

Applications of Nanotechnology: In Medicine

A. S. Pujar¹, Alfaz. M. Bagawan²

¹Professor, R L Science Institute, Belagavi

²R L Science Institute, Belagavi

Abstract: *Nanomedicine is an emerging and rapidly evolving field and includes the use of nanoparticles for diagnosis and therapy of a variety of diseases, as well as in regenerative medicine. In this mini-review, leaders in the field from around the globe provide a personal perspective on the development of nanomedicine. The focus lies on the translation from research to development and the innovation supply chain, as well as the current status of nanomedicine in industry. The role of academic professional societies and the importance of government funding are discussed. Nanomedicine to combat infectious diseases of poverty is highlighted along with other pertinent examples of recent breakthroughs in nanomedicine. Taken together, this review provides a unique and global perspective on the emerging field of nanomedicine. Applications of various nano systems in cancer therapy such as carbon nano tube, dendrimers, nano crystal, nano wire, nano shells etc.*

Keywords: Nanomedicine, nanoparticle, drug delivery, diagnosis

1. Introduction

Nanomedicine seeks to deliver a valuable set of research tools and clinically useful devices in the near future. The National Nanotechnology Initiative expects new commercial applications in the pharmaceutical industry that may include advanced drug delivery systems, new therapies, and in vivo imaging. Nanomedicine research is receiving funding from the US National Institutes of Health Common Fund program, supporting four nanomedicine development centers.

Functionalities can be added to nanomaterials by interfacing them with biological molecules or structures. The size of nanomaterials is similar to that of most biological molecules

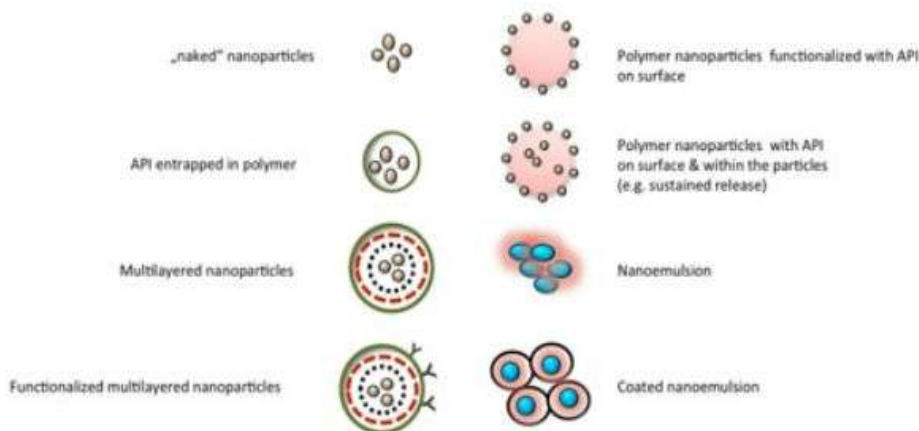
and structures; therefore, nanomaterials can be useful for both in vivo and in vitro biomedical research and applications. Thus far, the integration of nonmaterial with biology has led to the development of diagnostic devices, contrast agents, analytical tools, physical therapy applications, and drug delivery vehicles.

Nanomedicine sales reached \$16 billion in 2015, with a minimum of \$3.8 billion in nanotechnology R&D being invested every year. Global funding for emerging nanotechnology increased by 45% per year in recent years, with product sales exceeding \$1 trillion in 2013. As the nanomedicine industry continues to grow, it is expected to have a significant impact on the economy.

Drug delivery in present Scenario

Types of Nanoparticles

pH-sensitive & complex Drug-Delivery Systems



Nanotechnology has provided the possibility of delivering drugs to specific cells using nanoparticles. The overall drug consumption and side-effects may be lowered significantly by depositing the active agent in the morbid region only and in no higher dose than needed. Targeted drug delivery is

intended to reduce the side effects of drugs with concomitant decreases in consumption and treatment expenses. delivery focuses on maximizing bioavailability both at specific places in the body and over a period of time. This can potentially be achieved by molecular targeting by nanoengineered

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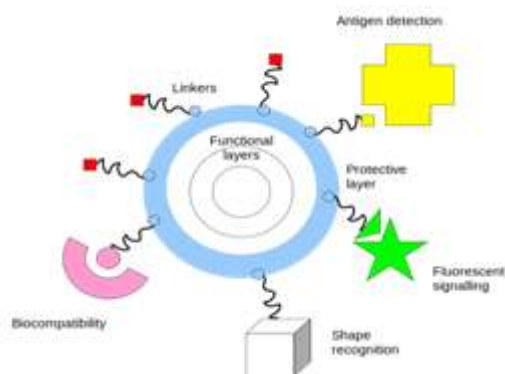
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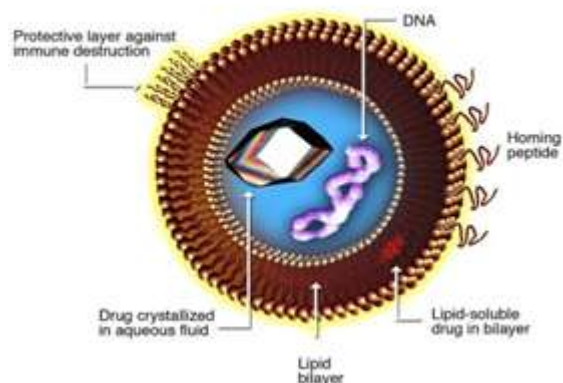
devices. A benefit of using nanoscale for medical technologies is that smaller devices are less invasive and can possibly be implanted inside the body, plus biochemical reaction times are much shorter. These devices are faster and more sensitive than typical drug delivery. The efficacy of drug delivery through nanomedicine is largely based upon: a) efficient encapsulation of the drugs, b) successful delivery of drug to the targeted region of the body, and c) successful release of the drug.

Drug delivery systems, lipid or polymer-based nanoparticles, can be designed to improve the pharmacokinetics and biodistribution of the drug. However, the pharmacokinetics and pharmacodynamics of nanomedicine is highly variable among different patients.^[16] When designed to avoid the body's defense mechanisms, nanoparticles have beneficial properties that can be used to improve drug delivery. Complex drug delivery mechanisms are being developed, including the ability to get drugs through cell membranes and into cell cytoplasm. Triggered response is one way for drug molecules to be used more efficiently. Drugs are placed in the body and only activate on encountering a particular signal. For example, a drug with poor solubility will be replaced by a drug delivery system where both hydrophilic and hydrophobic environments exist, improving the solubility.^[18] Drug delivery systems may also be able to prevent tissue damage through regulated drug release; reduce drug clearance rates; or lower the volume of distribution and reduce the effect on non-target tissue. However, the biodistribution of these nanoparticles is still imperfect due to the complex host's reactions to nano- and micro-sized materials and the difficulty in targeting specific organs in the body. Nevertheless, a lot of work is still ongoing to optimize and better understand the potential and limitations of nanoparticulate systems. While advancement of research proves that targeting and distribution can be augmented by nanoparticles, the dangers of nanotoxicity become an important next step in further understanding of their medical uses.

Nanoparticles are under research for their potential to decrease antibiotic resistance or for various antimicrobial uses. Nanoparticles might also be used to circumvent multidrug resistance (MDR) mechanisms.



Liposome for Drug Delivery



Systems under research

Two forms of nanomedicine that have already been tested in mice and are waiting human testing will use gold nanoshells to help diagnose and treat cancer, along with liposome's as vaccine adjuvants and drug transport vehicles. Similarly, drug detoxification is also another application for nanomedicine which has shown promising results in rats. Advances in Lipid nanotechnology were also instrumental in engineering medical nanodevices and novel drug delivery systems as well as in developing sensing applications. Another example can be found in dendrimers and nanoporous materials. Another example is to use block copolymers, which form micelles for drug encapsulation.

Polymeric nanoparticles are a competing technology to lipidic (based mainly on Phospholipids) nanoparticles. There is an additional risk of toxicity associated with polymers not widely studied or understood. The major advantages of polymers are stability, lower cost and predictable characterization. However, in the patient's body this very stability (slow degradation) is a negative factor. Phospholipids on the other hand are membrane lipids (already present in the body and surrounding each cell), have a GRAS (Generally Recognized As Safe) status from FDA and are derived from natural sources without any complex chemistry involved. They are not metabolized but rather absorbed by the body and the degradation products are themselves nutrients (fats or micronutrients)

Protein and peptides exert multiple biological actions in the human body and they have been identified as showing great promise for treatment of various diseases and disorders. These macromolecules are called biopharmaceuticals. Targeted and/or controlled delivery of these biopharmaceuticals using nanomaterials like nanoparticles and Dendrimers is an emerging field called nanobiopharmaceuticals, and these products are called nanobiopharmaceuticals.^[citation needed]

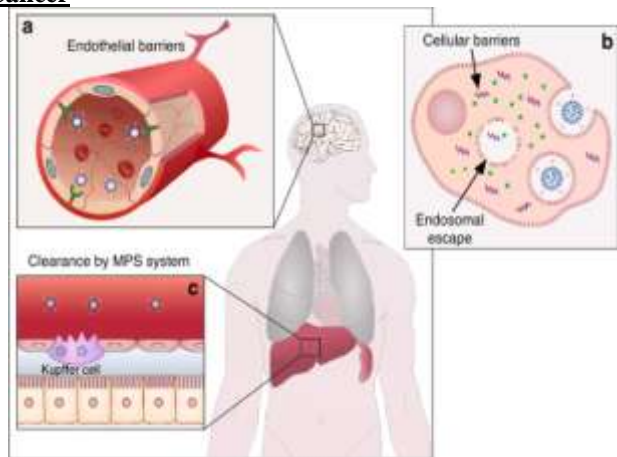
Another highly efficient system for microRNA delivery for example are nanoparticles formed by the self-assembly of two different microRNAs deregulated in cancer

Another vision is based on small electromechanical systems; nanoelectromechanical systems are being investigated for the active release of drugs and sensors. Some potentially important applications include cancer

treatment with iron nanoparticles or gold shells or cancer early diagnosis. Nanotechnology is also opening up new opportunities in implantable delivery systems, which are often preferable to the use of injectable drugs, because the latter frequently display first-order kinetics (the blood concentration goes up rapidly, but drops exponentially over time). This rapid rise may cause difficulties with toxicity, and drug efficacy can diminish as the drug concentration falls below the targeted range.

Nanoparticles have high surface area to volume ratio. This allows for many functional groups to be attached to a nanoparticle, which can seek out and bind to certain tumor cells. Additionally, the small size of nanoparticles (10 to 100 nanometers), allows them to preferentially accumulate at tumor sites (because tumors lack an effective lymphatic drainage system). Limitations to conventional cancer chemotherapy include drug resistance, lack of selectivity, and lack of solubility. Nanoparticles have the potential to overcome these problems.

Cancer

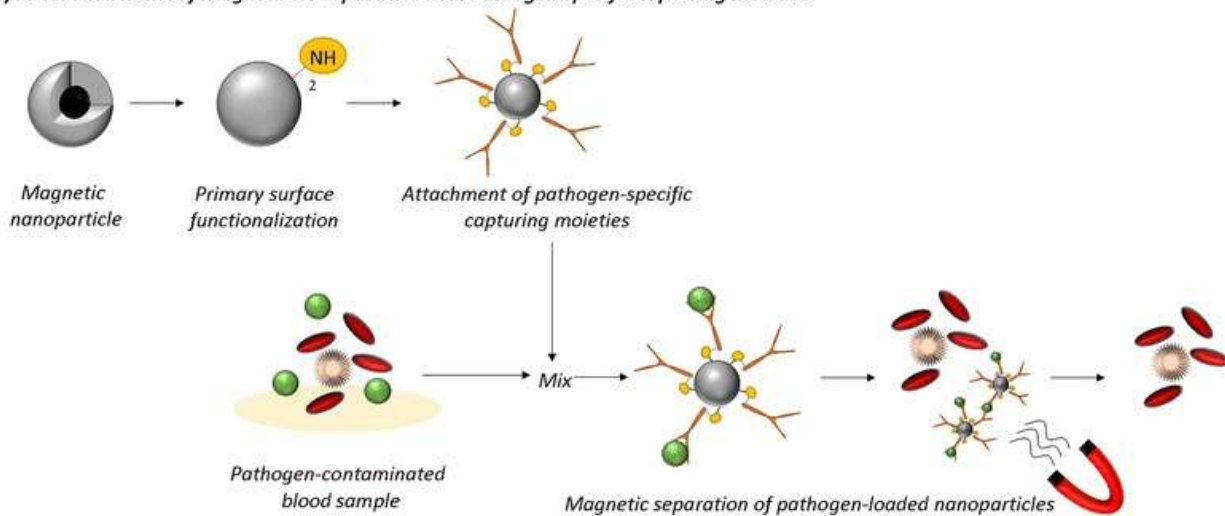


In photodynamic therapy, a particle is placed within the body and is illuminated with light from the outside. The light gets absorbed by the particle and if the particle is metal, energy from the light will heat the particle and surrounding tissue. Light may also be used to produce high energy oxygen molecules which will chemically react with and destroy most organic molecules that are next to them (like tumors). This therapy is appealing for many reasons. It does not leave a "toxic trail" of reactive molecules throughout the body (chemotherapy) because it is directed where only the light is shined and the particles exist. Photodynamic therapy has potential for a noninvasive procedure for dealing with diseases, growth and tumors. Kanzius RF therapy is one example of such therapy (nanoparticle hyperthermia). Also, gold nanoparticles have the potential to join numerous therapeutic functions into a single platform, by targeting specific tumor cells, tissues and organs.

Existing and potential drug nanocarriers have been reviewed.

Blood Purification

1.) Functionalization of Magnetic Nanoparticles with Pathogen-specific Capturing Moieties



2.) Magnetic Separation of Pathogen-loaded Nanoparticles from Blood

Magnetic micro particles are proven research instruments for the separation of cells and proteins from complex media. The technology is available under the name Magnetic-activated cell sorting or Dynabeads among others. More recently it was shown in animal models that magnetic nanoparticles can be used for the removal of various noxious compounds including toxins, pathogens, and proteins from whole blood in an extracorporeal circuit similar to dialysis.^{[60][61]} In contrast to dialysis, which works on the principle of the size related diffusion of solutes and ultrafiltration of fluid across a semi-permeable membrane, the purification with nanoparticles allows

specific targeting of substances. Additionally larger compounds which are commonly not dialyzable can be removed.

The purification process is based on functionalized iron oxide or carbon coated metal nanoparticles with ferromagnetic or super paramagnetic properties.

Binding agents such, as proteins, antibodies, antibiotics or synthetic ligands are covalently linked to the particle surface.

These binding agents are able to interact with target species forming an agglomerate. Applying an external magnetic field gradient allows exerting a force on the nanoparticles. Hence the particles can be separated from the bulk fluid, thereby cleaning it from the contaminants.

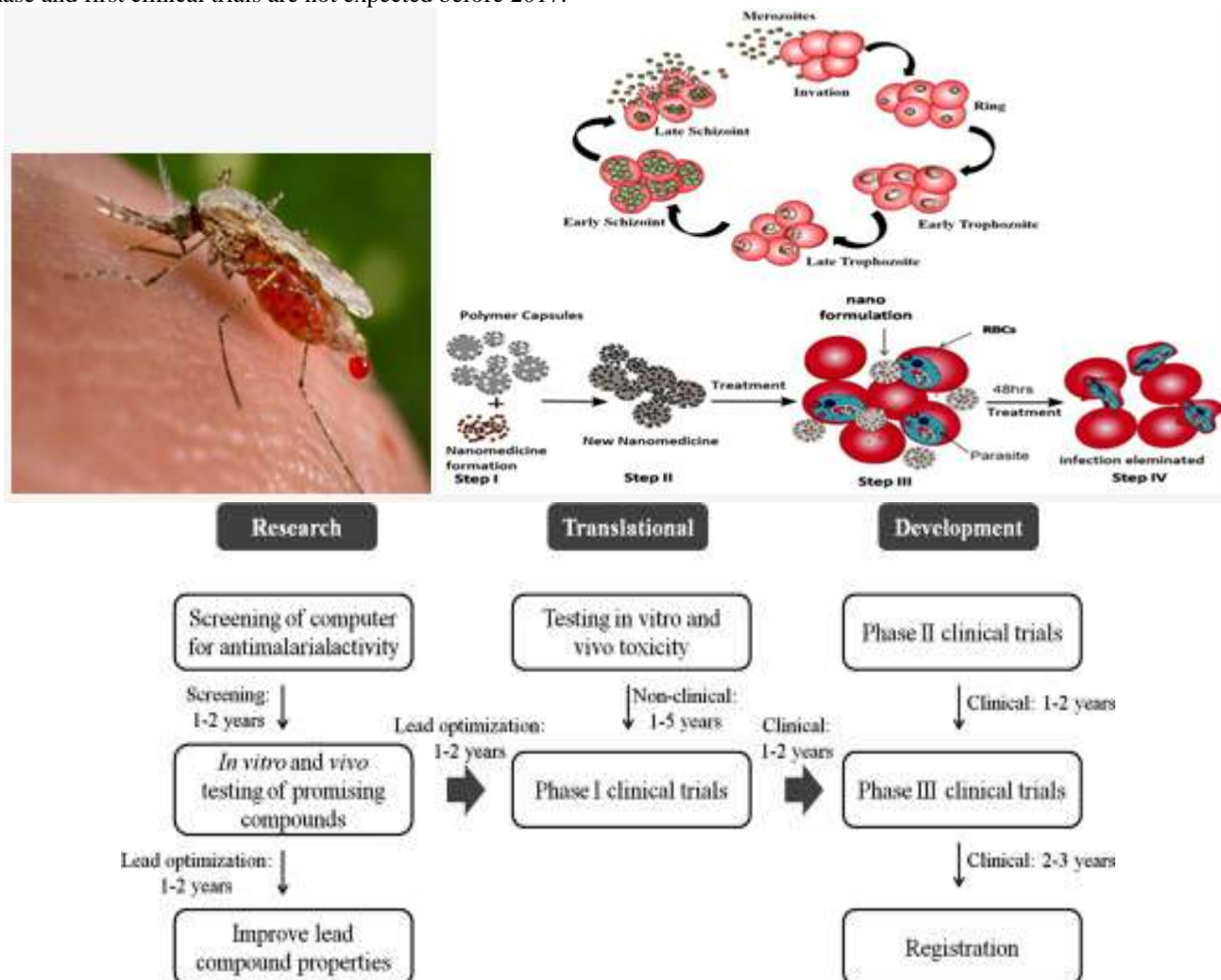
The small size (< 100 nm) and large surface area of functionalized nanomagnets leads to advantageous properties compared to hemoperfusion, which is a clinically used technique for the purification of blood and is based on surface adsorption. These advantages are high loading and accessibility of the binding agents, high selectivity towards the target compound, fast diffusion, small hydrodynamic resistance, and low dosage.

This approach offers new therapeutic possibilities for the treatment of systemic infections such as sepsis by directly removing the pathogen. It can also be used to selectively remove cytokines or endotoxins for the dialysis of compounds which are not accessible by traditional dialysis methods. However the technology is still in a preclinical phase and first clinical trials are not expected before 2017.

Malaria:

Malaria is an infectious disease that mainly affects children and pregnant women from tropical countries. The mortality rate of people infected with malaria per year is enormous and became a public health concern. The main factor that has contributed to the success of malaria proliferation is the increased number of drug resistant parasites. To counteract this trend, research has been done in nanotechnology and nanomedicine, for the development of new biocompatible systems capable of incorporating drugs, lowering the resistance progress, contributing for diagnosis, control and treatment of malaria by target delivery.

- Nanomedicine has contributed to the development of therapies for Malaria.
- Colloidal carriers are able to lower the drug resistance progress, contributing to diagnosis.
- Advanced colloidal carriers can be used to overcome multi-drug resistance.



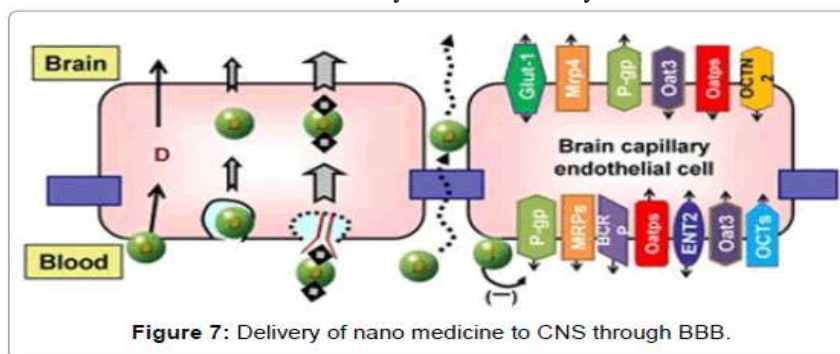
Nanotechnology in the treatment of neurodegenerative disorders

One of the most important applications of nanotechnology is in the treatment of neurodegenerative disorders. For the delivery of CNS therapeutics, various nano carriers such as, dendrimers, nano gels, nano emulsions, liposomes,

polymeric nano particles, solid lipid nano particles, and nano suspensions have been studied. Transportation of these nano medicines has been effected across various *in vitro* and *in vivo* BBB models by endocytosis and/or transcytosis, and early preclinical success for the management of CNS conditions such as, Alzheimer's disease, brain tumors, HIV

encephalopathy and acute ischemic stroke has become possible. The nanomedicine can be advanced further by

improving their BBB permeability and reducing their neurotoxicity



Aim of applied nanotechnology is regeneration and neuro protection of the central nervous system (CNS) and will significantly benefit from basic nanotechnology research conducted in parallel with advances in **neurophysiology**, neuropathology and cell biology. The efforts are taken to develop novel technologies that directly or indirectly help in providing neuro protection and/or a permissive environment and active signaling cues for guided axon growth. In order to minimize the peripheral side-effects of conventional forms of Parkinson's disease therapy, research is focused on the design, biometric simulation and optimization of an intracranial nano-enabled scaffold device (NESD) for the site-specific delivery of dopamine to the brain, as a strategy. Peptides and peptidic nano particles are newer tools for various CNS diseases.

Tuberculosis treatment: Tuberculosis(TB) is the deadly infectious disease. The long duration of the treatment and the pill burden can hamper patient lifestyle and result in the development of multi-drugresistant (MDR) strains. Tuberculosis in children constitutes a major problem. There is commercial non availability of the first-line drugs in pediatric form. Novel antibiotics can be designed to overcome drug resistance, cut short the duration of the treatment course and to reduce drug interactions with antiretroviral therapies. A nanotechnology is one of the most promising approaches for the development of more effective and compliant medicines. The advancements in nanobased drug delivery systems for encapsulation and release of anti-TB drugs can lead to development of a more effective and affordable TB pharmacotherapy.

2. Conclusion

The most important clinical applications of currently available nanotechnology are in the areas of Biomarker discovery, cancer diagnosis, and detection of infectious microorganisms. Nanomedicine promises to play an important role in the future development of diagnostic and therapeutic methods.

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Author Profile



A. S. Pujar is serving as Professor in R L Science Institute, Belagavi



Smt Alfaz .M.Bagawan, R L Science Institute, Belagavi