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A COMPREHENSIVE REVIEW ON NOVEL PHARMACEUTICAL NANOTECHNOLOGY AND ITS APPLICATIONS

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Abstract:
The health care industry is one ofhuge part of world industries today. With such a huge customer based and an increasing demand, pharmaceutical industries will respond to patient's demands by developing and successfully expanding their technologies. The nature of newly discovered drugs becomes more complex and toxicity also increased, new novel modes of delivery are necessary to deliver them to the desired sites of the body. Due to this reason the renowned pharmaceutical companies are concentrating on applying new methods and technologies. As compared to other technologies pharmaceutical nanotechnology is one of the most comprehensive technologies. Pharmaceutical nanotechnology gives novel tools with lots of opportunities and scope, which are expected to have a great impact not only on complicated diagnosis of disease but also on the therapeutics of diseases. Due to this advances, pharmaceutical nanotechnology is now popular and well-established for diagnostics, drug delivery and treatment of diseases through its nano-structured tools & devices. Pharmaceutical nanotechnology assists to develop novel technologies where current existing and conventional technologies may have their limits.It also provides opportunities to improve materials, medical devices performance. Due to current novel development in nano-technology, global interest shown by scientists, governments and industries assure that there is enormous potential and huge scope of nano-technology based drug delivery system in near future.

Keywords: *Pharmaceutical nanotechnology, Nano technology in drug delivery system, Nano technology in disease diagnosis.*

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INTRODUCTION:

Nanotechnology is a rapidly growing science of producing and utilizing nano-sized particles that they are having very small size, that measure in nano-meter. In other words, nanotechnology is the art of characterizing, manipulating and organizing matter systemically, at the nano-meter scale, which has created a revolution in all research perform in science, engineering, technology, drug delivery and therapeutics. The normal size of accessible structures is resides in the sub-micrometer range, being within the limits of optical resolution and visible barely with a light microscope. This scale is very smaller than structures that could be resolved by the naked eye, but still 1000 times larger than an atom. The nanotechnology is defined as developmentof a novelsizestructureresides is in the nano-meter range and the size range below these dimensions of a typical structure [1]. Today there are lots of treatments that require a more time and are also very expensive too. With the utilization of nanotechnology in pharmaceutical field, quicker and less expensive treatments can be developed. Normally, drugs flows and travels through the whole body before it reach the disease affected area or site. Using nanotechnology pharmaceuticals, the drug can be targeted to a precise location which would make the drug much more effective and reduce the chances of possible side-effects [2,3]. Current development in Pharmaceutical Nanotechnology provides a novel approach and complete technology against cancer for early diagnosis, prediction, prevention, personalized therapy and targeted drug delivery of anticancer drug or medicine.Nanotechnology would play important role in target-specific drug delivery and methods for early diagnosis of diseases and disorders [4].

Pharmaceutical Nanotechnology Based Systems

It is a challenging task developing a drug delivery system that enhances the pharmaceutical action of a drug whilereducing its toxic side effect in vivo. By using pharmaceutical nano-systems these challenging task can controlled. Nano-materials and nano-devicesaretwo basic type's pharmaceutical nanotechnology, which play a main role in pharmaceutical nanotechnology and other fields.The nano materials, are made from biomaterials; used in dental implants or orthopaedic. Their biocompatibility with the living cells can enhances by surface modified or coatings. These are further classified into two main type nano-structure materials and nano-crystals [5]. Nanostructured materials are vital because it can bridge the gap between molecular & bulk levels [6]. Nanostructured materials are processed forms of nano-materials with special size, shapes and functions. These include fullerenes, dendrimers, carbon nanotubes, quantum dots, and many more [7]. Nanomaterials are widely used in drug delivery due to their advantages like they can increase drug solubility; drug targetingand can lead to controlled release. They are used in various drug deliveries like genedelivery, hormone delivery through the skin, drug delivery through the eye and in oral and vaccine delivery systems and treatment like targeted anti-cancer treatment. Now a day's lot of companies worldwide employ nanoparticles in anti-cancer treatment. Nano devices are very small devices in the nanoscale and some of which include microarrays for the different kind of biological assay e.g. DNA, protein, cell, microfluidics for control and manipulation of micro or nanolitre of fluids, nano- and micro-electromechanical systems (NEMS/ MEMS), and disease signatures and some intelligent nano machines like respirocytes. Nanocrystals are prepared in special mills and the resulting nano sized drugscan be applied intravenously as nanosuspensions or bronchially through an inhaler. This reduced size drug size increases the surface/volume-ratio and altimetly enhancement in bioavailability of almost insoluble pharmaceuticals [8].

TYPES OF PHARMACEUTICAL NANOSYSTEMS WITH THEIR APPLICATIONS

The following are different types of nanosystems with their pharmaceutical applications

Dendrimers

Dendrimers are globular, highly branched, and synthetic polymers containing of an initiator core and multiple layers with active terminal groups. These layers are comprised of repeating units and each of these layer is called a generation. The core of a dendrimer is indicated as generation zero. The specific molecular structureof dendrimers with interior coremakes them suitable to carry various drugs using their multivalent surfaces throughelectrostatic adsorption or covalent conjugation. The advantages of dendrimers are that they are uniform in size to many proteins and biomolecules like insulin, and haemoglobin. Second generation dendrimers have a width similar to that of DNA (2.4 nm). Through hydrophobic interaction, hydrogen bond, or chemical linkage drugs can be loaded in the cavities in dendrimer cores. Researchers in Michigan developed a polyamidoamine-based G5 dendrimer for targeted drug delivery to tumour.The polyamidoamine-based G5 dendrimer has a diameter of about 5 nm and more than 100 functional primary amines on the surface. By attaching folate as the targeting molecule and methotrexate as the

therapeutic agent, the G5 dendrimer was many folds more effective than methotrexate alone in prohibiting tumourgrowth [9]. Dendrimers used in drug delivery and imaging are usually 10 to 100 nm in diameter with multiple functional groups on their surface, makes them ideal carriers for targeted drug delivery [10]. However, Dendrimers with poly cationic surface shown great potential in the targeted delivery of anticancer therapeutic agents, which can form multiple interactions with a number of target receptors. The poly cationic surface is also having main disadvantage in therapeutic delivery applications are due to their toxic effect on cell membranes [11].

Liposomes

In 1976 liposomes was first described as lipid vesicles that was applied in drug delivery [11].In 1995 liposomes were the first nanoscale drug delivery devices gets approval for clinical use. Since then, up to today many of developments are takes place in liposomes drug delivery system. Now a days liposomes are available not only for oral but also for topical and transdermal route. Long circulating liposomes, stimuli-responsive liposomes, elastic liposomes, nebulized liposomes are the new advances of liposomal drug delivery system [12]. Liposomes are spherical vesicles composed of amphiphilic phospholipids and cholesterol, which self-associate into bilayers to encapsulate an aqueous interior. The amphiphilic phospholipid molecules form a closed bilayer sphere in an attempt tostill maintaining contact with the aqueous phase via the hydrophilic head group, while shield their hydrophobic groups from the aqueous environment. Because a liposome can encapsulate an aqueous solution with a lipophilic outer membrane, hydrophilic solutes cannot pass through the lipids. So, liposomes can carry both lipophilic molecules as outer membrane and hydrophilic molecules in the inner aqueous core. Liposomes can be classified into three categories depending upon their size and number of bilayers as: multilamellar vesicles (multi bilayer), large unilamellar vesicles (large size, single bilayer), and small unilamellar vesicles (small size, single bilayer). Liposomes can be divided into five types based upon composition as well as mechanism of intracellular delivery: conventional liposomes, pH-sensitive liposomes, cationic liposomes, immune liposomes, and long-circulating liposomes [10]. The liposomeslipid bilayer fuse with bilayers of the cell membrane delivers its contents to the appropriate area. Liposomes have been intensivelyinvestigated for their use in cancer therapy. The effectiveness of drug delivery systems due to their small size, controlled time release of the drug, modification of drug pharmacokinetics, biological distribution and reduced drug toxicity [3].

Quantum dots

Quantum dots are nanocrystal or small tiny particles a semi conducting material with 2-10 nanometer diameter. Quantum dots are first discovered in 1980[13]. Quantum dots are used for periods ranging from milliseconds to minutes to track individual glycine receptors (GlyRs) and to analyse their dynamics in the neuronal membrane of living cells [14]. In recent years, semiconductor quantum dots have attracted the attention of many research groups because of their applications in scientific and technological significance in microelectronics, optoelectronics and cellular imaging [4]. Quantum Dots are semi conducting materials consisting of a semiconductor core coated by a shell to improve optical properties. Their properties originate from their physical size which ranges from 20-200A° in diameter [7]. Quantum dots are widely used in biological applications that require fluorescence, including cell biology and immune fluoresence assays, DNA array technology, particularly in the immune staining of proteins, microtubules and nuclear antigens [15]. The most commonly used Quantum dots are cadmium telluride, cadmium selenide, indium, arsenide and indium phosphide. In bio-imaging these particles serve as contrast agents, providing much greater resolution than existing fluorescent dyes. Quantum Dots particles absorbing white light and re-emit it with different bulk band gap energies corresponding to different combinations of particles within nanoseconds [10].

Carbon nanotubes

Carbon nanotubes are hexagonal networks of carbon atoms. Carbon nanotubes are 1nm in diameter and 1-100nm in length. Nanotubes are of two type's single walled nanotubes and multi walled nanotubes. These are small macro molecules have unique size, shape and remarkable physical properties [16]. Carbon nanotubes are carbon cylinders composed of benzene rings.Carbon nanotubeshave been used as diagnostic devices for the discrimination of different proteins from serum samples, biological sensors for detecting protein and DNA, and as carriers to deliver drug, protein or vaccine[4]. Single-walled carbon nanotubes have been usedto develop highly specific electronic biomolecule detectors as well as a platform for investigating surface–protein and protein–protein binding [14].

Polymeric nanoparticles

Polymeric nanoparticles having some inherent properties like biocompatibility, biodegradability,

non-toxicity and non-immunogenicity [7]. Polymeric nanoparticles are the combined name for nanospheres and nanocapsules [11]. Polymeric nanoparticles are solid colloidal particle with radius ranging from 0.5 to 500 nm [17]. Polymeric nanoparticles are developed as effective delivery vehicles because itsability to enhance the efficacy and minimizes the side effects of chemotherapeutic drugs due to their passive tumour-targeting properties. Polymeric nanoparticles having preferentially capacity to accumulate in and around the tumour mass also gives a platform for improved diagnostics of tumour, hereby this property laying the foundation for the new development of multi-functional nanoparticle systems in cancer diagnosis &therapy [18]. For preparation of polymeric nanoparticles natural macromolecules, such as proteins and polysaccharides, non-polar lipids, metal oxides and silica, and Polymers like poly (alkylcyanocrystalates), poly (mythylidenemalnolate 2.1.2), polyesters, e.g., poly (lactic acid), poly(e-caprolactone), and their copolymers are used [19]. Polymeric nanoparticles can be used for better application by overcoming obstacles in conventional drug delivery & effective drug delivery and would enhance treatment & patient compliance [20].

Polymeric micelles

Now a day's these micelles have emerged as a new promising colloidal carrier for targeted delivery of poor water soluble as well as amphiphilic drugs. Polymeric micelles can enhance solubilisation of hydrophilic compounds in their inner core. These are more stable as compared to surfactant micelles [21]. A polymer micelle is a nanoparticle consisting of two main parts one hydrophilic shell and one hydrophobic core. It can be divided into two main categories: hydrophobically assembled micelles and polyion-complex micelles. The hydrophobically assembled micelles consist of amphiphilic copolymers with a hydrophobic and a hydrophilic block. Balance between those two blocks in an aqueous medium induces spontaneous formation of nano-sized particulates. For most block copolymers, poly (ethylene glycol) is used as a hydrophilic block. Different micelle properties originate from the nature of hydrophobic core-forming materials, which include biodegradable polyesters polymers such as poly (glycolic acid), poly (lactic acid), and poly (e-caprolactone) [22]. These are usually of less than 100nm and their hydrophilic surface inhibit uptake by reticuloendothelial system. Micelles formed in solutions as aggregates in which the component molecules are arranged in a spherical structure with hydrophobic core shield from water by a mantle of hydrophilic groups. These are used for systemic delivery of water insoluble drugs [7].

Metallic nanoparticle:

Metallic nanoparticle can be prepared by various methods by using metals like gold etc. A metal nanoparticle shows similar optical properties which is dependent upon shape and size [23]. Researcher made nanoparticle by using various metals but out of all of themgoldand silver nanoparticles are important for biomedical use, a large number of ligands have been linked to nanoparticles such as peptides,sugar, proteins and DNA [7]. They have been used fordrug discovery, bioassays, active delivery of bioactive, detection, imaging and many other applications due to surface functionalization ability. Due these advantages it is an alternative to quantum-dots [8].

Fullerenes

A Fullerene isentirely composed of carbon in the forms of hollow sphere, ellipsoid or tubular and many more shapes. Buckminster Fuller who designed geodesic physical structures and buildings based on this geometry, fullerenes are commonly referred to as "Buckyballs". A Buckyball is a carbon consisting hollow geometric sphere, first found in soot developed from a laboratory experiment [24]. Fullerenes are similar to carbon nanotubes in that their molecular framework is entirely composed of an extensive p-conjugated carbon skeleton. They are typically synthesized by poorly understood empirical methods; for instance, the vaporization of graphite by resistive heating yields grunge from which fullerenes can be isolated chromatographically [25]. Fullerenes bind very efficiently and inactivate radicals that play a vital role in the development of diseases of the central nervous system e.g. Parkinson, Alzheimer diseases and cardiovascular diseases [26].

APPLICATION OF PHARMACEUTICAL NANOTECHNOLOGY

From the concept of the Nanotechnology, the current approach to Pharmaceutical therapy in which drug is systemically absorbed by whole body in order to affect a single localized organ, according to which that organ, or diseased part of it , should be targeted with molecular precision. The pharmaceuticals in current rely on slight differential selectivity of binding or uptake, and a dose sufficient to be effective against the diseased organ is likely to have significantly deleterious effects on the body as a whole when weak binding and uptake are summed over the entire rest of the body. The pharmaceutical nanotechnology has been also focusing the following applications.

Drug discovery and design

Nanotechnology is playing vital role for better understanding of mechanism of the drug action and identification of biomarker associated with specific disease which assist in new drug discovery and design. Byidentifying the protein present on the surface or target surface nanotechnology helps in identification and validation of target.Nanotechnology will enhance the drug discovery process, through miniaturization, automation, speed and reliability of assays. The examples of nanotechnology in drug discovery arequantum dots are used for periods ranging from milliseconds to minutes to track individual glycine receptors and to analyse their dynamics in the neuronal membrane of living cells, single walled nanotubes are successfully used to identity surface protein of pathogen. Similarly, gold nanoparticles, nanobodies which are smallest, intact, antigen-binding fragments produced by Ablynx are some commonly used nanomaterials in diagnostics [27].

Drug delivery

The pharmacokinetics profile of new discovered drug entity can be modified by using Pharmaceutical nanotechnology[7]. Nanoparticle-based drug delivery has many advantages over conventional drug delivery system, such as enhancing drug-therapeutic efficiency and pharmacological characteristics. Because nanoparticles having advantages such asmodify pharmacokinetics, improve the solubility of poorly water-soluble drugs, improve bioavailability,increase drug half-life by reducing immunogenicity, increase specificity towards the target cell or tissue therefore reducing side effects, diminish drug metabolism and enable a more controllable release of therapeutic compounds and the delivery of two or more drugs simultaneously for combination therapy [28]. The nanotechnology based drug delivery system also used for delivery of miconazole to the skin [29]. Nanotechnologies endue drug delivery system with optimized physical, chemical and biological properties can serve as effective delivery tools for currently available bioactives. Few nanotechnology based drug delivery devices are liposome,dendrimer,polymeric nanoparticles, polymer-drug conjugates, polymeric micelles, antibody- drug conjugates, which can broadly be classify as (i) stimuli sensitive delivery system, (ii)sustained and controlled delivery system, (iii) intracellular, cellular, tissue site specific targeting, (iii) multifunctional system for combined delivery of therapeutics, bio-sensing and diagnostic, and (iv)functional system for delivery of bioactives [30].

Molecular Diagnostics

The nano science of representing, characterizing, and quantifying subcellular biological processes in entire organisms is called as Molecular imaging. These processes include gene expression, protein-protein interaction, signal transduction, cellular metabolism, and both intracellular and intercellular trafficking. Some nanoparticles such as iron oxide nanocrystal, quantum dots and metallic nanoparticleswhich have inherent diagnostic properties. They have been successfully utilized in various magnetic resonance imagings, optical imaging, ultrasonic imaging and nuclear imaging [31]. The combination of other nanotechnology-based materialswithnanoparticles has the potential to address this emerging challenge and provide technologies that makes diagnoses possible at the level of single molecules and single cells [28]. In bio-imaging quantum dots particles such ascadmium telluride, cadmium selenide, indium phosphide, and indium arsenide serve as contrast agents, providing much higher resolution than existing fluorescent dyes [10].

Tissue Engineering

Tissue engineering makes use of artificially stimulated cell proliferation by using suitable nanomaterialbased growth factorsandscaffolds.Nanotechnology can assist to repair damaged tissueor toreproduce it. In future with more advances in tissue engineering might replace today's conventional treatments like organ transplants or artificial implants [32]. Nanotechnologies and micro technologies can be merged with biomaterials to generate scaffolds for tissue engineering that can maintain and regulate cell behaviour [33]. Nanotechnology can be used to create Nano patterns, nanofibers and control release nano particles with useful application in tissue engineering [34].

In gene therapy

In gene therapy, using a carrier moleculea normal gene is inserted in place of an abnormal diseasecausing gene. Conventional viral vectorsuse as a carrier molecule are associated with inflammatory reactions, adverse immunologic, and diseases in the host. Nanotechnology based drug delivery systems have currently emerged as potential carrierfor effective and promising tool in systemic gene treatment. Nanoparticles composed form polymer like chitosan, poly-l-lysine and modified silica nanoparticles have been reported to have enhanced transfection efficiency and reduced cytotoxicity. Nanotechnology provides viable option as ideal vector in gene delivery [35]. Nano sized liposomes can be used for delivery of genetic

material into desire cells. Liposomes incorporated with polyethylene glycol and galactose target liver cells effectively due to their rapid uptake by liver Kupffer cells. Thus gene therapy may be useful with such liposomal nanoparticles for variousliver disorders such ashereditary hemochromatosisand Wilson's disease [25]. A polymeric nanoparticle givesanti-proliferative effects by targeted delivery of gene therapy to breast cancer cells [36].

Stem cell therapy

Current research suggestsnanoparticles may be useful as effective tools for improving stem cell therapy. Chemical engineers have successfully used nanoparticles to enhance stem cells' ability to stimulate regeneration of damaged vascular tissue and reduce muscle degeneration in mice[36]. In stem cell therapy magnetic nanoparticles coupled to antibodies are added to a blood or bone marrow sample that contains the target adult stem cells. The magnetic particles bind the target cells, which then can be recovered using a magnet. This technique is used in cell therapies to isolate adult stem cells that are then retransplanted in the patient e.g. to treat blood disorders or cardiac diseases [26]. Theuse of iron oxide nanoparticles to develop magnetodendrimers that can be used to label human neural stem cells and mesenchymal stem cells through nonspecific membrane adsorption processes [37]. The use of super paramagnetic iron oxide particles to label human mesenchymal stem cells to track their migration using MRI after transplanting it for cartilage repair [38].

In Cancer treatment

The research going on their conclusions shows that nanoparticles are useful for cancer treatments these includes are liposomes, quantum dots, solid lipid nanoparticles, nano shells, gold nanoparticles. Due to small size nanoparticles penetrate small capillary and are taken up by the cell which allows for efficient drug accumulation at the target sites in the body [39]. The effectiveness of nanotechnology based drug delivery systems have few advantages such as their small size, reduced drug toxicity, controlled time release of the drug and modification of drug pharmacokinetics and biological distribution overcome drawbacks of conventional anti-cancer drug delivery system [40].

Artificial organs and implants

Transplantation is often the only option for many patients those suffering from end-stage organ failure. Application of nanotechnology in artificial organ and implant development generates hope for those patients. Nanotechnology can be useful for the development of artificial organs and implants but still safety and clinical approvals yet to grant by respective regulatory authority. Current research and investigations are going on for replacement of defective or incorrectly functioning cells and organs with artificial cells [14].

FUTURE ASPECTS OF PHARMACEUTICAL NANOTECHNOLOGY

Now a day's materials with nanostructure by combination with nanotechnology techniques are being used to make better composite materials, materials with enhanced catalytic activity, hardness and scratch resistance, and a wide range of consumer products that improve human life. Pharmaceutical nanotechnology has emerged as a discipline having tremendous potential as a carrier delivery of bioactives and diagnostics and provides smart materials for tissue engineering. It offers novel tools, scope and opportunities, which are anticipated to have a great impact on many areas in diagnostics of disease and treatment of diseases through its nano-engineered tools. Pharmaceutical nanotechnology gives better opportunities to enhance materials, medical devices and assist to develop novel technologies where existing and more conventional technologies may have their limits. In coming future nanotechnology will provide us the new nanotechnology such as Nano cocoons, smart medicine and nanorobots to make important contributions to disease diagnosis, detection, therapy, and prevention.

CONCLUSION:

New innovations in pharmaceutical nanotechnology provide new tools, opportunities and scope, which are expected to have a great impact on many areas in disease diagnostics and therapeutics. Pharmaceutical nanotechnology has emerged as a discipline having enormous potential as carrier for spatial and temporal delivery of bioactives and diagnostics and provides smart materials for tissue engineering. Pharmaceutical nanotechnology is now well-established as specialized area for drug delivery, diagnostics, prognostic and treatment of diseases through its nanoengineered tools. Few products and delivery systems of nanotechnology base are already approved by regulatory bodies are also they in market. Nanotechnology creates new hope to pharmaceutical industries by providing new age patentable technologies in view of revenue loss caused due to off-patent drugs. Various researcher and scientist of scientific industries, research societies and governments all over world are looking with great expectations and contributing their best to discover and unleash the potential of nanotechnology.

Nanotechnology has the great potential to make remarkable contributions to disease diagnosis, therapy, and prevention. However, few suggested initiative must be taken in order to utilize the advantage of this growing potential of nanotechnology. We still don't have sufficient data and guidelines regarding safe use of devices and materials based upon nanotechnology. There are few unresolved issues related with safety of nanotechnology. But still with all these considerations pharmaceutical nanotechnology have very good potential to solve many issue related with pharmaceutical industry.

REFERENCES:

1.Aboofazel, R. Kinam Park Alexander Florence 'Nanotechnology: A new approach in pharmaceutics', Journal of Controlled Release, 2010, Vol. 141, pp. 263–264.
2.Sagar R. Mudshinge , Amol B. Deore, Sachin Patil , Chetan M. Bhalgat, Nanoparticles: Emerging carriers for drug delivery, Saudi Pharmaceutical Journal, 2011, 19, 129–141.
3.Misra, R, Acharya, S. and Sahoo, S.K., 'Cancer nanotechnology: application of nanotechnology in cancer Therapy', Drug Discovery Today, 2010, Vol. 15, pp. 777-782.
4.Darshana, P. and Joshi, K., 'Emerging nanopharmaceuticals' Int. J. Pharm. Phytopharmacol. Res., 2012, Vol. 2 (1), pp. 60-65.
5.Jain, N.K. 'Pharmaceutical Nanotechnology', J Nanomedicine, 2007, Vol. 2(7), pp. 210-215.
6.Bera, D., Qian, L., Tseng, T., Holloway, P. 'Quantum dots & their multimodal applications' Materials, 2010, 3(4), 2260-2345.
7.The Nanotech Revolution in Drug Delivery Establishing a New Paradigm in Pharmaceuticals, 2007, published by Cientifica Ltd. London.
8.Rangasamy, M., et al 'Nano Technology: A Review', Journal of Applied Pharmaceutical Science, 2011Vol. 1(2), pp. 8-16.
9.Zhang, L., Gu, F. X., Chan, J. M., Wang A. Z., Langer, R. S. and Farokhzad, O.C. 'Nanoparticles in Medicine: Therapeutic Applications and Developments', Clinical Pharmacology & therapeutics,2008, Vol. 83, pp. 54-57.
10.Bawarski W.E., 'Nanomedicine', Nanotechnology, Biology and Medicine, 2008, Vol. 4, pp. 273–282.
11.Semete, B., Kalombo, L., Katata, L. and Swai, H., 'Nano-drug delivery systems: Advances in TB, HIV and Malaria treatment', Medicine, VBRI Press. 2010, ISBN: 978-81-920068-01
12.Zylberberg, C., Matosevic, S., 'Pharmaceutical liposomal drug delivery: a review of new delivery systems and a look at the regulatory landscape'. Journal drug delivery, 2016, Vol 23, issue-9, pp. 3319-3329.
13.Ekimov, A. I., Onushchenko, A. A., JETP Lett. 34, 345-349 (1981)
14.Kewal K. and Jain., 'The role of nanobiotechnology in drug discovery', Drug dis. therp, 2005, 10 (21): 23-27.
15.Michalet, X., Pinaud, F. F., Bentolila, L. A., Tsay, J. M., Doose, S., Li, J. J., Sundaresan, G., Wu, A. M., Gambhir, S. S. and Weiss S., 'Quantum dots for live cells- in vivo imaging and diagnostics', Science, 2005, Vol. 307, pp. 1268-1272.
16.Niraj Sinha, John T.-W. Yeow, Carbon Nanotubes for Biomedical Applications, IEEE transactions on nanobioscience, JUNE 2005, VOL. 4, NO. 2.
17.Gref, R.,Minamitake, Y., Peracchia, MT. Trubetskoy, V. Torchilin, V. Langer, R. 'Biodegradable long circulating nanospheres' Science 1994, 236:1600-3.
18.Lilian E van Vlerken, L. E. V. V. and Amiji, M. M., 'Multi-functional polymeric nanoparticles for tumour-targeted drug delivery', Ashley Publications, 2006, Vol. 10, pp.151-157.
19.Kubik, T., Bogunia-Kubik K. and Sugisaka, M., 'Nanotechnology on Duty in Medical Applications', Curr Pharm Biotechnol. 2005 Feb; 6(1):17-33.
20.Jawahar, N., Meyyanathan S.N., Polymeric nanoparticles for drug delivery and targeting: a comprehensive review. International journal helath allied science, 2012, 1:217-223.
21.Leroux, C., Jones jean, M., 'Polymeric micelles a new generation of colloidal drug carriers' European journal of pharmaceutical and biopharmaceuticals, 1999, Vol. 48 (2);101-111.
22.Kim, S., Shi, Y., Young Kim, J. Y., Kinam Park and Ji-Xin Chen, 'Overcoming the barriers inmicellar drug delivery: loading efficiency, in vivo stability, and micelle–cell interaction', Expert. Opin. Drug Deliv., 2010, Vol. 7 (1), pp. 86-89.
23.E. Dulkeith, T. Niedereichholz, T. A. Klar, J. Feldmann, G. von Plessen, D. I. Gittins, K. S. Mayya, and F. Caruso, Plasmon emission in photoexcited gold nanoparticles, Phys Rev B 70 (2004) 205424.
24.Andrew, W., Salamon S., Courtney, P. and Shuttler, I., 'Nanotechnology and engineered nanomaterials' Expert Opin. Drug Deliv., 2000, Vol. 9 (3), pp. 76-89.
25.Faraji, A. H., Wipf , V., 'Bioorganic Nanoparticles in cellular drug delivery', Med. Chem. 2009, 17, pp. 2950–2962
26.Barbel, V. W., Husing K., SibylleY.and Bock, A. K., 'Nanomedicine Drivers for development and possible impacts', Expert Opin. DrugDeliv., 2004, Vol. 7 (1), pp. 86-89.

27.K. K. Jain, Nanotechnology-based Drug Delivery for Cancer, Technology in Cancer Research & Treatment, Volume 4, Number 4, August (2005).
28.Sanvicens, N. and Marco, M.P., 'Multifunctional nanoparticles -properties and prospects for their use in human medicine' Elsevier Ltd. 2008, Vol. 10, pp. 1016.
29.Gajanan S. Sanap, Ajay Kharche , Pankaj Khuspe, Novel Carriers In Topical Antifungal Therapy Of Miconazole, World Journal of Pharmaceutical Research, 2016, Vol 5, Issue 3, ,553-569.
30.Vasir, J. K. Reddy M.K. and Labhasetwar V. D., 'Nanosystems in Drug Targeting: Opportunities and Challenges'. Current Nanoscience. 2005, 1, 47-64.
31.Wickline S.A., Lanza G.M., 'Molecular Imaging, Targeted Therapeutics, and Nanoscience'. J Cellular Biochem 2005, Supp39, 90–97.
32.Reddy, J. R. K, Sagar, E.G., Prathap, S. B. C. and Kumar, B. R., 'Nanomedicine and drug delivery - revolution in health system', Journal of Global Trends in Pharmaceutical Sciences, 2011, Vol. 2 (1), pp. 21-30.
33.Ali Khademhosseini, Robert Langer, Jeffrey Borenstein, and Joseph P. Vacanti, Microscale technologies for tissue engineering and biology, Proc Natl Acad Sci U S A. 2006 Feb 21; 103(8): 2480–2487.
34.Chung HJ, Park TG, Surface engineered and drug releasing pre-fabricated scaffolds for tissue engineering, Adv Drug Deliv Rev. 2007 May 30;59(4-5):249-262.
35.Liu, C., Zhang, N., 'Nanoparticles in gene therapy principles, prospects, and challenges' Prog. Mol. Biol. Transl Sci. 2011, 104:509-62.
36.M. Abhilash, Potential applications of Nanoparticles, International Journal of Pharrm. Bio. Sci. 2010, 1(1).
37.Bulte, J. W. M., Douglas, T., Witwer, B., Zhang, S. C., Strable, E., Lewis, B. K., Zywicke, H., Miller, B., Magnetodendrimers allow endosomal magnetic labeling and in vivo tracking of stem cells, Nat Biotechnol. 2001 Dec; 19(12):1141-7.
38.Heymer, A., Haddad, D., Weber, M., Gbureck, U., Jakob, P. M., Eulert, J. and Noth, U., 'Iron oxide labelling of human mesenchymal stem cells in collagen hydrogels for articular cartilage repair', Biomaterials, 2008, Vol. 29 (10), pp.1473-1483.
39.Vinit Kumar, Stefano Palazzolo, Samer Bayda, Giuseppe Corona, Giuseppe Toffoli, and Flavio Rizzolio, DNA Nanotechnology for Cancer Therapy, Theranostics. 2016; 6(5): 710–725.
40.Ki Hyun Bae, Hyun Jung Chung, and Tae Gwan Park, Nanomaterials for Cancer Therapy and Imaging, Mol Cells. 2011 Apr 30; 31(4): 295–302.