e-ISSN: 2347-7857
p-ISSN: 2347-7849

Research and Reviews: Journal of Pharmaceutics and Nanotechnology

Nano-Medicine: Promising Drug for Future

Jagmeet Singh[1]*, Poonam Jaggi[2] and Simranjeet Kaur[3]

[1]Department of Biotechnology, Lovely Professional University, Jalandhar, Punjab, India
[2]Department of Biotechnology, Amity University, Noida, New Delhi, India
[3]Department of Pharmacy, Chandigarh Group of Colleges, Landran, Mohali, Punjab, India

Research Article

Received: 02/08/2016
Accepted: 05/08/2016
Published: 12/08/2016

*For Correspondence
Jagmeet Singh, Department of Biotechnology, Lovely Professional University, Jalandhar, Punjab, India.

E-mail: er.meet3031@yahoo.com

Keywords: Nano-medicine, Nanomachines, Nanobots, Drug delivery, Quantum dot

ABSTRACT

In the last few decades, the nanotechnology field has significantly been progressed, leads to achieve success in synthesis and design of functional nanoparticles for diagnostic and therapeutic applications. Nanomedicine is one of the applications of nanotechnology in medical field that can be used to formulate novel formulas for targeted drug delivery that are potentially effective and safer, thus can lead to a reduction in drug side effects and better patient outcomes. However, the clinical production of these formulations has been limited due to costly and lengthy regulatory processes and the inefficiency to assess the efficacy and safety of the nanomedicines. Thus, innovative and rigorous models for preclinical testing are needed to appraise these formulations to assure their future commercial availability and successful clinical translation.

INTRODUCTION

The study of nanomedicine has been started almost 50 years ago with the description of first lipid vesicles. In last 15 years, nanoparticle-based medicine has really taken off. Nanomedicine is used for the preservation and improvement of human health with the use of molecular tools and knowledge of the human anatomy [1-3]. If we scale down the material size to its molecular level, it will radically improve physical and chemical changes of the material. Hence, use of nanomaterial in medicine provides a great progress in the prevention and treatment of various deadly diseases. However nanomedicines are economic, promising and health impacts can be manipulated in an integrated and safe way [4-6]. Technical and medical understanding of nanomedicines will help in future development and it is also crucial to understand the social and economic hurdles that hamper the commercialization of nanomedicines.

Nanomedicines play a vital role in repairing, diagnosing and regulating human biological system at the molecular level, with the use of engineered nanostructures and Nano devices [7-10]. Nanomedicine is an industry that comprise of more than 200 companies and 38 products worldwide with a minimum investment of $3.78 billion per year in research and development of nanomedicines. In 2004, nanomedicines sale has crossed $6.36 billion and in April 2006, it was anticipated that more than 125 nanotech-based drugs and delivery systems have been developed globally. This gradual growth of nanomedicine industry will have crucial impact on the economy and health care of the human race [11-16].

According to European Medical Research Councils of European Society of Foundation (EMRC- ESF) nanomedicine is science of diagnosing, preventing and treating health issues, and also helps in relieving pain, with the help of molecular tools and knowledge of the human structure [17-20]. Broadly nanomedicines are categorized into five disciplines: Nano imaging, analytical tools, Nano-devices and nanomaterial, new methods of pharmaceutical treatment, ethics, toxicology, etc. in specific area of healthcare. In coming future, nanomedicine will provide tools and methods useful for research and practice for clinical practice, which can revolutionize the way of thinking and treatments applied in the health care sector [18-24].

e-ISSN: 2347-7857
p-ISSN: 2347-7849

DIFFERENT DEVICES AND STRUCTURES USED BY NANOMEDICINE

Nanoparticles

Nanoparticles are designed to improve the bioavailability of drugs, as we know the bioavailability of several drug is the major limitation in achieving more effective treatments [25-27]. However, very small size helps nanoparticles to easily penetrate into cells and is a best carrier for different drugs. Nanomedicine has capacity to deliver drug in the specific target cells and increases the efficacy of drug by eliminate the risk of toxicity [28-30].

Nanotubes

Physical modifications of nanostructures are done by nanotubes. Nanotubes are intensively used to determine in-vitro and in-vivo drug delivery, because nanotubes can penetrate into cells without causing any toxic effect to the cells. In present era Carbon nanotube based devices are being utilized in stem cell therapies and tissue engineering, including neuronal regeneration [31-34].

Dendrimers

Dendrimer are type of synthetic nanostructures that are used in gene therapy or imaging. Dendrimers are complex, nano-sized, branched polymer with nanometer scale dimensions [35,36]. Dendrimers are comprised of three main components: a central core, an interior dendritic structure and an exterior surface having functional surface groups [37].

Liposomes

Liposomes are small spherical shaped artificial vesicles that can be developed from natural non-toxic phospholipids and cholesterol. Due to small size, hydrophilic and hydrophobic nature liposomes are best drug delivery carrier. Properties of liposome vary considerably with lipid composition, preparation method, size, and surface charge [38-40].

Quantum dot

Quantum dots are small luminescent crystals that emit different colors. Researchers determining the use of crystals in image-guided surgery, sensitive diagnostic tests and light-activated therapies [41,42]. Cadmium selenide quantum dots are the mostly used, due to their applications not only in medicine, but also in solar cells, quantum computers, light-emitting diodes etc [43].

Fullerene

Since the discovery of fullerenes in 1985, they have considerable attention in various fields of science. Fullerenes are carbon spheres that are being used for a broad range of its applications in Nano medicine [44-47]. Fullerenes have unique electronic properties that make them fascinating candidate for diagnostic and therapeutic applications. The fullerene family, and especially C60, has alluring physical and electrochemical properties, which can be utilized in different fields of medicine [48-51].

Nanodevices

Implantable medical nanodevices help researchers perform automatic treatment from inside the patient's body. Bionic devices, interface with the neural systems and substitute the native function of the system, such as bionic pressure controller, pacemaker are the potential candidates to reduction [52,53]. Nanobots are the future of nanomachines. In future nanobots can sense and easily adapt to environmental stimuli such as sounds, heat, light, chemicals and surface textures. Nanobots can also perform difficult calculations; communicate, work together and move [54,55].

NANOSIZED TECHNOLOGIES FOR MEDICAL IMAGING AND TARGETED DRUG DELIVERY

Research's main focus in medical disease diagnostics is molecular imaging. It can facilitate early stage diagnosis, provide basic required knowledge on pathological processes of disease and can be applied to follow the efficacy of therapy [56-58]. Nanoparticulate probes have shown remarkable advantages over single molecule-based contrast agents, such as generating excellent contrast, incorporate multiple properties, more circulation time. Basically, nanoparticles allow the components of a contrast agent to easily get assembled in adequate ratio. That

result in an appropriate molecular imaging, such agents can be detected by multiple imaging techniques. Agents also deliver therapeutic agents that detect cell types precisely [59-62].

Nanoparticles with inherent diagnostic properties

Nanotechnology is field of science dedicated to do manipulation at atomic or molecular level lead to development of nanostructures in scale size range less than 100 nm, which possess exclusive properties. The chemical and physical properties of materials get improved or changed as the size of material is scaled down to nanosize [63,64]. Smaller size means there are different arrangement and spacing available for surface atoms that will manage the physical and chemical properties of material. Quantum dots (QDs), Colloidal gold and ironoxide semiconductor nanocrystals are potential examples of nanoparticles, having size range in between 1-20 nm, and have medical diagnostic applications in medical and biological field [65-68]. Gold nanoparticles can be used as quenchers in fluorescence resonance energy transfer measurement. The distance-dependent optical property of gold nanoparticles generates opportunities for estimation of the binding of DNA-conjugated gold nanoparticles and complementary RNA sequence [69]. Super paramagnetic iron oxide nanocrystals can be used as contrast agents in magnetic resonance imaging (MRI), as they cause modifications in spin-spin relaxation times of water molecules in surroundings, to monitor the expression of gene or to detect the pathologies such as brain inflammation, cancer, atherosclerotic plaques or arthritis [70]. Quantum Dots can be tagged to biological systems for detection by electrical or optical means in vitro and upto some extent in vivo. The luminance wavelength (from the UV to the near-IR) of Quantum Dots can be tuned by changing the particle size; therefor nanosystems have the capability to reform cell, antigen, receptor and enzyme imaging [71-74].

Nanovehicles and drug carriers

However there are various engineered constructs, architectures, particulate systems, and assemblies, whose consolidate feature is its size in nanometer scale range i.e. less than 240 nm. Nanovehicals include protein cage architectures, polymeric micelles, polymeric and ceramic nanoparticles, dendrimers, viral-derived capsid nanoparticles, liposomes and polyplexes [75,76]. Initally, therapeutic or diagnostic agents can be covalently attached, adsorbed or encapsulated on these nanocarriers. These approaches can smoothly overcome issue of drug stability and solubility, particularly with new drug candidates come up from high-throughput drug screening initiatives are hydrophobic [77,78]. But some carriers such as dendrimers have a poor bonding with active compounds. There are various alternative approaches for the solubilization of hydrophobic drugs. One approach is to mill the substance and then with the help of coating stabilize the smaller particles which form nanocrystals in size ranges suitable for oral delivery and for intravenous injection [79]. Thus, the reduced particle size encompasses large surface area and hence a scenario for faster release of drug. Pharmacokinetic profiles of such injectable nanocrystals may lies from briskly soluble in the blood stream to slow dissolving. Second approach is by advantage of their small size and by functionalizing their surface with synthetic polymers and appropriate ligands, Nano carriers can be targeted to specific cells in the body after intravenous and subcutaneous routes of injection [80-83].

Targeting

There are two basic requirements needed in the design of Nano carriers to achieve effective drug delivery [84]. First, the drugs must reach the desired targeted cell after administration with minimal loss to their activity and volume in blood stream. Second, drugs must only affect the targeted cells without having harmful effects to healthy tissue. Two strategies for Nano carrier targeting: passive and active targeting of drugs [85,86].

Passive Targeting

Passive targeting takes advantage of pathophysiological characteristics of effected cell, enabling nanodrugs to accumulate in effected tissue [87]. Tumor vessels are highly disorganized and have large number of pores, resulting in enlarged gap junctions between endothelial cells and compromised lymphatic drainage. The leaking vascularization, which refers to the EPR effect, that allows movement of macromolecules up to 390 nm in diameter into the surrounding effected cell [88]. One of the earliest nanoscale technologies for passive targeting of drugs was based on the use of liposomes. To protect the liposome from immune destruction, liposomes are coated with a synthetic polymer. Passive targeting approaches form the basis of clinical therapy; they also suffer from several limitations. Targeting cells inside a tumor is not always feasible because some drugs cannot penetrate the tumor efficiently and due to the random nature of approach it becomes more difficult to control the process. Another limitation is, certain tumors do not exhibit an EPR effect due to which permeability of blood vessels may not be the same throughout a single tumor [89-92].

Active Targeting

To overcome the limitations of passive targeting attaching affinity ligands Such as peptides, aptamers or antibodies, to the Nano carriers surface by a variety of conjugation chemistries. Nano carriers recognize the target cells and bind them through ligand–receptor interactions by the expression of receptors on the cell surface. To achieve specificity, those receptors should be highly expressed on targeted cells, but not on normal cells. The receptors should express themselves homogeneously and should not get dissolved in the blood. Internalization of targeting conjugates can also happen by receptor-mediated endocytosis after binding to the target cells, that initiates drug release inside the cells. On the basis of receptor-mediated endocytosis mechanism, targeting conjugates bind to their receptors, then plasma membrane encloses around the ligand–receptor complex to form endosome. Newly formed endosome is then moved to specific cell organelles, and the drugs can be released by enzymes or acidic pH. Nanodrugs currently approved for medical or clinical use are simple and generally have less active targeted drug release components. Moreover, nanodrugs that are currently in clinical development phase, lacks specific targeting. To fully determine the application of targeted drug delivery, researchers should need to investigate whether we can use them on specific diseases for targeting, whether the properties, target site and mode of action of the therapeutic drugs, are suitable for targeted delivery of drug [93,94].

Macrophage as a target

The tadency of macrophages of the reticuloendothelial system for fast recognition and clearance of foreign matter has provided an approach to macrophage-specific targeting with nanovehicles. The macrophage is a specialized cell in human body whose contribution to pathogenesis is very well known. Changes in immune effector functions and macrophage clearance cause common disorders such as autoimmunity, atherosclerosis and various infections. The macrophage, therefore, is a valid pharmaceutical target and there are numerous opportunities for a focused macrophage-targeted approach. For example, almost all microorganisms can be killed by macrophages, many pathogenic organisms developed resistance against macrophage destruction. Passive targeting of nanovehicles with encapsulated antimicrobial agents to the defected macrophages is a suitable strategy for effective microbial killing. The endocytic pathway will direct the carrier to lysosomes where pathogens are resident [56,77,95]. The carrier is then degraded by lysosomal enzymes that releases drug into phagosome-lysosome vesicle or in the cytoplasm either by specific transporters or by diffusion, depending on the physico-chemical nature of the drug molecule. Formulations that are approved for human are limited to lipid-based nanosytems with entrapped amophotericin B (Amp-B), and are recommended for treatment of infections that are caused by specific fungal species. This mode of targeting has significantly minimized the effective quantity of Amp-B for treatment. Other beneficial effects are significant minimize in nephrotoxicity and pro-inflammatory release of cytokine. Another possibility to explore is liposome emulsification, as this can also stabilize Amp-B association with the nanocarrier. Others have used multifunctional carriers to deliver antimicrobials to macrophages. Such as, injecting tuftsin-bearing liposomes intravenously to infected animals not only result in the delivery of liposome-encapsulated drugs to the macrophage phagolysosomes, also in the nonspecific stimulation of spleen macrophage and liver macrophage functions against parasitic, fungal and bacterial infections [82,92,96].

Extravasation: targeting of solid cancers

The development of “stealth” technologies has created the opportunities for passive accumulation of intravenously injected nanoparticles on targeted site having leakage in vasculature by extravasation. Although, many attempts have been made which includes drug delivery and imaging agents with various different nanoscale technologies to the underlying parenchyma of injured arteries, the majority of research is concentrated on solid tumors. The distribution of stealth nanoparticles in solid tumors is heterogeneous, because of perfusion heterogeneity and unpredictable. Functional and Structural abnormalities of blood vessels and lymphatic vessels inside the solid tumors prevent efficient delivery of systemic nanoparticles and macromolecules [1,7,97]. These are compromised by abnormal hydrostatic pressure gradients and compressive mechanical forces generated by effected tumor cell proliferation compress and collapse the intratumoral vessels. Tumor-specific cytotoxic therapy that reduces the number of tumor cell may result in more effective delivery, by decompressing same vessels; however, this enhanced perfusion could provide a route for metastasis. Organization, distribution, and relative levels of hyaluronan, decorin, and collagen prevent diffusion of nanoparticles and macromolecules inside the tumors. Thus, diffusion of nanoparticles and macromolecules can vary with type of tumor, anatomical locations, and factors that affects extracellular matrix composition or structure. But, a major problem is the amount of drug release from internalized nanovehicles. In an acidic environment such as lysosome/endosome conditions may not favor rapid release of doxorubicin from the ammonium sulfate gradient loaded doxorubicin liposomes [85,93,98].

e-ISSN: 2347-7857
p-ISSN: 2347-7849

TOXICITY ISSUES

Nano vehicles may overcome stability or solubility issues for the drug and minimize drug side effects. There can be some significant toxicity issues that are associated with the Nano carriers, which require proper attention. Over the past few years, toxicology reports showed that the nanotechnology derived particles cause serious risks to biological systems. For example, exposure of human keratinocytes to insoluble single-wall carbon nanotubes was associated with oxidative stress and apoptosis. The issue of toxicity has becomes more problematic for intravenously injected nanoparticles [75,84,97-99].

Cell death and altered gene expression

Though we are using cadmium selenide QDs in imaging very much, but have very little knowledge about their metabolism and deleterious effects on human body. Cadmium selenide QDs are dangerous to cells in UV irradiation, as reaction releases highly toxic ions of cadmium. Depending on the nature of the monomer units, some polymeric micelles can cause cell death via necrosis or apoptosis, or by both. Differential gene expression has been observed in various cells after delivery of cisplatin with polymeric micelles as compared to that of free cisplatin treatment. Products produced from poly(L-lactic acid) nanoparticles show cytotoxicity to immune cells, thus bringing up the concern of their use for uninterrupted cytosolic drug release [67,87-88]. Some polymeric components that are used in nanoparticle engineering and design behave as inhibitors of P-glycoprotein efflux pumps expressed in polarized endothelial cells that creates the outer membrane of the blood-brain barrier, and can also interfere with transport of a number of modulators and homeostatic mediators in the central nervous system.

Cell death and gene therapy

A clear warning is conspicuous from the poor success rate in human gene therapy with the help of viruses. However, viral vectors are very efficient carrier system for nucleic acids, they can cause severe immunotoxicity and unintented gene expression changes after random integration into the host human genome. These issues of viral vector have generated a surge in engineering and design of synthetic poly-cationic non-viral gene transfer carriers/systems. However, the poly-cationic nature of the gene delivery carrier can cause immediate or delayed cytotoxicity by the mechanisms of necrosis and apoptosis. Necrosis can be occurred due to destabilization of membrane or formation of pores after interaction between cationic constituents of the carrier system with cell surface proteoglycans and negatively charged proteins in cytoskeleton. In Jurkat T cells the mechanism of apoptotic occurs due to polycation-mediated release of Bcl-2-sensitive proteins (cytochrome c) from the intermembrane space of mitochondria and altered the function of mitochondrial. Different cationic materials, their molecular weights and polydispersity of these materials can initiate apoptosis at different times and by different modes of ation. The effect of these materials on cell death may depend on nature of cell, the extent mitochondrial heterogeneity and mitochondrial content. Still, cytotoxic gene-delivery carrier systems can be compromised of translation or transcription processes and potentially limits protein expression [98-101].

CONCLUSION AND FUTURE OF NANOMEDICINE

Nanotechnology is startup to bring changes in the scale and methods of drug delivery and vascular imaging. The NIH Roadmap's 'Nanomedicine Initiatives' thinks that nanoscale technologies can start producing more medical benefits within coming 12-15 years. This constitutes the development of nanoscale laboratory-based drug discovery platform devices and diagnostic nanomachines such as nanoscale cantilevers for chemical force microscopes, nanopore sequencing, microchip devices and many more. The National Cancer Institute has started programs with the goal to produce multifunctional entities at nanometer scale that can perform diagnosis, monitor cancer treatment progress, and deliver therapeutic agents. These include engineering and design of targeted contrast agents that enhance the consistency of cancer cells to the single cell level and nanodevices that are capable to address the evolutionary and biological diversity of multiple cancer cells that make tumor within an individual. Thus, to achieve full potential of nanotechnology in targeted drug delivery and imaging, nanocarriers should have to be smarter. These form the base of complex interactions essential to the fingerprints of nanovehicle and its surrounding microenvironment. Such as, stability of carrier, intracellular and extracellular drug release rates in carious different pathologies, interaction with biological microenvironment such as opsonization and other biological barriers that enroute to the target site. Toxicity issues are of very important concern but are often ignored by researchers. Therefore, it is needed that basic research should be carried out for these issues if we want to achieve successful and effective application of these technologies. The future of nanomedicine will directly depend on the design of nanotechnology materials and tools to generate nanomachines based around a thorough and detailed knowledge of biological processes.

REFERENCES

1. Ahmad U and Faiyazuddin Md. Smart Nanobots: The Future in Nanomedicine and Biotherapeutics. J Nanomedine Biotherapeutic Discov. (2016); 6: e140.
2. Benyettou F and Motte L. Nanomedicine: Towards the "Magic Bullet" Science. J Bioanal Biomed. (2016); 8: e137.
3. Balabathula P. Nanomedicines can Offer Improved Therapeutic Efficacy through Various Parenteral Routes of Administration. J Nanomed Nanotechnol. (2016); 7: e136.
4. AbouAitah KEA, et al. pH-controlled Release System for Curcumin based on Functionalized Dendritic Mesoporous Silica Nanoparticles. J Nanomed Nanotechnol. (2016); 7: 351.
5. Krukemeyer MG, et al. History and Possible Uses of Nanomedicine Based on Nanoparticles and Nanotechnological Progress. J Nanomed Nanotechnol. (2015); 6: 336.
6. Ji HF, et al. Nanomedicine and Biotherapeutics for Antiobiotic Resistance Bacteria. J Nanomedine Biotherapeutic Discov. (2015); 5: e138.
7. Lenoir T and Herron P. The NCI and the Takeoff of Nanomedicine. J Nanomedine Biotherapeutic Discov. (2015); 5: 135.
8. Li W, et al. Effects of Intracellular Process on the Therapeutic Activation of Nanomedicine. Pharm Anal Acta. (2015); 6: 368.
9. Narayanasamy P and Nanomedicines: Future Against Infections. Chem Sci J. (2014); 5: e105.
10. Kazemi A, et al. The Question of Ethics in Nanomedicine. J Clinic Res Bioeth. (2014); 5: 193.
11. Vukoman Jokanovic. The Deep Scientific and Philosophic Approach to the Future Nanomedicine, Given on the Base of Author Introduction in the Monograph "Nanomedicine, the Greatest Challenge of the 21st Century". Drug Des. (2014); 3: 113.
12. Bragazzi NL and Nicolini C. Nanogenomics for Personalized Nanomedicine: An Application to Kidney Transplantation. Cell Mol Biol. (2014); 60: 115.
13. Leary JF. Nanomedicine – Reality will trump hype! J Nanomedine Biotherapeutic Discov. (2013); 4: e125.
14. Menaa F. Global Financial Model for Responsible Research and Development of the Fast Growing Nanotechnology Business. J Bus Fin Aff. (2014); 3: e139.
15. Lai L, et al. Nanomedicine: Economic Prospect and Public Safety. J Develop Drugs. (2013); 2: e127.
16. Bell IR, et al. Nonlinear Response Amplification Mechanisms for Low Doses of Natural Product Nanomedicines: Dynamical Interactions with the Recipient Complex Adaptive System. J Nanomed Nanotechol. (2013); 4: 179.
17. Menaa F, et al. Importance of Fluorine and Fluorocarbons in Medicinal Chemistry and Oncology. J Mol Pharm Org Process Res. (2013); 1: 104.
18. Krukemeyer MG and Wagner W. Nanomedicine in Cancer Treatment. J Nanomed Nanotechol. (2013); 4: 166.
19. Bregni C. Nanomedicines in Cancer Therapy. J Mol Pharm Org Process Res. (2013); 1: 101.
20. Motte L. What are the Current Advances Regarding Iron Oxide Nanoparticles for Nanomedicine? J Bioanal Biomed. (2012) 4: e110.
21. Quan L. Macromolecular Nanomedicine of Glucocorticoids for the Treatment of Rheumatoid Arthritis. J Nanomed Nanotechol. (2013); 4: e126.
22. Peramo A. Nanomedicine in Thrombosis. J Nanomedic Nanotechnol. (2012); 3: e106.
23. Rahiman S and Tantry BA. Nanomedicine Current Trends in Diabetes Management. J Nanomed Nanotechol. (2012); 3: 137.
24. Uckun FM. Stat3-Syk Molecular Complex as A Target for Anti- Cancer Nanomedicines. J Nanomed Nanotechol. (2012); 3: e110.
25. Hosseini PM, et al. Gaps in the Iranian Patenting System: A Barrier to Nanomedicine Commercialization. J Nanomed Biotherapeut Discov. (2012); 2: 108.
26. Lin E. Novel Drug Therapies and Diagnostics for Personalized Medicine and Nanomedicine in Genome Science, Nanoscience, and Molecular Engineering. Pharmaceut Reg Affairs. (2012); 1: e116.
27. Ostafin AE and Batenjany MM. Nanomedicine Making Headway across the Blood Brain Barrier. J Nanomed Nanotechol. (2012); 3: e123.
28. Yun Y, et al. Nanomedicine-based Synthetic Biology. J Nanomedic Biotherapeu Discover. (2011); 1: 102e.
29. Suh KS and Tanaka T. Nanomedicine in Cancer. Translational Medic. (2011) 1: 103e.
30. Tsigelny IF and Simberg D. Has the Time for In silico Design of Nanomedicines Finally Arrived? J Nanomedic Biotherapeu Discover. (2011); 1: 104e.
31. Muro S. Efficient and Safe Intra-cellular Transport of Targeted Nanomedicines: are we there Yet? J Nanomedic Biotherapeu Discover. (2011); 1: 106e.
32. Chapman M and Pascu SI. Nanomedicines Design: Approaches towards the Imaging and Therapy of Brain Tumours. J Nanomedic Nanotechnol. (2012); S4: 006.

33. Alaqad K and Saleh TA. Gold and Silver Nanoparticles: Synthesis Methods, Characterization Routes and Applications towards Drugs. J Environ Anal Toxicol. (2016); 6:384.
34. Heidari A. Pharmacogenomics and Pharmacoproteomics Studies of Phosphodiesterase-5 (PDE5) Inhibitors and Paclitaxel Albumin-stabilized Nanoparticles as Sandwiched Anti-cancer Nano Drugs between Two DNA/RNA Molecules of Human Cancer Cells. J Pharmacogenomics Pharmacoproteomics. (2006); 7: e153.
35. Sreelakshmy V, et al. Green Synthesis of Silver Nanoparticles from Glycyrrhiza glabra Root Extract for the Treatment of Gastric Ulcer. J Develop Drugs. (2016); 5:152.
36. Israel LL, et al. Ultrasound-Mediated Surface Engineering of Theranostic Magnetic Nanoparticles: An Effective One-Pot Functionalization Process Using Mixed Polymers for siRNA Delivery. J Nanomed Nanotechnol. (2016); 7: 385.
37. Yadav JP, et al. Characterization and Antibacterial Activity of Synthesized Silver and Iron Nanoparticles using Aloe vera. J Nanomed Nanotechnol. (2016); 7: 384.
38. Heydrnejad MS and Samani RJ. Sex Differential Influence of Acute Orally-administered Silver nanoparticles (Ag-NPs) on Some Biochemical Parameters in Kidney of Mice Mus musculus. J Nanomed Nanotechnol. (2016); 7: 382.
39. Jibowu T. The Formation of Doxorubicin Loaded Targeted Nanoparticles using Nanoprecipitation, Double Emulsion and Single Emulsion for Cancer Treatment. J Nanomed Nanotechnol. (2016); 7: 379.
40. Hafez EM, et al. The Neonicotinoid Insecticide Imidacloprid: A Male Reproductive System Toxicity Inducer-Human and Experimental Study. Toxicol open access. (2016); 2: 108.
41. Motamed K, et al. IG-001 - A Non-Biologic Nanoparticle Paclitaxel for the Treatment of Solid Tumors. J Nanomater Mol Nanotechnol. (2014); 3: 1.
42. Yari A and Gravand E. ZnO-nanoparticle Coated Multiwall Carbon Nanotube as a New Sensing Element for Highly Sensitive Potentiometric Determination of Thiosulfate Ion. J Nanomater Mol Nanotechnol. (2015); 4: 2.
43. Yari A, et al. Sensing Element Based on a New Nanoparticle to Develop a Carbon past Electrode for Highly Sensitive Determination of Ag+ in Aqueous Solutions. J Nanomater Mol Nanotechnol. (2015); 4: 4.
44. Adesina SK, et al. Nanoparticle Characteristics Affecting Efficacy. J Pharm Drug Deliv Res. (2016); 5: 1.
45. Lokesh BVS and Kumar PV. Enhanced Cytotoxic Effect of Chemically Conjugated Polymeric Sirolimus against HT-29 Colon Cancer and A-549 Lung Cancer Cell Lines. J Pharm Drug Deliv Res. (2015); 4: 2.
46. Bajaj L and Sekhon BS. Nanocarriers Based Oral Insulin Delivery. J Nanomater Mol Nanotechnol. (2014); 3: 1.
47. Khosroshahi ME and Tajabadi M. Characterization and Cellular Fluorescence Microscopy of Superparamagnetic Nanoparticles Functionalized with Third Generation Nano-molecular Dendrimers: In-vitro Cytotoxicity and Uptake study. J Nanomater Mol Nanotechnol. (2016); 5: 3.
48. Pathrose B, et at. Stability, Size and Optical Properties of Silver Nanoparticles Prepared by Femtosecond Laser Ablation. J Nanomater Mol Nanotechnol. (2016); 5:3.
49. Alvi S, et al. Survivability of Polyethylene Degrading Microbes in the Presence of Titania Nanoparticles. J Nanomater Mol Nanotechnol. (2016); 5: 3.
50. Raza A, et al. In-situ Synthesis, Characterization and Application of Co0.5Zn0.5Fe2O4 Nanoparticles Assisted with Green Laser to Kill S. enterica in Water. J Nanomater Mol Nanotechnol. (2016); 5: 2.
51. Ma L, et al. Silver Sulfide Nanoparticles as Photothermal Transducing Agents for Cancer Treatment. J Nanomater Mol Nanotechnol. (2016); 5: 2.
52. Salehi M, et al. An Alternative Way to Prepare Biocompatible Nanotags with Increased Reproducibility of Results. J Nanomater Mol Nanotechnol. (2016); 5: 2.
53. Selvarani S, et al. Ocimum Kilimandscharicum Leaf Extract Engineered Silver Nanoparticles and Its Bioactivity. J Nanomater Mol Nanotechnol. (2016); 5:2.
54. Adesina SK, et al. Nanoparticle Characteristics Affecting Efficacy. J Pharm Drug Deliv Res. (2016); 5:1.
55. EL-Moslamy SH, et al. Bioprocess Development for Chlorella vulgaris Cultivation and Biosynthesis of Anti-phytopathogens Silver Nanoparticles. J Nanomater Mol Nanotechnol. (2016); 5: 1.
56. Shehata MM, et al. Influence of Surfactants on the Physical Properties of Silica Nanoparticles Synthesis via Sol-Gel Method. J Nucl Ene Sci Power Generat Technol. (2016); 5: 1.
57. Barua A, et al. Sustainable and Effectual Bio Fabrication of Gold Nanoparticles for Screening of Milk Adulteration. J Nanomater Mol Nanotechnol. (2015); 4: 5.
58. Kumar S, et al. Synthesis, Characterization, and Formation Mechanism of Nanoparticles and Rods of 1,5-Bis(2-Halophenyl) Penta-1,4-Dien-3-One. J Nanomater Mol Nanotechnol. (2015); 4: 5.
59. Anitha P and Sakthivel P. Microwave Assisted Synthesis and Characterization of Silver Nanoparticles using Tridax Procumbens and its Anti-Inflammatory Activity against Human Blood Cells. J Nanomater Mol Nanotechnol. (2015); 4:5.
60. Ramani T, et al. Synthesis, Characterization of Phosphine, Phosphine Oxide and Amine Stabilized Platinum Nanoparticles in Organic Medium. J Nanomater Mol Nanotechnol. (2015); 4: 4.

61. Yari A, et al. Sensing Element Based on a New Nanoparticle to Develop a Carbon past Electrode for Highly Sensitive Determination of Ag+ in Aqueous Solutions. J Nanomater Mol Nanotechnol. (2015); 4:4.
62. Panchangam RBS and Dutta T. Engineered Nanoparticles for the Delivery of Anticancer Therapeutics. J Pharm Drug Deliv Res. (2015); 4: 1.
63. Sengupta J, et al. Immuno-Potentiating Activity of Gold Nanoparticles on Experimental Animal Models. J Nanomater Mol Nanotechnol. (2015); 4: 3.
64. Chaudhary R, et al. Zinc Ferrite Nanoparticles as Highly Effective Magnetic Resonance Imaging Contrast Agents with Emphasis on Atherosclerosis. J Nanomater Mol Nanotechnol. (2015); 4: 3.
65. Stab J, et al. Flurbiprofen-loaded Nanoparticles Can Cross a Primary Porcine In vitro Blood-brain Barrier Model to Reduce Amyloid-ß42 Burden. J Nanomedine Biotherapeutic Discov. (2016); 6: 140.
66. oradpour M, et al. Establishment of in vitro Culture of Rubber (Hevea brasiliensis) from Field-derived Explants: Effective Role of Silver Nanoparticles in Reducing Contamination and Browning. J Nanomed Nanotechnol. (2016); 7: 375.
67. Bhattacharyya S, et al. Modulating the Glucose Transport by Engineering Gold Nanoparticles. J Nanomedine Biotherapeutic Discov. (2016); 6: 141.
68. Francisco JC, et al. Acellular Human Amniotic Membrane Scaffold Loaded with Nanoparticles Containing 15d-PGJ2: A New System Local Anti-Inflammatory Treatment of Eye Diseases. J Clin Exp Ophthalmol. (2016); 7: 537.
69. Ghanbari M, et al. Study of the Cytotoxicity Effect of Doxorubicin-loaded/Folic acid-Targeted Super Paramagnetic Iron Oxide Nanoparticles on AGS Cancer Cell Line. J Nanomed Nanotechnol. (2016); 7: 368.
70. Pereira da Silva S, et al. Iron Oxide Nanoparticles Coated with Polymer Derived from Epoxidized Oleic Acid and Cis-1,2-Cyclohexanedicarboxylic Anhydride: Synthesis and Characterization. J Material Sci Eng. (2016); 5: 247.
71. Heidari A. Manufacturing Process of Solar Cells Using Cadmium Oxide (CdO) and Rhodium (III) Oxide (Rh2O3) Nanoparticles. J Biotechnol Biomater. (2016); 6: e125.
72. Gandhi H and Khan S. Biological Synthesis of Silver Nanoparticles and Its Antibacterial Activity. J Nanomed Nanotechnol. (2016); 7: 366.
73. Murgueitio E, et al. Synthesis of Iron Nanoparticles using Extracts of Native Fruits of Ecuador, as Capuli (Prunus serotina) and Mortiño (Vaccinium floribundum). Biol Med (Aligarh). (2016); 8: 282.
74. Aparicio-Caamaño M, et al. Iron Oxide Nanoparticle Improves the Antibacterial Activity of Erythromycin. J Bacteriol Parasitol. (2016); 7: 267.
75. AbouAitah KEA, et al. Mesoporous Silica Materials in Drug Delivery System: pH/Glutathione- Responsive Release of Poorly Water-Soluble Pro-drug Quercetin from Two and Three-dimensional Pore-Structure Nanoparticles. J Nanomed Nanotechnol. (2016); 7: 360.
76. Bakare AA, et al. Genotoxicity of Titanium Dioxide Nanoparticles using the Mouse Bone Marrow Micronucleus and Sperm Morphology Assays. J Pollut Eff Cont. (2016); 4: 156.
77. Sivaramasamy E, et al. Enhancement of Vibriosis Resistance in Litopenaeus vannamei by Supplementation of Biomastered Silver Nanoparticles by Bacillus subtilis. J Nanomed Nanotechnol. (2016); 7:352.
78. Dai M, et al. Engineered Protein Polymer-Gold Nanoparticle Hybrid Materials for Small Molecule Delivery. J Nanomed Nanotechnol. (2016); 7: 356.
79. AbouAitah KEA, et al. pH-controlled Release System for Curcumin based on Functionalized Dendritic Mesoporous Silica Nanoparticles. J Nanomed Nanotechnol. (2016); 7:351.
80. Kumar P, et al. Synthesis of Dox Drug Conjugation and Citric Acid Stabilized Superparamagnetic Iron-Oxide Nanoparticles for Drug Delivery. Biochem Physiol. (2016); 5: 194.
81. Vinoda BM, et al. Photocatalytic Degradation of Toxic Methyl Red Dye Using Silica Nanoparticles Synthesized from Rice Husk Ash. J Environ Anal Toxicol. (2015); 5: 336.
82. El-Hussein A. Study DNA Damage after Photodynamic Therapy using Silver Nanoparticles with A549 cell line. J Nanomed Nanotechnol. (2016); 7: 346.
83. Mitra S, et al. Therapeutic use of Fisetin and Fisetin Loaded on Mesoporous Carbon Nanoparticle (MCN) in Thioglycollate-induced Peritonitis. J Nanomed Nanotechnol. (2015); 6: 332.
84. Awad H, et al. Study of Label- Free Detection and Surface Enhanced Raman Spectroscopy (SERS) of Fibrinogen Using Arrays of Dielectric Core-Metal Nanoparticle Shell. J Anal Bioanal Tech. (2015); S13: 010.
85. Shareena Dasari TP, et al. Antibacterial Activity and Cytotoxicity of Gold (I) and (III) Ions and Gold Nanoparticles. Biochem Pharmacol (Los Angel). (2015); 4: 199.
86. Hajiyeva FV, et al. Luminescent Properties of Nanocomposites on the Basis of Isotactic Polypropylene and Zirconium Dioxide Nanoparticles. J Nanomedic Nanotechnol. (2015); S7: 003.
87. Yasir M, et al. Haloperidol Loaded Solid Lipid Nanoparticles for Nose to Brain Delivery: Stability and In vivo Studies. J Nanomedic Nanotechnol. (2015); S7: 006.
88. Iannuccelli V and Maretti E. Inhaled Micro- or Nanoparticles: Which are the Best for Intramacrophagic Antiinfectious Therapies?. J Infect Dis Diagn. (2015); 1: e102

89. Levy I, et al. Tumor Necrosis Factor Related Apoptosis Inducing Ligand-conjugated Near IR Fluorescent Iron Oxide/Human Serum Albumin Core-shell Nanoparticles of Narrow Size Distribution for Cancer Targeting and Therapy. J Nanomed Nanotechnol. (2015); 6: 333.
90. Fayemi OE, et al. Metal Oxide Nanoparticles/ Multi-walled Carbon Nanotube Nanocomposite Modified Electrode for the Detection of Dopamine: Comparative Electrochemical Study. J Biosens Bioelectron. (2015) 6: 190.
91. Comber JD and Bamezai A. Gold Nanoparticles (AuNPs): A New Frontier in Vaccine Delivery. J Nanomedine Biotherapeutic Discov. (2015); 5: e139.
92. Bindhani BK and Panigrahi AK. Biosynthesis and Characterization of Silver Nanoparticles (Snps) by using Leaf Extracts of Ocimum sanctum L (Tulsi) and Study of its Antibacterial Activities. J Nanomed Nanotechnol. (2015); S6: 008.
93. Yasuda M, et al. BSA Adsorption and Immobilization onto Charged Monodisperse Polymer Nanoparticles. J Biosens Bioelectron. (2015); 6: 183.
94. Curtis A, et al. Heat Dissipation of Hybrid Iron Oxide-Gold Nanoparticles in an Agar Phantom. J Nanomed Nanotechnol. (2015); 6: 335.
95. Muniz-Miranda M. Application of the SERS Spectroscopy to the Study of Catalytic Reactions by Means of Mono and Bimetallic Nanoparticles. J Anal Bioanal Tech. (2015); 6: 286.
96. Krukemeyer MG, et al. History and Possible Uses of Nanomedicine Based on Nanoparticles and Nanotechnological Progress. J Nanomed Nanotechnol. (2015); 6: 336.
97. Vincze Gy, et al. Nanoheating without Artificial Nanoparticles. Biol Med (Aligarh). (2015); 7: 249.
98. Ghosh S, et al. Antidiabetic and Antioxidant Properties of Copper Nanoparticles Synthesized by Medicinal Plant Dioscorea bulbifera. J Nanomed Nanotechnol. (2015); S6: 007.
99. Abdellatif AAH. Targeting of Somatostatin Receptors using Quantum Dots Nanoparticles Decorated with Octreotide. J Nanomed Nanotechnol. (2015); S6: 005.
100. Radhakrishan Y, et al. Chitosan Nanoparticles for Generating Novel Systems for Better Applications: A Review. J Mol Genet Med. (2015); S4: 005.
101. Andocs G, et al. Nanoheating without Artificial Nanoparticles Part II. Experimental Support of the Nanoheating Concept of the Modulated Electro-Hyperthermia Method, Using U937 Cell Suspension Model. Biol Med (Aligarh). (2015); 7:247.