Review Article

Nanomedicine: Promising Tiny Machine for the Healthcare in Future-A Review

Moni Saha

Abstract

One of the 21st century's most promising technologies is nanotechnology. 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. Nanotechnology is a collective term referring to technological developments on the nanometer scale, usually 0.1-100 nm. A nanometer is one-billionth of a meter, too small to be seen with a conventional laboratory microscope. It is at this size scale - about 100 nanometers or less - that biological molecules and structures inside living cells operate. Therefore, nanotechnology is engineering and manufacturing at the molecular scale.

Utilities of nanotechnology to biomedical sciences imply creation of materials and devices designed to interact with the body at sub-cellular scales with a high degree of specificity. This could be potentially translated into targeted cellular and tissue-specific clinical applications aimed at maximal therapeutic effects with very limited adverse-effects. Nanomedicine can offer impressive resolutions for various life threatening diseases. Disease areas which can be expected to benefit most from nanotechnology within the next few years are cancer, diseases of the cardiovascular system, the lungs, blood, neurological (especially neurodegenerative) diseases, diabetes, inflammatory/infectious diseases, Parkinson's or Alzheimer's disease and orthopaedic problems. In the first half of the 21st century, nanomedicine should eliminate virtually all common diseases of the 20th century, and virtually all medical pain. This article presents an overview of some of the applications of nanotechnology in nanomedicine.

From the Department of Pharmacy, Stamford University Bangladesh, Bangladesh.

Received: 02 Jul 2009
Accepted: 29 Sep 2009

Address correspondence and reprint request to: Dr. Moni Saha, Department of Pharmacy, Stamford University Bangladesh, Bangladesh.
E-mail: saha_moni1978@yahoo.com

Saha M. *OMJ.* 24, 242-247 (2009); doi:10.5001/omj.2009.50

Introduction

Nanomedicine uses nano-sized tools for the diagnosis, prevention and treatment of disease and to gain increased understanding of the complex underlying pathophysiology of disease. The ultimate goal is to improve the quality of life. The aim of nanomedicine may be broadly defined as the comprehensive monitoring, repairing and improvement of all human biological systems, working from the molecular level using engineered devices and nanostructures to achieve medical benefit. Most broadly, nanomedicine is the process of diagnosing, treating, and preventing disease and traumatic injury, relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body.[1]

Nanomedicine offers the prospect of powerful new tools for the treatment of human diseases and the improvement of human biological systems using molecular Nanotechnology. The term 'Nanotechnology' generally refers to engineering and manufacturing at the molecular or nanometer length scale (A nanometer is one-billionth of a meter, about the width of 6 bonded carbon atoms).[1]

Nanotechnology, 'the manufacturing technology of the 21st century', will provide an opportunity to build a broad range of economically complex molecular machines (including, not incidentally, molecular computers). It will lead to the building of computer controlled molecular tools much smaller than a human cell with the accuracy and precision of drug molecules. Such tools will allow medicine, for the first time to intervene in a sophisticated and controlled way at the cellular and molecular level.[2]

A growing interest in the medical applications of nanotechnology has led to the emergence of a new field called nanomedicine.[3, 4] They could remove obstructions in the circulatory system, kill cancer cells, or take over the function of subcellular organelles. Just as today the artificial heart has been developed, so in the future, perhaps artificial mitochondrion would be developed.[2] Nanomedicine offers the prospect of powerful new tools for the treatment of human diseases and the augmentation of human biological systems.[3] Diamondoid-based medical nanorobotics may offer substantial improvements in capabilities over natural biological systems, exceeding even the improvements possible via tissue engineering and biotechnology. This review is aimed to explore several of the worst medical problems and how nanotechnology can be used to cure them.

Diseases and Cures by Nanomedicine

Medical science has scored some impressive successes. Antibiotics have reduced diseases caused by bacteria remarkably. Nowadays, vitamin and mineral deficiency diseases are rare in developed nations. However, there are still many diseases that limit our lifespan, and the medicines concerned can only postpone them but are not able to cure. Life cannot be extended indefinitely without curing each disease that threatens to shorten it.

Table 1: A Partial Nanomedicine Technologies Taxonomy [5]

Raw nanomaterials	**Cell simulations and cell diagnostics**	**Biological research**
Nanoparticle coatings	Cell chips,	Nanobiology
Nanocrystalline materials	Cell stimulator	Nanoscience in life sciences
Nanostructured materials	**DNA manipulation, sequencing,**	Drug delivery
Cyclic peptides	**diagnostics**	Drug discovery
Dendrimers	Genetic testing	Biopharmaceutics
Detoxification agents	DNA microarrays	Drug encapsulation
Drug encapsulation	Ultrafast DNA sequencing	Smart drugs
Fullerenes	DNA manipulation and control	**Molecular medicine**
Functional drug carriers Smart drugs	**Tools and diagnostics**	Genetic therapy
MRI scanning (nanoparticles)	Bacterial detection systems	Pharmacogenomics
Nanobarcodes	Biochips	**Artificial enzymes and enzyme control**
Molecular medicine	Biomolecular imaging	Enzyme manipulation and control
Nanoemulsions	Biosensors and biodetection	**Nanotherapeutics**
Nanofibers	**Diagnostic and defense applications**	Antibacterial and antiviral nanoparticles
Nanoparticles	Endoscopic robots and microscopes	Fullerene-based pharmaceuticals
Nanoshells	Fullerene-based sensors	Photodynamic therapy
Carbon nanotubes	Imaging (cellular, etc.)	Radiopharmaceuticals
Noncarbon nanotubes	Monitoring	**Synthetic biology and early nanodevices**
Quantum dots	Lab on achip	Dynamic nanoplatform nanosome
Artificial binding sites	Nanosensors	Tecto-dendrimers
Artificial antibodies	Point of care diagnostics	Artificial cells and liposomes
Artificial enzymes	Protein microarrays	Polymeric micelles and polymersomes
Artificial receptors	Scanning probe microscopy	**Biotechnology and biorobotics**
Molecularly imprinted polymers	Intracellular devices	Biologic viral therapy
Control of surfaces		Virus-based hybrids
Artificial surfaces-adhesives	Intracellular biocomputers	Stem cells and cloning
Artificial surfaces—nonadhesive	Intracellular sensors/reporters	Tissue engineering
Artificial surfaces—regulated	Implants inside cells	Artificial organs
Biocompatible surfaces		Nanobiotechnology
Biofilm suppression	BioMEMS	Biorobotics and biobots
Engineered surfaces		
Pattern surfaces (contact guidance)	Implantable materials and devices	Nanorobotics
Thin-film coatings	Implanted bioMEMS, chips, and electrodes	DNA-based devices and nanorobots
	MEMS/Nanomaterials-based prosthetics	Diamond-based nanorobots
Nanopores	Sensory aids (artificial retina, etc.)	Cell repair devices
Immunoisolation	Microarrays	
Molecular sieves and channels	Microcantilever-based sensors	
Nanofiltration membranes	Microfluidics	
Separations	Microneedles	
	Medical MEMS	
	MEMS surgical devices	

Table 2: Application of Nanomedicine for the Healthcare [6-11]

Application of nanomedicine	Nanomaterial Name & Type	Pharmacological function	Diseases
Nanomedicines in the clinic	Liposome (30-100 nm)	Targeted drug Delivery	Cancer
	Nano particle (Iron oxide, 5-50 nm)	Contrast agent for magneting resonance imaging	Hepatic (Liver)
Nanomedicines under development	Dendrimer (5-50 nm)	Contrast agent for magneting resonance imaging	Cardiovascular Phase III clinical trial
	Fullerene (Carbon bucky ball 2-20 nm)	Antioxidant	Neurodegenerative, Cardiovascular
	Nanoshells (Goldcoated silica 60 nm)	Hyperthermia	Cancer Preclinical

Treatment of Cancer

At a cellular level, cancerous tissues are usually quite different from normal tissues. Many cancer cells change the chemicals on their surface, and are therefore easy to identify. However, most cancer cells grow faster or change shape and every cancer involves a genetic change that causes a difference in the chemicals inside the cell. The immune system takes advantage of surface markers to destroy cancer cells; but this is not enough to keep us cancer-free. Nanobots will have several advantages. Firstly, they can physically enter cells and scan the chemicals inside. Secondly, they can have on board computers that allow them to do calculations not available to immune cells. Thirdly, nanobots can be programmed and deployed after a cancer is diagnosed, whereas the immune system is always guessing about whether a cancer exists.

Nanobots can scan each of the body's cells for cancerous tendencies, and subject any suspicious cells to careful analysis; if a cancer is detected, they can wipe it out quickly, using more focused and vigorous tactics than the immune system is designed for. Given such molecular tools, a small device can be designed to identify and kill cancer cells. The device would have a small computer, several binding sites to determine the concentration of specific molecules, and a supply of some poison which could be selectively released and able to kill a cell identified as cancerous. The device would circulate freely throughout the body and would periodically sample its environment by determining whether the binding sites were occupied or not. Occupancy statistics would allow determination of concentration.

Today's monoclonal antibodies are able to bind to only a single type of protein or other antigen, and not proved effective against most cancers. The cancer-killing device mentioned here could incorporate a dozen different binding sites and so could monitor the concentrations of a dozen different types of molecules. The computer could determine if the profile of concentrations fit a pre-programmed "cancerous" profile and would, when a cancerous profile was encountered, release the poison.[2, 12]

Prevention of Brain Damage in Neurodegenerative Diseases

The brain is unique among the body's organs; it stores our memories and personality, and therefore, t it cannot simply be replaced if it starts to wear out. This poses a special problem for life extension; the information stored in the brain must be preserved over extended periods of time, safe from disease and accident. Obviously, it is good to prevent the premature death of neurons. Poisons such as alcohol, accidents such as stroke, and diseases such as Alzheimer's can all cause neurons to die. In each of these cases, neuron death can be greatly slowed if not prevented entirely by controlling the chemistry inside the cell. Injurious chemicals can be vacuumed up and converted into harmless ones.

Damaged neurons, like other cells, sometimes go into suicide mode (called "apoptosis"); as mentioned above, this can be chemically prevented, and the neuron can be stabilized until the problem is fixed and the damage is repaired. It is now acknowledged that brain cells do regenerate; the brain is generating new cells all the time. This implies that some neural death is normal. How do the new cells know how to behave? It seems that a new neuron can take its cues from the existing ones; this means that a person's mind may be intact even after the death and replacement of a large percentage of their neurons. Finally, it may be possible to measure neural connections and/or activity in enough detail to simulate the firing pattern. This may make it possible to create an artificial neuron or even an artificial neural net that can be used to replace missing neurons and retain old memories. But even if this proves to be impossible, the worst-case scenario is one in which people cannot remember much farther than a century back. More memory loss than this can be accepted as a natural consequence of aging.[12]

Hormone Deficiency

Aging is associated with changes in the levels of many hormones; perhaps the best known example is menopause, which is caused by a reduction in estrogen. It is likely that treating glands against aging at the cellular level would restore age-appropriate hormone production. However, if this is not enough to bring the body to a younger state, artificial glands could be built that would maintain the desired hormone levels. In fact, different hormone levels could be supplied to different organs -something that the body cannot do for itself. This would be an example of heterostasis.[12]

For the treatment of Infection

Bacteria, viruses, and parasites are continuing problems. Antibiotics work well against most bacteria; however, antibiotic-resistant strains are developing. Since viruses are not active until they take over a cell, they are immune to antibiotics, and medicine cannot do much against them. There are many kinds of parasites that may need individual medical techniques. Our immune system is quite effective in dealing with most infections but the immune system needs to learn about it by experience.

It is generally most effective at fighting organisms that it can recognize on a molecular level. Some diseases, such as Ebola, progress too rapidly for the immune system to respond. Syphilis survives by being stealthy and by surrounding itself with the chemicals of the body to camouflage itself. Herpes splices itself into the genes of the body's cells, so the immune system cannot detect it and wipe it out. HIV directly attacks the immune system. Nanobots have several advantages over the immune system. They will not be susceptible to attack by natural pathogens. They will have computational resources unavailable to immune cells. They can be programmed to find and fight diseases they have never encountered (when a new disease shows up), as soon as it is analyzed everyone's nanobots can benefit.

Likewise, the system can be activated based on external knowledge of the likelihood of a disease; the nanobots would not have to waste energy looking for malaria in winter. Nanotech will provide more options for cleaning up after a disease, since corrupted genes will be repairable without killing the affected cell. Some diseases, such as cholera and tetanus, live in the environment; without scrubbing the whole earth, we cannot get rid of them entirely, therefore, we will need to maintain an immune system against them. But many diseases cannot survive without humans to infect.

With great effort, we managed to eradicate smallpox using 1970's technology. Cheap manufacturing would allow the creation of billions of doses of highly effective treatments that would be easy to distribute and administer; the main obstacles to wiping out many diseases worldwide would be political, not economic or technological. Nanorobotic 'Microbivores' the nanorobotic phagocytes (artificial white cells) traveling in the bloodstream could be 1000 times faster-acting than white blood cells and eradicate 1000 times more bacteria, offering a complete antimicrobial therapy without increasing the risk of sepsis or septic shock (as in traditional antibiotic regimens) and without the release of biologically active effluents. Microbivores could also be useful for treating infections of the meninges or the cerebrospinal fluid (CSF) and respiratory diseases involving the presence of bacteria in the lungs or sputum, and could also digest bacterial biofilms. These handy nanorobots could quickly rid the blood of nonbacterial pathogens such as viruses (viremia), fungus cells (fungemia), or parasites (parasitemia). Outside the body, microbivore derivatives could help clean up biohazards, toxic biochemicals or other environmental organic materials spills, as in bioremediation.[5, 12]

For Life Saving after Accidents

Accidents, especially motor vehicle accidents, are a leading cause of death in all ages. Although an accident is not itself a disease, it kills as it damages the body, and that damage can be treated or prevented like a disease. Most accidents involve mechanical injury (trauma) and many involve chemical injury, either by poisoning or oxygen starvation.

A permanent nanorobot installation can ensure survival. Nanobots embedded in a tissue can strengthen it against tearing, or repair once it is torn. It is common for a blow to the head to rattle the brain against the skull; a specially shaped nano-built device could cushion the brain, preventing this damage. Other devices could vacuum up common poisons before they could cause damage, or barricade poisoned areas to keep the poison from spreading through the body. 'Respirocytes' the artificial red blood cells could allow the body to function normally for several minutes without breathing or blood circulation, giving more opportunity to restore normal functioning. In cases of extreme injury, heterostasis could be used to stabilize the body until help can arrive. As long as the brain is not physically damaged, it can be functionally separated from the body and forced into a low-power state.

With today's medicine, paramedics refer to the "golden hour"; if an accident victim can be brought to a hospital in less than an hour,the chance of survival is greatly increased. People have recovered after drowning in cold water for over an hour; artificial mimicry of this state, combined with the ability to aggressively repair the body, might extend the "golden hour" significantly. 'Respirocytes' - artificial red blood cells comprised of microscopic diamondoid pressure tanks that are operated at up to 1000 atmospheres of pressure - could carry greater than 200 times more respiratory gases than an equal volume of natural red blood cells. The injection of a 5-mililitre therapeutic dose of 50% respirocyte saline suspension, a total of 5 trillion individual nanorobots, into the human bloodstream would exactly duplicate the gas-carrying capacity of the patient's entire 5.4 liters of blood.

Primary medical applications of respirocytes would include transfusable blood substitution; partial treatment for anemia, perinatal/neonatal, and lung disorders; enhancement of cardiovascular/neurovascular procedures, tumor therapies and diagnostics; prevention of asphyxia; artificial breathing; and a variety of sports, veterinary, battlefield, and other uses. The clottocytes are artificial platelets that could stop human bleeding within ~1 second of physical injury, but using only 0.01% the bloodstream concentration of natural platelets. In other words, nanorobotic clottocytes would be around 10,000 times more effective as clotting agents than an equal volume of natural platelets. Nanorobotic artificial mechanical platelets (Clottocytes) could allow for complete hemostasis in as little as one second - 100 to 1000 times faster than the natural system. They could also work internally. Using acoustic pulses, a blood vessel break could be rapidly communicated to neighboring clottocytes, immediately triggering a progressive controlled mesh-release cascade.[12-16]

For Blood-Related Diseases

Many diseases, from heart attacks and strokes to sepsis and metastasizing cancer, involve the blood in some way. The author has proposed an aggressive nanomedical device, a "Vasculoid" that would replace the blood volume and take over its functions by lining the entire vascular system with a multi-segmented robot. In addition to preventing many diseases, and limiting the scope of others (such as poisoning), such a system would provide detailed control of the body's chemical environment around each individual capillary, allowing heterostasis to be used extensively.

The vasculoid is a single, complex, multi-segmented nanotechnological medical robotic system capable of duplicating all essential thermal and biochemical transport functions of the blood, including circulation of respiratory gases, glucose, hormones, cytokines, waste products, and cellular components. This nanorobotic system, a very aggressive and physiologically intrusive macroscale nanomedical device comprised of around 500 trillion stored or active individual nanorobots, weighs around 2 kg and consumes from 30-200 watts of power in the basic human model, depending on activity level. The vasculoid system conforms to the shape of existing blood vessels and serves as a complete replacement for natural blood. The Vasculoid is extremely complicated and would require much research to build and use successfully. This particular device may never be used, but it can provide a hint of the possibilities inherent in advanced nanomedicine.

A second application would be to provide metabolic support in the event of impaired circulation. Poor blood flow, caused by a variety of conditions, can result in serious tissue damage. A major cause of tissue damage is inadequate oxygen. A simple method of improving the levels of available oxygen despite reduced blood flow would be to provide an "artificial red blood cell." We will consider a simple design here: a sphere with an internal diameter of 0.1 microns (100 nanometers) filled with high pressure oxygen at ~1,000 atmospheres (about 10^8 pascals). The oxygen would be allowed to trickle out from the sphere at a constant rate (without feedback). Diamond has a Youngs modulus of about 10^{12} pascals. An atomically precise diamondoid structure should be able to tolerate a stress of greater than 5 x 10^{10} pascals (5% of the modulus). Thus, a 0.1 micron sphere of oxygen at a pressure of 10^8 pascals could be contained by a hollow diamondoid sphere with an internal diameter of 0.1 microns and a thickness of less than one nanometer.

While providing oxygen to healthy tissue should maintain metabolism, tissues already suffering from ischemic injury (tissue injury caused by loss of blood flow) may no longer be able to properly metabolize oxygen. In particular, the mitochondria will, at some point, fail. Increased oxygen levels in the presence of nonfunctional or partially functional mitochondria will be ineffective in restoring the tissue. However, more direct metabolic support could be provided. The direct release of ATP, coupled with selective release or absorption of critical metabolites (using the kind of selective transport system mentioned earlier), should be effective in restoring cellular function even when mitochondrial function had been compromised. The devices restoring metabolite levels, injected into the body, should be able to operate autonomously for many hours (depending on power requirements, the storage capacity of the device and the release and uptake rates required to maintain metabolite levels). Advances in medical technology necessarily depend on the understanding of living systems. With the kind of devices discussed earlier, it would be possible to explore and analyze living systems in greater detail than ever considered possible before.

Autonomous molecular machines, operating in the human body, could monitor levels of different compounds and store that information in internal memory. They could determine both their location and the time. Thus, information could be gathered about changing conditions inside the body, and that information could be tied to both the location and the time of collection. Physical samples of small volumes (nano tissue samples) could likewise be taken. These molecular machines could then be filtered out of the blood supply and the stored information (and samples) could be analyzed. This would provide a picture of activities within healthy or injured tissue. This new knowledge would give us new insights and new approaches to curing the sick and healing the injured.[2,12,17]

In the first half of the 21st century, nanomedicine should eliminate virtually all common diseases of the 20th century, and virtually all medical pain and suffering as well.[18] Only conditions that involve a permanent loss of personality and memory information in the brain – such as an advanced case of Alzheimer's disease or a massive head trauma may remain incurable in the nanomedical era. Because aging is believed to be the result of a number of interrelated molecular processes and malfunctions in cells, and because cellular malfunctions will be largely reversible, middle-aged and older people who gain access to an advanced nanomedicine can expect to have most of their youthful health and beauty restored. Hence they may find few remaining limits to human longevity in this wonderfully vigorous state.[1]

Nanomedicine can offer impressive resolutions for various life threatening diseases. Disease areas which can be expected to benefit most from nanotechnology within the next few years are cancer, diseases of the cardiovascular system, the lungs, blood, neurological (especially neurodegenerative) diseases, diabetes, inflammatory/ infectious diseases, Parkinson's or Alzheimer's disease and orthopaedic problems. In the longer term, perhaps 10–20 years from today, the earliest molecular machine systems and nanorobots may join the medical armamentarium, finally giving physicians the most potent tools imaginable to conquer human disease, ill-health, and aging.[19] The future prospect of nanomedicine is bright and we are required to work very hard and long to make it fruitful.

Acknowledgements

The author reported no conflict of interest and no funding was received on this work.

References

1. Freitas RA Jr. The future of nanofabrication and molecular scale devices in nanomedicine. Stud Health Technol Inform 2002;80:45-59.
2. Ralph C. Merkle. Nanotechnology and Medicine, Advances in Anti-Aging Medicine, Vol. I, edited by Dr. Ronald M. Klatz, Liebert press, 1996. p. 277-286. http://www.zyvex.com/nanotech/nanotechAndMedicine.html.
3. Freitas RA Jr Nanomedicine, Volume I: Basic Capabilities, Landes Bioscience, Georgetown, TX, 1999; http://www.nanomedicine.com.
4. Freitas RA Jr. The Nanomedicine Page, http://www.foresight.org/Nanomedicine/index.html.
5. Freitas RA Jr. What is nanomedicine? Nanomedicine: NBM 2005;1:2-9.
6. Bharali DJ, Khalil M, Gurbuz M, Simone TM, Mousa SA. Nanoparticles and cancer therapy: a concise review with emphasis on dendrimers. Int J Nanomedicine 2009;4:1-7.
7. Park JW. Liposome-based drug delivery in breast cancer treatment. Breast Cancer Res 2002;4(3):95-99.
8. Thorek DL, Chen AK, Czupryna J, Tsourkas A. Superparamagnetic iron oxide nanoparticle probes for molecular imaging. Ann Biomed Eng 2006 Jan;34(1):23-38.
9. Partha R, Conyers JL. Biomedical applications of functionalized fullerene-based nanomaterials. Int J Nanomedicine 2009;4:261-275.
10. Stya Kumar S, Srinivasa Babu P. Nanotechnology: A new approach in cancer therapy. Pharm Times 2006;39:17-20.
11. Hirsch LR, Gobin AM, Lowery AR, Tam F, Drezek RA, Halas NJ, West JL.. Metal nanoshells. Ann Biomed Eng. 2006; 34:15-22. Chris Phoenix. Nanotechnology and Life Extension, January 2003, Forsight.
12. Phoenix C. Nanotechnology and Life Extenssion. 2003 Forsight.
13. Freitas RA Jr. Microbivores: Artificial Mechanical Phagocytes, KurzweilAI.net, 2002; http://www.kurzweilai.net
14. Freitas RA Jr. Exploratory design in medical nanotechnology: a mechanical artificial red cell. Artif Cells Blood Substit Immobil Biotechnol 1998 Jul;26(4):411-430. http://www.foresight.org/Nanomedicine/Respirocytes.html.
15. Freitas RA Jr. Clottocytes: Artificial Mechanical Platelets, Foresight Update No. 41, 30 2000, pp. 9-11. http://www.imm.org/Reports/Rep018.html.
16. Freitas RA Jr. Clottocytes: Artificial Mechanical Platelets, KurzweilAI.net 2002.
17. Freitas RA Jr., Christopher J. Phoenix. Vasculoid: A Personal Nanomedical Appliance to Replace Human Blood. Journal of Evolution and Technology 2002; Vol. 11. http://jetpress.org/volume11/vasculoid.html.
18. Freitas RA Jr. Nanodentistry. J Am Dent Assoc 2000 Nov;131(11):1559-1565. jada.ada.org.
19. Freitas RA Jr. Current Status of Nanomedicine and Medical Nanorobotics. J. Comput. Theor. Nanosci. 2005;2:1-25.