyme produced by the microbes cleaves the linker and gentamicin is released to kill the bacteria. This is highly desirable because the indiscriminate prophylactic use of antibiotics is associated with the emergence of drug-resistant bacterial strains .

Robert A. Freitas has designed an artificial red blood cell called respirocyte, a spherical nanorobot of about the bacterium size. This respirocyte, as represented in figure 1, would be made up of 18 billion atoms, precisely arranged in a crystalline structure to form a miniature pressure tank. The tank would hold as many as nine billion oxygen and carbon dioxide molecules. When respirocytes are injected into an individual's bloodstream, sensors on the surface would detect oxygen and carbon dioxide levels in the blood. The sensors would then signal when it is time to load oxygen and unload carbon dioxide, or *vice versa*. Respirocytes could store and transport 200 times more gas than red blood cells. It also consists of glucose engine which will release glucose when there is deficiency in the body.

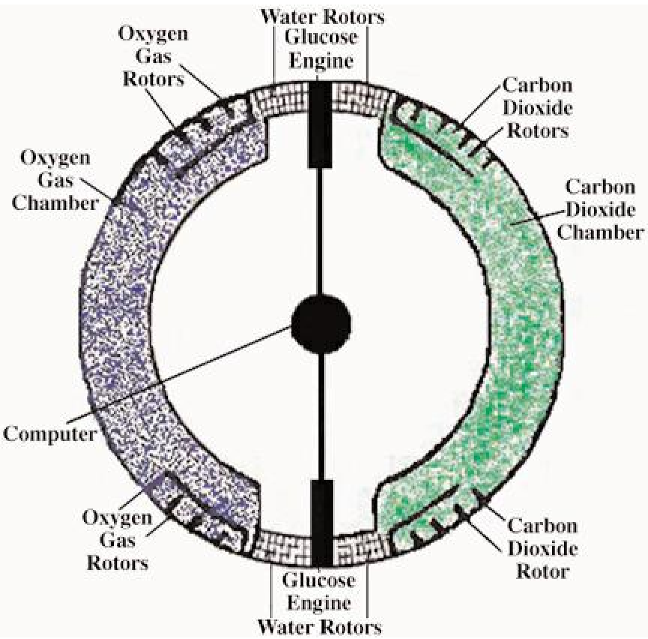

Figure 1: Pictorial representation of a respirocyte

Artificial engineered microbes are already being used to produce human hormones, for example. Human DNA is incorporated in the genome of the bacteria, which then start to produce human hormones, used to cure endocrine diseases.

NANOMEDICINE IN ANESTHESIOLOGY (7)

More than million people in this world are undergoing surgery where anesthesia is essential. Currently an anesthesiologist is required to give the anesthesia and careful titration of the drugs is essential to prevent the side effects like hypotension, desaturation, preventing the intubation response. Advancement in the field of nanotechnology gives hope by applying in anesthesia by the use of nano robots. This gives excellent pain relief to million patients who undergo various types of surgery and also pain relief to ill cancer patients. In the design of nano robot there are two spaces: An interior space which will be a closed vacuum environment into which liquids from the outside cannot normally enter unless it is needed for chemical analysis. The exterior space will be subjected to various chemical liquids in our bodies. The nanorobots of typically 0.5-3 microns in size with 1-100 nm parts can freely flow inside the body exploring and detect the various receptors eg: GABA receptors in the brain, opioid receptors, neuromuscular junction receptors. It mainly consists of three main parts - the receptor sensor, central processing unit (CPU), effector and the power system. The purpose of receptor sensor is to identify the different anesthesia receptors on the cell. The effector is used to produce the post receptor event. The CPU controls all the activities. The power system provides the necessary energy for the working of the nanorobot.

Respiratory sensor may provide new tool for emergency responders:

Researchers have created a tiny device that can monitor a victim's breathing in emergency situations by effectively shrinking an operating room machine into a small, disposable tool that can be carried to a disaster site.

NSF-supported researchers at Nanomix, Inc., have created a transistor that fuses carbon nanotubes, polymers and silicon into a capnography sensor -- a human breathing monitor. Alexander Star and his colleagues at Nanomix and the University of California, Los Angeles, have described the new sensor as depicted in figure 2. Their study shows that carbon nanotube transistors fused with carbon dioxide-detecting polymers can determine carbon dioxide (CO_2) concentrations in both ambient and exhaled air.

Capnography sensors detect subtle changes in the concentration of carbon dioxide gas in a person’s breath, revealing respiratory diseases in children and adults, and allowing anesthesiologists to monitor a patient’s breathing during surgery. In the field, emergency responders may be able to use the new sensor to verify proper breathing tube placement, monitor the patient's respiratory patterns and assess the effect of life support measures. While the Nanomix device is already capable of monitoring human breathing in laboratory settings, the researchers are collaborating with anesthesiologists and other specialists at the University of California, San Francisco, to design and test a field-ready medical device. The same electronic interactions between polymers and carbon nanotubes that sense CO_2 can also yield photo-sensitive devices that record the binary "on" and "off" patterns of digital memory. The memory is written optically, but read and erased electronically. When researchers shine light on the polymer-coated nanotube transistors, electric signals are stored as charges in the nanotubes. Because different polymers absorb light differently, engineers can tune the device to work under specific light waves. By changing the voltage in the device, one can control the read and erase functions (8).

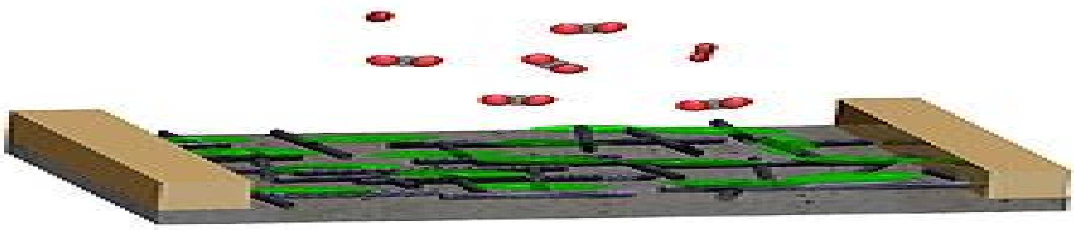

Figure 2: Conceptual illustration of the carbon nanotube network device coated with poly(ethylene imine) and starch polymer layer for detection of CO_2 gas

MANAGEMENT OF DIABETES MELLITUS

Use of nanotechnology in the detection of insulin and blood sugar

A new method that uses nanotechnology to rapidly measure minute amounts of insulin and blood sugar level is a major step toward developing the ability to assess the health of the body's insulin-producing cells. It can be achieved by following ways;

By microphysiometer

The microphysiometer is built from multiwalled carbon nanotubes, which are like several flat sheets of carbon atoms stacked and rolled into very small tubes. The nanotubes are electrically conductive and the concentration of insulin in the chamber can be directly related to the current at the electrode and the nanotubes operate reliably at pH levels characteristic of living cells. Current detection methods measure insulin production at intervals by periodically collecting small samples and measuring their insulin levels. The new sensor detects insulin levels continuously by measuring the transfer of electrons produced when insulin molecules oxidize in the presence of glucose. When the cells produce more insulin molecules, the current in the sensor increases and vice versa, allowing monitoring insulin concentrations in real time (9,10).

By implantable sensor

Use of polyethylene glycol beads coated with fluorescent molecules are injected under the skin and stay in the interstitial fluid. When glucose in the interstitial fluid drops to dangerous levels, glucose displaces the fluorescent molecules and creates a glow. This glow is seen on a tattoo placed on the arm. Sensor microchips are also being developed to continuously monitor key body parametersincluding pulse, temperature and blood glucose. A chip would be implanted under the skin and transmit a signal that could be monitored continuously (10).

Examination of contact lenses

Professor Jin Zhang at the University of Western Ontario has developed contact lenses that would change color as the user's glucose levels varied. The new device is made by embedding nanoparticles into standard hydrogel. These particles react with glucose in the tears and change color. The effect is slight, but it could alert diabetics to dangerous sugar levels without the need for regular blood tests (11).

Nanotechnology in the treatment of diabetes (10)

Diabetes is considered to be one of the major afflictions of modern western society. To date, diabetic patients control their blood-sugar levels via insulin introduced directly into the bloodstream using injections. This unpleasant method is required since stomach acid destroys protein-based substances such as insulin, making oral insulin consumption useless. The new system is based on inhaling the insulin (instead of injecting it) and on a controlled release of insulin into the bloodstream (instead of manually controlling the amount of insulin injected). The treatment of diabetes includes the proper delivery of insulin in the blood stream which can be achieved by nanotechnology in the following ways:

Development of oral insulin

It has become more feasible for the production of insulin through nanotechnology. When insulin is given via oral route, the intestinal epithelium is a major barrier for the absorption of hydrophilic drugs, as they cannot diffuse across epithelial cells through lipid-bilayer cell membranes to the bloodstream. Therefore, attention has been given to improving the paracellular transport of hydrophilic drugs and so, a carrier system is needed to protect protein drugs from the harsh environment in the stomach and small intestine, if given orally. To overcome this variety of intestinal permeation enhancers polymers such as chitosan (CS) are used. The insulin loaded Nanoparticles coated with mucoadhesive chitosan has the property of prolonging its residence in the small intestine, infiltrate into the mucus layer and subsequently mediate transiently opening the tight junctions between epithelial cells while becoming unstable and broken apart due to their pH sensitivity and/or degradability (12-19). The insulin released from the broken-apart NPs could then permeate through the paracellular pathway to the bloodstream, its ultimate destination.

At UCSF Professor of bioengineering, Tejal Desai, implants millions of pancreatic cells that secrete insulin into tiny capsules that can be implanted into the body in an effort 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, pores so small 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.

One great alternative for pancreatic tissue transplantation could be so-called artificial beta cell. There are many attempts worldwide to develop such a cell. One possible way to accomplish this is to change certain molecules on the beta cell surface that are normally targets for an immune attack.

Another approach is to insert new genes into naturally occurring cells. The cells can be genetically altered so that they could not only produce insulin, but could also respond to the rise and fall of blood glucose, just as normal pancreatic beta cells do.

Illani Atwater, Ph.D., from Sansum Medical Research Institute, Santa Barbara, CA,(24) is working on inserting the proinsulin gene into a keratinocyte cell line attached to a glucose sensitive promoter gene, as well as the genes for GLUT2 glucose transporters and glucokinase phosphorylation enzymes. No matter which way leads toward the solution, the result will be the same, i.e. artificial beta cell that will produce insulin in response to the rise of blood glucose, and no target for the immune system.

The nanopump is a powerful device and has many possible applications in the medical field. An American company, Medtronic MiniMed, has developed a device called Long Term Sensor System (LTSS), which links an implantable long-term glucose mini sensor with an implantable insulin mini pump. The pump injects Insulin to the patient's body in a constant rate, balancing the amount of sugars in his or her blood. The pump can also administer small drug doses over a long period of time. The main problem is how to develop and refine a sophisticated algorithm to translate glucose levels determined by the sensor into appropriate insulin dosages.

NANONEPHROLOGY (21-23)

According to a study, nearly 900,000 patients worldwide suffer from end-stage renal disease and require treatment through dialysis or transplantation. Nanonephrology is a branch of nanomedicine and nanotechnology that seeks to use nano-materials and nano-devices for the diagnosis, therapy, and management of renal diseases. It includes the following goals

- The study of protein structures of kidney at the atomic level
- To study the cellular processes in kidney cell through nanoimaging approaches
- nanomedical treatments that utilize nanoparticles, nanorobots etc to treat various kidney diseases.

Advances in nanonephrology will be based on discoveries in the above areas that can provide nano-scale information on the cellular molecular machinery involved in normal kidney processes and in pathological states. By understanding the physical and chemical properties of proteins and other macromolecules at the atomic level in various cells in the kidney, novel therapeutic approaches can be designed to combat major renal diseases. The nano-scale artificial kidney is a goal that many physicians dream of. Nano-scale engineering advances will permit programmable and controllable nano-scale robots to execute curative and reconstructive procedures in the human kidney at the cellular and molecular levels.

Researchers have developed a human nephron filter (HNF) that would eventually make possible a continuously functioning, wearable or implantable artificial kidney. The HNF is the first application in developing a renal replacement therapy (RRT) to potentially eliminate the need for dialysis or kidney transplantation in end-stage renal disease patients. The HNF utilizes a unique membrane system created through applied nanotechnology. In this nanonephrology,the bottom-up nanotechnology, is to produce the nanoparticles, which is the assembly of new molecules or taking molecules and assembling them into new machines. The basic concept of the device is that, it contains two membranes in an attempt to emulate the normal nephron so the way it works is blood first flows over the first membrane, which we say as the G membrane and is configured to reflect the function of the glomerular basement membrane, so it's a fully porous membrane removing solute up to the molecular weight of albumin. The ultrafiltrate that's produced by blood passing over this membrane then passes over a second membrane we say as the T membrane, which is probably the critical part of the device. This is meant to emulate the tubular membrane in the renal tubules. The tubular membrane, the T membrane, has been developed so that it will reabsorb all of those substances we want to retain, some sodium, some potassium, calcium, a little bit of phosphorous.

Since there are hundreds of uremic toxins and it would be impossible to identify them individually so the best approach would be to just get rid of all of them but then retain those things that we know are important and maintain body homeostasis from a biochemical point of view. That is the basic concept. To do this, the T membrane, the tubular membrane, is manufactured using nanotechnology and contains specially developed pores that are very tiny. The distance between the pores is about 1 to 5 nanometers and the length of the pore is only about 1 nanometer so these are very, very thin membranes that are created with these very, very thin pores. The pores are created in a way that they differentially permit movement of solute through independent of molecular weight so as to substances of an identical molecular weight are trying to get through a pore, one can be permitted to go through and one can be blocked.

CONCLUSION

Pharmaceutical nanotechnology has provided more fine-tuned diagnosis and focused treatment of diseases at a molecular level. Pharmaceutical nanotechnology is most innovative and highly specialized field, which will revolutionize the healthcare in near future. Pharmaceutical nanotechnology presents revolutionary opportunities to fight against many diseases. It helps in detecting the antigen associated with diseases such as cancer, diabetes mellitus, neurodegenerative diseases, as well as detecting the microorganisms and viruses associated with infections. Pharmaceutical nanotechnology provides opportunities to improve materials, medical devices and help to develop new technologies where existing and more conventional technologies may be reaching their limits. Further advances in the application of nanotechnology in treatment of diseases would improve the quality of life of patients.

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