Advances in Biochemistry & Applications in Medicine

Chapter 2

Nanotechnology and Nanomedicine: Going Small Means Aiming Big

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Abstract

Nanotechnology is an emerging multidisciplinary field of science and technology that works at the molecular and atomic level. It has a major contribution in the development of key novel products in different regimes of science. In field of medicine, development of novel imaging agents, pharmaceutical nano-formulations are being developed for the betterment of the human health. Drug delivery using nanoparticles is an attractive advancement in medicine that enables targeted drug-delivery to attain attractive therapeutic efficacy. Recently used drug delivery system includes, polymeric micelles, liposomes, dendrimers and many others reveal a wide variety of useful properties. Conventional drug delivery methods represent several disadvantages because of off-target action and shows severe toxic health effects. Nanomedicine is an approach of nanotechnology, being applied for diagnosis and treatment of highly infectious diseases like cardiovascular diseases, Alzheimer's disease, Parkinson's disease, using nanoscale particles and nanorobots which is a major risk to mankind. Here, we provide a broad overview of nanoparticles, its novel applications, formulations and commercialization in the field of medicine using synthetic and natural nanopolymers.

Keywords: nanotechnology; nanomedicine; nanoparticles; drug delivery; cancer therapy.

1. Introduction

Nanotechnology is an area of science that involves working with materials and devices on a nanoscale level. This molecular level investigation is at a range usually below 100 nm. On scalable terms, a nanometer is approximately 1/80,000 of the diameter of a human hair,

or 10 times the diameter of a hydrogen atom (**Figure 1**). Advancements in the emergence of biological probes, nanomaterials and analytical tools of nanoscale range, referred to as "nanotechnology" are currently being applied in diagnosis and treatment of human health disorders. Its functions are spread across all areas of sciences including physics, chemistry and biology.

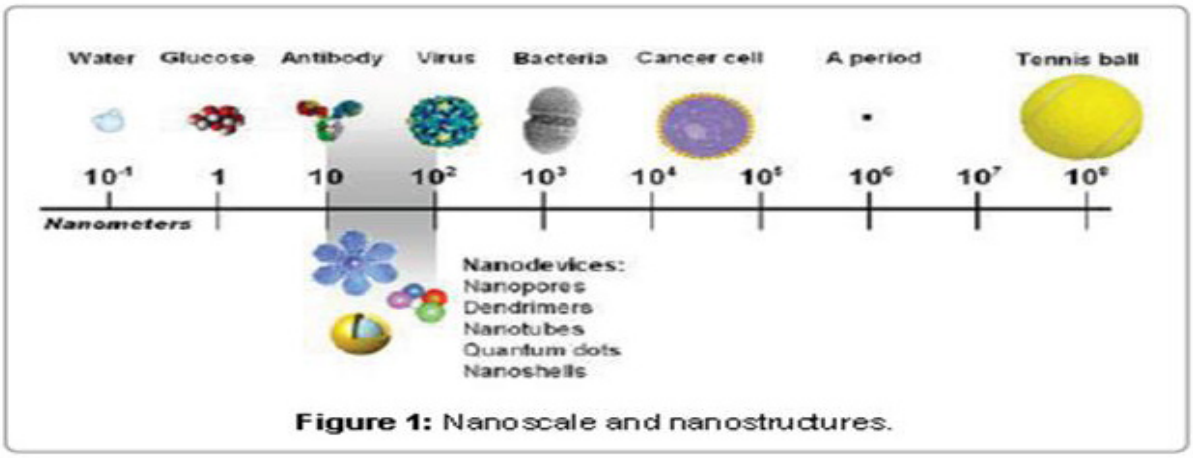


Figure 1: Nanoscale and nanostructures [1]

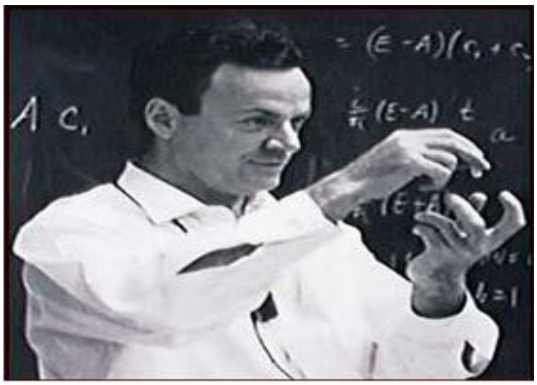
Nanotechnology has grown in leaps and bounds over the last few years. Although, the initial properties of nanomaterials studied were for its physical, mechanical, electrical, magnetic, chemical and biological applications, recently, attention has been geared towards its pharmaceutical application, especially in the area of drug delivery. Nanotechnology will offer the tools to explore the frontiers of medical science at a cellular level. Nanostructures display unique mechanical, electrical, chemical and optical properties. Understanding and controlling such properties is challenging, but harnessing them will provide exciting new opportunities for research, diagnosis and therapy of heart, lung, and blood and sleep disorders. Applications of nanotechnology for the diagnosis, treatment, monitoring and control of biological systems have recently been called as "Nanomedicine" by the National Institutes of Health (NIH).

Recent researches in nanodrug delivery have been designed to overcome the challenges through the development and fabrication of nanostructures. The technology helps in delivery of drugs that are poorly water soluble and can provide means of bypassing the liver, thereby preventing the first pass metabolism. Nanotechnology improves performance and acceptability of dosage forms by increasing their effectiveness, safety, patient adherence, as well as ultimately reducing health care costs. It may also enhance the performance of drugs that are unable to pass clinical trial phases. It definitely promises to serve as drug delivery carrier of choice for the more challenging conventional drugs used for the treatment and management of chronic diseases such as cancer, asthma, hypertension, HIV and diabetes.

2. A Brief History of Nanotechnology

'Nano' comes from the Greek word 'dwarf'. Nanotechnology is defined as the research and development of materials, devices, and systems exhibiting physical, chemical and biological properties that are different from those found on a larger scale (matter smaller than scale of

things like molecules and viruses). The vision of nanotechnology introduced in 1959 by late Nobel Physicist Richard P Feynman in dinner talk said, "There is plenty of room at the bottom," [2].



R. P. Feynman- Father of Nanotechnology

He suggested nanomachines, nanorobots and nanodevices ultimately could be used to develop a wide range of automatically precise microscopic instrumentation and manufacturing tools, could be applied to produce a vast quantity of ultra small computers and various nanoscale microscale robots.

3. Potential of Nanotechnology

Nanotechnology has received a lot of consideration because of its future prospective that can factually reform each field in which it is being applied. The current drug delivery systems are remnants of conventional drug delivery mechanisms that occur in the nanometer array like dendrimers, liposomes, nanocrystals and polymeric micelles, referred to as "nanovehicles". Colloidal gold nanoparticles were first prepared by Michael Faraday more than 150 years ago, but were never related with nanotechnology till now. For targeting the staining techniques, the particles were conjugated with antibodies termed as 'immunogold staining' and it may be considered as a precursor of recent explosive applications of gold particles in nanotechnology. The importance of nanotechnology in drug delivery is its ability to manipulate the molecules and supramolecular structures to generate the devices with programmed utility.

4. Clinical Efficacy of Nanotechnology in Drug Delivery

Clinically useful drug delivery systems need to deliver a certain amount of a drug that can be therapeutically effective over an extensive period of time. Such prerequisites can be met by the nano scale drug delivery system produced by nanotechnology. The existing techniques of constructing nanoparticles are chiefly based on double emulsion methods or solvent exchange technique. The main drawbacks with the existing methods are the low drug loading capability, low loading effectiveness and reduced ability to control the size distribution. Utilizing nanotechniques such as nanopatterning may allow construction of nanoparticles with high loading efficiency and highly homogeneous particle sizes [3].

5. Nanoparticles as Drug Delivery Carrier

Nanoparticles have been documented to in use since the use 9th century in Mesopotamia for ancient pottery. Nanoparticles represent a promising drug delivery system of controlled and targeted release. A schematic comparison of untargeted and targeted drug delivery systems is shown in **Figure 2**. Nanoparticles cover mostly all types of sciences and manufacturing technologies. The properties of this particle are flying over today scientific barriers and have passed the limitations of conventional sciences. This is the reason why nanoparticles have been evaluated for the use in many fields.

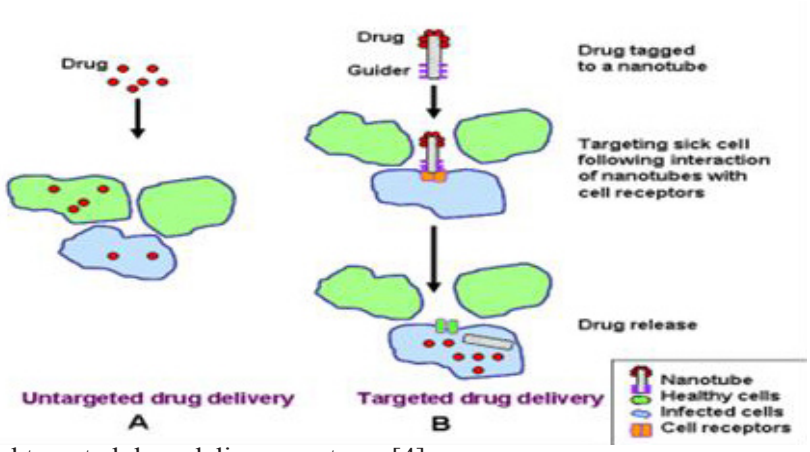


Figure 2: Untargeted and targeted drug delivery systems [4]

5.1. Assets of nanoparticles

Several properties of nanoparticles that are important for application in drug delivery mechanism comprise simple, inexpensive manufacturing method that is easy to scale up. The manufacturing process eliminates potentially toxic ingredients or organic solvents. All the components of the formulation should be commercially accessible, affordable, non-hazardous, safe and eco-friendly. The nanoparticles should be stable with respect to size, size distribution, surface morphology and other significant physical and chemical properties.

6. Formulations of Nanoparticles used in Drug Delivery Mechanism

Nanoparticles applied in drug delivery mechanisms are submicronsized particles (3-200 nm), or devices that uses a wide variety of materials which includes viruses (viral nanoparticles), polymers (polymeric nanoparticles, micelles, or dendrimers), lipids (liposomes) and organometallic compound (**Table 1**).

6.1. Polymer-drug conjugates

Polymer–drug conjugates come under the class of polymer therapeutics which consists of water-soluble polymers which are chemically conjugated to a drug through a biodegradable linker **(Figure 3B)**. The idea came into subsistence in 1975 when Ringsdorf proposed the use of polymer–drug conjugates to transport hydrophobic small molecules [6] because small drug molecules, particularly hydrophobic compounds have a low aqueous solubility and an

extensive tissue distribution profile such that administration of the free drug may cause severe side effects. Therefore, conjugation of these compounds to the biocompatible, hydrophilic polymers would considerably increase their aqueous solubility, modify their tissue distribution profile and boost the half-life in plasma circulation. The colloidal character or size of these vehicles can assist their retention within the circulation for extended periods as compared with small low molecular weight molecules.

Polymer-conjugate technology has proved to be a feasible formulation approach. A number of reports are available [7,8] on bioconjugation of protein and peptide to PEG that significantly improve the usefulness of these polymer drugs by decreasing their immunogenicity and increasing their stability in the presence of proteases. In 1994, in therapeutics, these were first used in anti-cancer therapy approved by FDA through introduction of PEG-L-asparagines (Oncaspar1). The conjugate consists of polymer of PEG having a molecular weight of 5Kd which is attached to the L-asparagines enzyme for the treatment of acute lymphoblastic leukemia [9].

Table 1: Types of nanocarriers for drug delivery [5]

System	Structure	Characteristics	Examples of compounds
Polymeric nanoparticles (polymer-drug conjugates)	Drugs are conjugated to theside chain of a linear polymer with a linker (deavable bond)	(a)Water-soluble, nontoxic, biodegradable (b)Surface modification (pegylation) (c)Selective accumulation and retention in tumor tissue (EPR effect) (d)Specific targeting of cancer cells while sparing normal cells—receptor-mediated targeting with a ligand	Albumin-Taxol (Abraxane) PGA-Taxol (Xyotax) PGA-Camptotheon (CT-2106) HPMA-DOX (PK1) HPMA-DOX- galactosamine (PK2)
Polymeric micelles	Amphiphilic block copolymers assemble and form a micelle With a hydrophobic core and hydrophilic shell	(a)Suitable carrier for water-Insoluble drug (b)Biocompatible, self-assembling, biodegradable (c)Ease of functional modification (d)Targeting potential	PEG-pluronic-DOX PEG-PAA-DOX (NK911) PEG-PLA-TaXol (GeneXol-PM)
Dendrimers	Radially emerging hyperbranched synthetic hyperbranched synthetic and repeated units	(a)Biodistribution and PK can be tuned (b)High structural and chemical homogeneity (c)Ease of functionalizati on, high ligand density (d)Controlled degradation (e)Multifunctionality	PAMAM-MTX PAMAM-plati nate
Liposomes	Self-assembling closed colloidal structures composed of lipid bilayers	(a)Amphiphilic, blocompatible (b)Ease of modification (c)Targeting potential	Pegylated liposomal DOX (Doxil) Non- pegylated liposomal DOX (Myocet) Liposomal daunorubicin

Viral nanoparticles	Protein cages, which are multivalent, self-assembled structures	(a)Surface modification by mutagenesis or bioconjugation—multivalenCY (b)Specific tumor targeting, multifunctionality (c)Defined geometry and remarkable uniformity (d)Biological compatibility and inert nature	HSP-DOX CPMV-DOX
Carbon nanotubes	Carbon cylinders composed of benzene ring	(a) Water-soluble and biocompatible through chemical modification (organic functlonalization) (b) Multifunctionality	CNT-MTX CNT-amphoteri O n B

Abbreviations: PGA: poly-(L-glutamate); HPMA: N-(2- hydroxypropyI)-methacrylamide copolymer; PEG: polyethylene glycol; PAA: poly-(--aspartate); PLA: poly-(.-lactide); PAMAM: poly(amidoamine); DOX: doxorubicin; MTX: methotrexate; PK: pharmacokinetics; EPR: enhanced permeability and retention; CNT: carbon nanotube; HSP: heat shock protein; CPMV: cowpea mosaic virus.

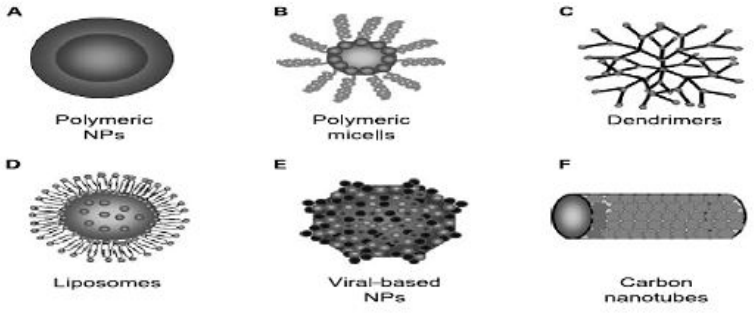


Figure 3: Types of nanocarriers for drug delivery. A, polymeric nanoparticles. B, polymeric micelles. C, dendrimers. D, liposomes. E, viral-based nanoparticles. F, carbon nanotubes [5].

6.2. Polymeric micelles

The efficient properties of micelles are based on amphiphilic block copolymers, which bring together to form a nano sized shell structure in aqueous media (**Figure 3B**). The reservoir for hydrophobic drugs are hydrophobic core region while the hydrophilic shell region stabilizes the hydrophobic core and turn into water-soluble polymers, making it an apposite candidate for *in vitro* administration [10]. The drug can be laden into a polymeric micelle in two ways: physical encapsulation [11] or chemical covalent binding [12]. Paclitaxel, Genexol-PM (PEG-poly (D, L-lactide-paclitaxel) is the first formulation of polymeric micelle which is a cremophor- free polymeric micelle-formulated paclitaxel. Multifunctional polymeric micelles with targeting ligands and imaging and therapeutic agents are currently being actively developed [13] which will become the conventional between numerous models of micelle formulation in future.

6.3. Dendrimers

A dendrimer is a synthetic polymeric macromolecule (nm), consists of several extremely pronged monomers that appear radially from the central core (**Figure 3C**). Properties associated with these dendrimers such as their monodisperse size, modifiable surface functionality, multivalency, water solubility, and available internal cavity make them attractive for drug

delivery [14]. Polyamidoamine dendrimer, the dendrimer most widely used as a scaffold, was conjugated with cisplatin [15]. The easily modifiable surface characteristic of dendrimers enables them to be simultaneously conjugated with several molecules such as imaging contrast agents, targeting ligands, or therapeutic drugs, yielding a dendrimer-based multifunctional drug delivery system [14].

6.4. Lipid coated nanoparticles (liposomes)

Liposomes are self-assembled closed colloidal structures consists of lipid bilayers with spherical shape in which a central aqueous space is present surrounded by an outer lipid bilayer (**Figure 3D & 4**). At present, different types of anticancer drugs have been applied to the lipid-based system by using an array of preparation techniques. Amongst all, lipid-based formulations of the anthracyclines doxorubicin (Doxil, Myocet) and daunorubicin (DaunoXome) are approved for the treatment of AIDS-related Kaposi's sarcoma and metastatic breast cancer [16]. Furthermore, many liposomal chemotherapeutics approved agents are recently being assessed in clinical trials [17]. The next generation liposomal drugs may be immunoliposomes, which selectively release the drug to the preferred site of action [18].

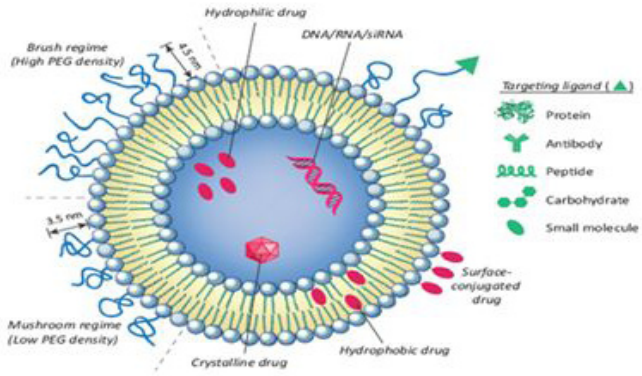


Figure 4: A Liposome used as nanoparticle for drug delivery

6.5. Viral nanoparticles

A diversity of viruses like, canine parvovirus, cowpea chlorotic mottle virus, cowpea mosaic virus and bacteriophages have been constructed for biomedical applications which consist of tissue targeting and drug delivery (**Figure 3E**). A number of peptides and targeting molecules can be exhibited in a biologically active form on the surface their capsid by using genetic or chemical processes. Therefore, a large number of ligands or antibodies plus together with folic acid, transferrin and single-chain antibodies have been conjugated in viruses for *in vivo* tumor specific targeting [19]. Through targeting of heat shock protein, specific targeting can be achieved by a dual-function protein cage that leads to the encapsulation of doxorubicin [20].

6.6. Carbon nanotubes

Carbon nanotubes are carbon cylinders consisting of benzene rings (**Figure 3F**) cur-

rently being applied as sensors in biology for detecting protein and DNA, carriers to transport protein or vaccine or diagnostic tools for the discrimination of variety of proteins from serum samples [21]. These are completely insoluble in almost all types of solvents, causing health related and toxicity problems. On the other hand, introduction of chemical conversion to carbon nanotubes can turn them into functionalized and water-soluble so that they can be associated to a broad range of active molecules, for example, as nucleic acids, therapeutic agents, proteins and peptides. Anticancer drugs (methotrexate) or antifungal agents (amphotericin B) have been covalently attached to carbon nanotubes with a fluorescent agent (FITC).

In vitro studies indicates that the drugs coupled to carbon nanotubes revealed to be more efficiently internalized into cells as compared with free drug alone and proved to have effective antifungal activity [22]. The multiple covalent functionalizations on the tips of carbon nanotubes permit them to transport a large number of molecules instantly and this approach offers a fundamental advantage in anticancer therapy.

6.7. Gold nanoparticles (GNPs)

Gold nanoparticles (GNPs) have several implementations in various fields, for example, diagnosis and cancer therapy, protein and DNA determination, drug and gene delivery, etc. Because of their exclusive properties such as, large surface area to volume ratio, small size, constancy over high temperatures, high reactivity to the living cells and translocation into the cells [23]. GNPs are appropriate for the transport of drugs to cellular targets due to their simplicity of synthesis, biocompatibility and functionalization (**Figure 5**). GNPs can successfully destroy cancer cells or bacteria functionalized with targeted specific biomolecules [24]. The efficiency of conjugation of GNPs with different kinds of antibiotics had been extensively studied [25], [26]. They observed that conjugates of GNPs showed more efficacy in inhibiting the growth of Gram-positive and Gram-negative bacteria as compared with the same dosage of antibiotics consumed alone. Their results suggested that GNPs can serve to be an efficient drug carrier in a drug delivery system [25], [26]. Some durable gold nanoparticles enclosed with vancomycin showed significant improvement of antibacterial activity compared with free antibiotic [27].

7. Smart Drug Delivery Systems

Preferably, nanoparticles drug delivery system should accumulate selectively in the target organ or tissue and simultaneously, enter target cells to transport the bioactive agent. It has been recommend [28] accumulation in the organ or tissue could be attained by the passive or antibody-mediated active targeting [29] whereas certain ligands or cell-penetrating peptides could mediate the intracellular delivery. Therefore, when necessary, a drug delivery system should be multifunctional and should acquire the ability to switch on and switch off certain functions. Another important prerequisite of multifunctional drug delivery system is

that different properties coordinated in an optimal fashion. Accordingly, if a system is generated which can provide combination of both the requirements i.e. target accumulation and specific cell surface binding; the half life of carrier in circulation should be long enough and subsequently, accumulation of drug delivery system in the target cells should proceed fast so as to prevent carrier degradation and loss of drug in interstitial space. The key problem in drug delivery system is the intracellular transport of bioactive agents. Drug delivery system nanoparticulate, such as micelles, gold nanoparticles and liposomes (**Figure 5**). are repeatedly used to increase the effectiveness of drug and DNA transport and targeting [30].

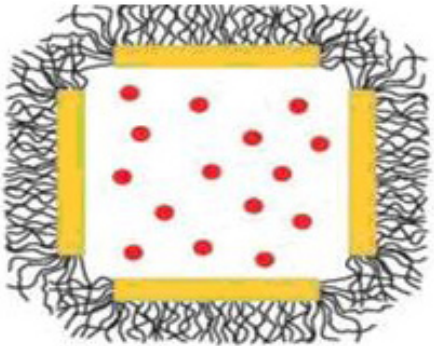


Figure 5: Smart drug delivery system - Gold nanocage covered with polymer

In drug delivery field, the most outstanding achievements were the development of smart drug delivery systems also called as stimuli-sensitive delivery systems. The idea is based on fast transitions of a physicochemical property of polymer systems when got a stimulus. This stimulus comprises physical (light, mechanical stress, electricity, temperature, ultrasound), chemical (ionic strength, pH), or biological (biomolecules, enzymes) signals and these stimuli can either be external stimuli which is artificially induced to trigger the desired events or if internal, it results into change in physicochemical changes in a living thing. Smart drug delivery systems provide a predictable and programmable drug delivery profile in response to different sources of stimulation. Smart drug delivery system has numerous advantages in comparison to conventional drug delivery systems. At the time of application, the conventional controlled transport systems are based on the programmed drug release rate in spite of the external environmental conditions, whereas, smart drug delivery system is based on release-on-demand strategy, which results into the liberation of therapeutic drug by drug carrier only at the time of receiving a specific stimulus. The best example of smart drug delivery system has been shown in self-regulated insulin transport systems which can act in response to changes in the level of glucose environment [31], [32].

7.1. Multifunctional drug carriers

A multifunctional drug delivery system refers to drug delivery carrier which shows several properties of active or passive internalization at specific disease site, capability to transport drug into intracellular target organelles or imaging ability, prolonged blood circulation, stimuli-sensitivity, etc. [33]. Practically, it shows two or more functions, in actual fact, polymer-drug conjugates and smart drug delivery system as discussed above can be regarded

as multifunctional drug delivery system. Multifunctional drug delivery system shows secondary functions as they also have internal hydrolysis inside cells or specific stimuli responsiveness in addition to delivery of drugs.

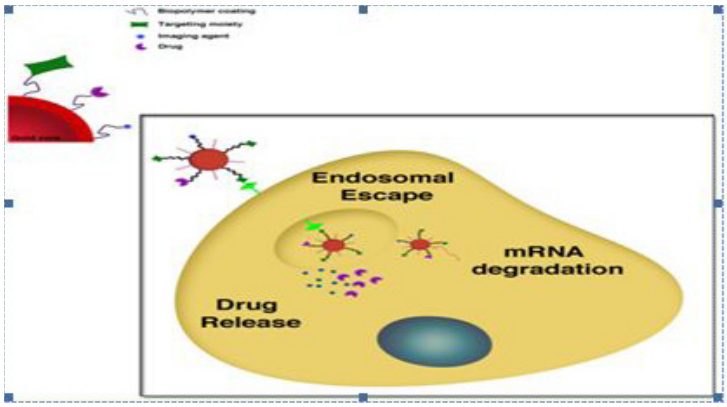


Figure 5: Multifunctional nanoparticle. The following are illustrated: the ability to carry one or more therapeutic agents; biomolecular targeting through one or more conjugated antibodies or other recognition agents; imaging signal amplification, by way of co-encapsulated contrast agents [5].

8. Role of Nanotechnology in Therapeutics

Nanoparticulates and devices can be constructed to interact with cells and tissues at a sub-cellular (i.e. molecular) level, with a high level of functional specificity, for implications in medicine and physiology, therefore, permitting a degree of combination between biological systems and technology not previously achieve. It should be esteemed that nanotechnology is not a distinct emerging scientific subject, but a multidisciplinary of conventional sciences, such as, physics, chemistry, materials science and biology, to assemble the mandatory group expertise required to exploit these novel technologies [34]. The promise that nanotechnology brings is versatile which shows improvements not only in current practices, but may also offering entirely new tools and techniques with full potential. At nanometer scale, manipulation of drugs and other materials may modify the fundamental properties and bioactivity of the materials [35]. These implements can give authorization to control over the several characteristics of drugs or agents such as restricted delivery over short or long periods of time, environmentally initiated restricted discharge or highly specific site-targeted delivery and change in solubility and blood pool retention time.

8.1. Nanomedicine

"Nanomedicine" is the discipline of science and technology dealing with diagnosis, treatment and prevention of diseases, alleviation of pain to recover the human health in short period of time through administration of micro/nanoscale particles, genetic engineering and biotechnology and ultimately multifaceted machinery systems and nonorobots [36]. It was alleged as implementating the five major subdisciplines which may overlap each other through universal technical concerns.

8.1.1. nanaomedicine in anticancer therapy

Cancer is one of the primary causes of death worldwide, inhabiting the second position in developing countries with fast growing occurrence over the time. Existing anti-cancer therapy approaches are based on chemotherapy, radiotherapy and surgery, in which chemotherapy is the one which shows the greater efficacy for cancer remedy, mainly in higher stages [37]. Implementation of new bioactive agents in anticancer therapy has greatly enhanced patient survival rate yet there are different biological hurdles that provoke drug delivery to the targeted cells and tissues. These are mainly critical blood half-life and physiological nature with excessive off-target effects and successful clearance from the human being [38,39].

The advancement and optimization of drug delivery strategies based nanoparticles concerns the early detection of cancer cells and/or specific tumor biomarkers, and the enhancement of the efficacy of the treatments applied [40]. The most important biomedical applications of nanoscale materials can be organized as shown in **Figure 6**.

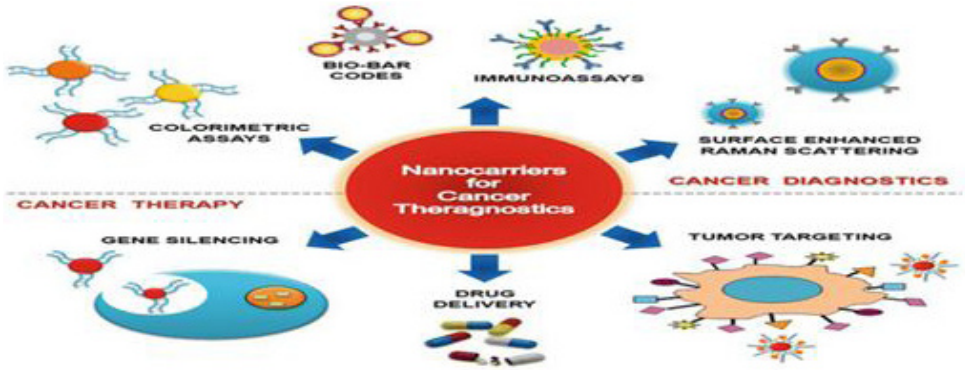


Figure 6: Biomedical applications of nanoscale materials in cancer therapy.

8.1.1.1. tumor cell targeting

Cancer cells display diverse targets on their surface, highly specific in each type of cancer. In cancer treatment, active targeting through nanoparticles is generally associated with specific type of cancer coupled with specific target. Chemotherapy is the leading approach of care for patients with targeted agents in an effort to improve the result. In various types of signaling pathways, these targeted agents are the key components in these pathways. The potential of targeted treatments has activated the study of targeted nanoparticulates that can permit synergistically act by binding and inhibiting cancer pathways while delivering therapeutic payloads. Tumor cell targeting involves many targets associated with the uncontrolled cell proliferation and the angiogenesis and others specifics for the different types of cancer.

9. Nanoparticles in Pulmonary Infections

Micronization of drugs plays a crucial role in enhancing the drug dosage form and therapeutic efficacy today. If a drug is micronized into microspheres with appropriate particle size, it can be delivered directly to the lung by the mechanical interception of capillary bed. If a drug is constructed as microspheres in the range of 7–25 μm, the microspheres can be localized in lung through i.v. administration (**Figure 7**). This approach can improve pulmonary drug con-

centration to maximize its effectiveness against some pulmonary infections such as mycoplasmal pneumonia and reduce the harmful side effects. The final nanoparticulate formulation may be administered either as a dry powder inhalers or nebulizer (metered dose inhalers). Being at nanoscale, nanoparticles are highly suitable for pulmonary transport because they can easily be air borne and delivered to the alveolus. The components of the nanoparticle formulation are biodegradable to evade deposition in the lungs, which prevents irritation of the air ways and lung tissue.

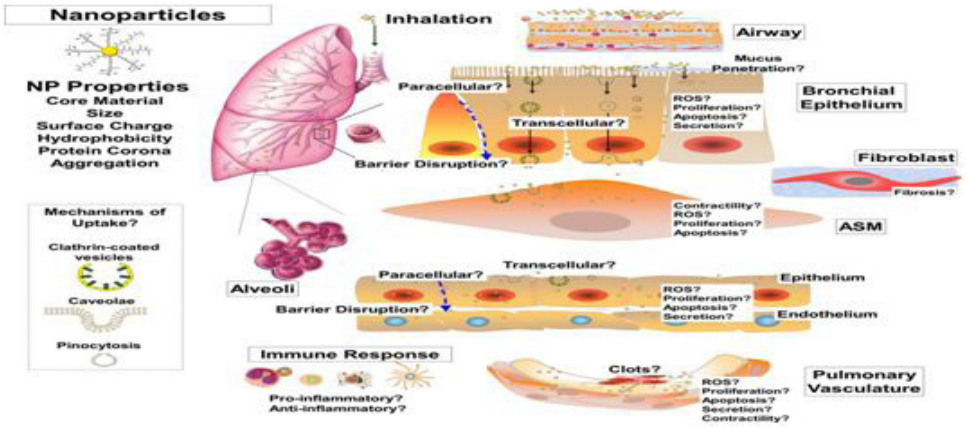


Figure 7: Pulmonary Administration of nanoparticles

10. Nanorobots in Cardiovascular Dieses

The techniques offered by nanotechnology in medical and cardiac sciences are in the fields of, imaging, diagnosis and tissue engineering. Implementation of nanotechnology approaches has offered insight into the potential benefits of nanotechnology in cardiovascular sciences. However, the benefits of nanotechnology exceed all features of medicine which is one of the important applications of nanomedicine in the area of cardiovascular sciences. Conventional surgical practices includes opening of the chest through the sternum and connects the patient to a cardiopulmonary bypass machine and arrested the heart. Different types of surgical techniques are executed on the arrested heart. Although, these practices can lead to additional morbidity such that they trigger central nervous system disorders and also the gastrointestinal complications.

Nanoscience offers approaches to design and build up innovative cardiac equipments, which are smaller in size and also more efficient. Surgical systems using robotics are being developed to give extraordinary control over equipments to offer accuracy to surgeons. This is predominantly useful to minimize invasive cardiac surgery. Instead of manipulating surgical instruments, surgeons use their fingers to move joystick handles on a control console to maneuver robot arms containing miniature instruments that are inserted into ports in the patient. The key novel implementation of nanotechnology in diagnostics and medical research are nanorobots. In the human body, nanorobots could monitor the degree of different compounds and document the information required in their internal memory. They can be quickly used in the inspection of a given tissue, examining its biomechanical and histometrical appearance

in larger aspect. As biotechnology expand the range and efficiency of treatment alternatives available from nanoparticles, the beginning of molecular nanotechnology will again extremely enlarge the comfort, effectiveness and speed of future medical therapies and significantly elevating their cost, risk and invasiveness [41].

11. Alzheimer's Disese with Nanotherapeutics

Alzheimer's disease is the major brain syndrome adversely affecting the elderly population worldwide. It is estimated to become a major health concern with severe socio-economic consequence in the coming decades. The total number of people affected by Alzheimer's disease worldwide today is about 15 million people which are expected to grow by four times by 2050. One of the FDA-approved commercially available drugs used for reducing the symptom in dementia is Rivastigmine. Due to its inability to cross the blood brain barrier and its consequences on peripheral organs, unable to attain its complete therapeutic potential.

In drug delivery mechanism of brain, biodegradable polymeric nanoparticles may be considered as relevant source [42]. Administration of rivastigmine injected intravenously rivastigmine was coupled to Poly (n-butylcyanoacrylate) (PnBCA) nanoparticles coated with the chemical polysorbate 80, which can be efficiently taken up as compared with free drug (an enhancement of up to 3.82 fold was found). This improved delivery is explained in terms of a mechanism which involves the binding of lipoproteins present in the blood to the nanoparticle surface.

11.1. Nanaogels

Ikeda and his coworkers elucidated an example for the Aβ anti-assembly strategy [43]. They designed an amphipathic nanogel that incorporates proteins and controls their folding and aggregation, similar to natural chaperones (proteins assisting the non-covalent folding and/or unfolding). In the case of Aβ, these nanogels would inhibit the amyloidogenesis process effectively through this mechanism (**Figure 8**).

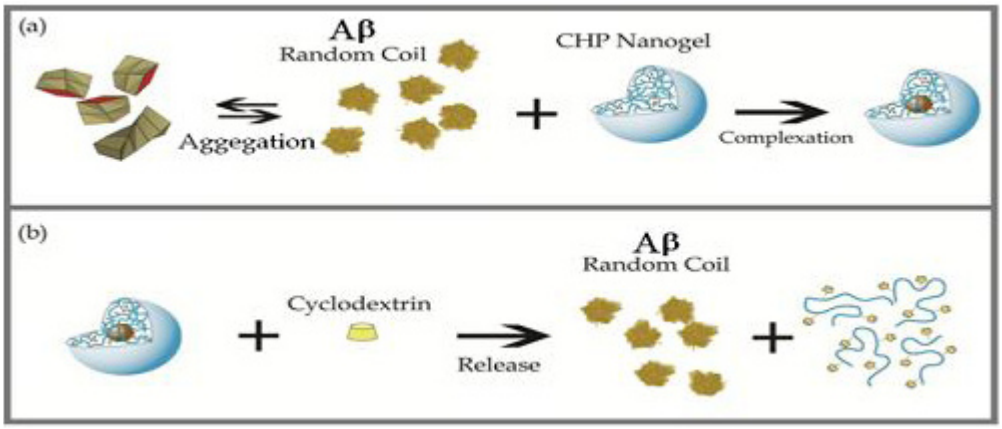


Figure 8: Schematic representation of the interactions between artificial nanoscale chaperone system and misfolded Aβ. (b). Refolded Aβ monomers are released after addition of cyclodextrin.

12. Parkinson's Disease

This can enhance current therapy of Parkinson's disease. Parkinson's disease is the second major neurodegenerative disorder after Alzheimer's disease. It influences one in every 100 persons with age above 65 years. Parkinson's disease is a disorder of the central nervous system. In this disorder, neuro-inflammatory reactions are implicated which leads to serious difficulties in body motions. Recent therapies goal to develop the functional capacity of the patient for long period of time if possible but they cannot modify the succession of the neurodegenerative process.

13. Conclusion

Nanoparticle mediated drug delivery is going to have a great potential impact on the society. It will drastically improve patient's quality of life associated with healthcare, early detection of pathologic conditions, reduce the severity of disease and result in improved clinical outcome for the patient. Together with the progression of nanoscale drug delivery systems, advances in nanoscale imaging suggest the potential for the development of multifunctional ‘‘smart’’ nanoparticles that may facilitate the realization of individualized cancer therapy and early diagnosis and treatment of highly infectious diseases like AD. Almost all types of nanoparticles including polymeric nanoparticles, nanocrystals, polymeric micelles, dendrimers and carbon nanotubes have been evaluated for their suitability as multifunctional nanoparticles that can be applied for simultaneous *in vivo* imaging and treatment of cancers. But realizing such a potential requires harmonized efforts among scientists in different disciplines and continued support by funding agencies.

14. References

1. Nikalje, A.P. (2015). Nanotechnology and its Applications in Medicine. Med Chem. 5: 81-89.

2. Feynman, R.P. (1960). There's plenty of room at the bottom. Eng Sci. 23: 22-36.

3. Rita, M., Fiore, P.N, Sonia, T., Roberta, C., Francesca, I. and Nevio, Pi. (2007). A new crown ether as vesicular carrier for 5-fluoruracil: Synthesis, characterization and drug delivery evaluation. Colloids and Surfaces B: Biointerfaces. 58(2):197-202.

4. Suri, S.S., Fenniri, H. and Singh, B. (2007). "Nanotechnology-based drug delivery systems." J. Occupational Medicine Toxicology. 2(1): 16.

5. Cho, Y.J., Kim, C.J., Kim, N., Kim, C.T. and Park, B. (2008). Some cases in applications of nanotechnology to food and agricultural systems. Biochip J. 2(3): 183-185.

6. Ringsdorf, H. (1975). Structure and properties of pharmacologically active polymers. J Polym Sci Polym Sympo. 51135153.

7. Duncan, R., Ringsdorf, H. and Satchi-Fainaro, R. (2006). Polymer therapeutics: Polymers as drugs, drug and protein conjugates and gene delivery systems: Past, present and future opportunities. Advances in Polymer Sci. 192(1): 18.

8. Harris, J.M. and R.B. (2003). Chess of. Effect on pegylation, pharmaceuticals, Nature Reviews Drug Discovery.

21421.

9. Veronese, F.M., Pasut, G. and P.E. (2005). Gylation, approach. Successful drug to delivery. Nature Reviews Drug Discovery. 14518

10. Adams, M.L., Lavasanifar, A, and Kwon, G.S. (2003). Amphiphilic block copolymers for drug delivery. J Pharm Sci. 92: 1343-1355.

11. Batrakova EV, Dorodnych TY, Klinskii EY, et al. (1996). Anthracycline antibiotics non-covalently incorporated into the block copolymer micelles: *in vivo* evaluation of anti-cancer activity. Br J Cancer.74: 1545-1552.

12. Nakanishi, T,, Fukushima, S., Okamoto, K,, et al. (2001). Development of the polymer micelle carrier system for doxorubicin. J Control Release. 74: 295-302.

13. Nasongkla, N., Bey, E., Ren, J., Ai, H., Khemtong, C. and Guthi, J.S. (2006). Multifunctional polymeric micelles as cancer-targeted, MRI-ultrasensitive drug delivery systems. Nano Lett. 6: 2427-2430.

14. Svenson S, Tomalia DA. (2005). Dendrimers in biomedical applications reflections on the field. Adv Drug Deliv Rev. 57: 2106-2129.

15. Malik, N., Evagorou, E.G. and Duncan, R. (1999). Dendrimerplatinate: a novel approach to cancer chemotherapy. Anticancer Drugs. 10: 767-776.

16. Markman, M. (2006). Pegylated liposomal doxorubicin in the treatment of cancers of the breast and ovary. Expert Opin Pharmacother. 7: 1469-1474.

17. Hofheinz, R.D., Gnad-Vogt, S.U., Beyer, U. and Hochhaus. (2005). A Liposomal encapsulated anti-cancer drugs. Anticancer Drugs. 16: 691-707.

18. Wu, J., Liu, Q. and Lee, R,J. (2006). A folate receptor-targeted liposomal formulation for paclitaxel. Int J Pharm. 316: 148-153.

19. Manchester M, Singh P. (2006). Virus-based nanoparticles (Vnanoparticles): platform technologies for diagnostic imaging. Adv Drug Deliv Rev. 58: 1505-1522.

20. Flenniken, M.L., Willits, D.A., Harmsen, A.L., et al. (2006). Melanoma and lymphocyte cell-specific targeting incorporated into a heat shock protein cage architecture. Chem Biol. 13: 161-170.

21. Bianco, A., Kostarelos, K., Partidos, C.D. and Prato, M. (2005). Biomedical applications of functionalised carbon nanotubes. Chem Commun. 5: 571.

22. Pastorin, G., Wu, W., Wieckowski, S., et al. (2006). Double functionalisation of carbon nanotubes for multimodal drug delivery. Chem Commun. 11: 1182-1184.

23. Sheikhloo, Z., Salouti, M. and Katiraee, F. (2011). Biological synthesis of gold nanoparticles by fungus Epicoccum nigrum. J Clust Sci. 22: 661-665.

24. Tiwari, P.M., Vig, K., Dennis, V.A. and Singh, S.R. (2011). Functionalized Gold Nanoparticles and Their Biomedical Applications. Nanomaterials. 1: 31-63.

25. Grace, N.A. and Pandian. K. (2007). Antibacterial efficacy of aminoglycosidic antibiotics protected gold nanoparticles-A brief study. Colloids Surf A Physicochem Eng Asp. 297: 63-70.

26. Saha, B., Bhattacharya, J., Mukherjee, A., et al. (2007) *In vitro* structural and functional evaluation of gold nanoparticles conjugated antibiotics. Nanoscale Res Lett 2: 614-22.

27. Gu, H. et al. (2003). Presenting vancomycin on nanoparticles to enhance antimicrobial activities. Nano Lett. 3: 1261-1263.

28. Maeda, H., Wu, J., Sawa, T., Matsumura, Y. and Hori, K. (2000).Tumor vascular permeability and the EPR effect in macromolecular therapeutics: A review J. Controlled Release. 6527184

29. Jaracz, S., Chen, J., Kuznetsova, L.V. and Ojima, I. (2005). Recent advances in tumor-targeting anticancer drug conjugates. Bioorg Med Chem. 13504354.

30. Torchilin, V.P. (2005). Recent advances with liposomes as pharmaceutical carriers. Nat Rev Drug Discovery. 414560.

31. Chu, L.Y., Liang, Y.J., Chen, W.M., Ju, X.J. and Wang, H.D. (2004). Preparation of glucose-sensitive microcapsules with a porous membrane and functional gates. Colloids Surf. B: Biointerfaces. 37914.

32. Kim, J.J. and Park, K. (2001). Modulated insulin delivery from glucose-sensitive hydrogel dosage forms. J Control Release. 773947.

33. Lee, E.S., Na, K., and Bae, Y. H. (2005). Super p^H-sensitive multifunctional polymeric micelle. Nano. Lett. 53259.

34. Silva, G.A. (2004). Introduction to nanotechnology and its applications to medicine. Surg Neurol. 61: 216-20.

35. Caruthers, S.D., Wickline, S.A. and Lanza, G.M. (2007). Nanotechnological applications in medicine. Curr Opin Biotechnol. 18: 26–30.

36. Patil, M., Mehta, S.D. and Guvva, S. (2008). Future impact of nanotechnology on medicine and dentistry. J Indian Soc Periodontol. 12(2): 34-40.

37. Blanco, E., Hsiao, A., Mann, A.P., Landry, M.G., Meric-Bernstam, F, and Ferrari, M. (2011). Nanomedicine in cancer therapy: Innovative trends and prospects. Cancer Sci. 102(7): 1247-1252.

38. Conde, J., Doria, G. 0 and Baptista, P. (2012). Noble Metal Nanoparticles Applications in Cancer. J Drug Delivery. 2012(2012): 1-12.

39. Sanna, A., Pala, N., Sechi, M. (2014). Targeted therapy using nanotechnology: focus on cancer. Int J Nanomedicine. 9: 467-483.

40. Baptista, P.V. (2012). Could gold nanoprobes be an important tool in cancer diagnostics? Expert Reviews of Molecular Diagnostics. 12(6): 541-543.

41. Ernest, H. and Rahul, S. (2005). Impact of nanotechnology on biomedical sciences. Review of current concepts on convergence of nanotechnology with biology. Online Journal of Nanotechnology.

42. Wilson, B., Samanta, M.K., Santhi, K., Kumar, K.P.S., Paramakrishnan, N. and Suresh, B. (2008). "Poly(n-butylcyanoacrylate) Nanoparticles Coated with Polysorbate 80 for the Targeted Delivery of Rivastigmine into the Brain to Treat Alzheimer's Disease". Brain Res. 1200: 159-168.

43. Ikeda, K., Okada, T., Sawada, S., Akiyoshi, K. and Matsuzaki. K. (2008). Inhibition of the formation of amyloid beta-protein fibrils using biocompatible nanogels as artificial chaperones. FEBS Lett. 580(28-29): 6587-6595.