MEDWIN PUBLISHERS
Committed to Create Value for Researchers

Nanomedicine & Nanotechnology Open Access
ISSN: 2574-187X

Nanotechnology: Applications in Cancer Therapy and Diagnosis

Nikam R*, Sharma Y and Patil D

Department of Pharmaceutics, SSS's, Savitribai Phule University, India

***Corresponding author:** Rutuja Nikam, Department of Pharmaceutics, SSS's, Divine College of Pharmacy, Nashik, affiliated to Savitribai Phule University, Maharashtra 422301, India, Tel: +919172489088; Email: nikamrutuja105@gmail.com

Review Article

Volume 9 Issue 3

Received Date: May 14, 2024

Published Date: July 17, 2024

DOI: 10.23880/nnoa-16000312

Abstract

These days, Probably the most serious diseases in the entire globe is cancer in the world, and its prevalence is rapidly increasing. Uncontrolled cell development is the cause of it. Although It is always critical for higher specificity and concern about toxic waste across the system, cancer medicines have made significant progress. Recent technological breakthroughs, particularly in the area of biomaterials, have contributed to the spike in early identification, which is crucial for improving patients' prognosis and quality of life. Many of the drawbacks associated with conventional pharmaceutical formulations can be resolved with the use of nanotechnology. Customized nanomaterials have made great strides toward high specificity, sensitivity, and efficacy in cancer detection and treatment. The application of nanoparticles in nanotechnology allows for the integration of nanoscience into medicine. The application of nanoscience to cancer diagnosis and therapy will enhance patient assessment and management, benefit doctors, and enhance the quality of healthcare services. This review article describes the various nanotechnology modalities employed, their limitations and potential side effects, and the therapeutic uses of nanoscience in the contemporary care of cancer.

Keywords: Nanotechnology; Prognosis; Treatment; Diagnosis; Cancer; Nanomedicine

Abbreviations

CT: Computed Tomography; RES: Reticulo-Endothelial System; EPR: Enhanced Permeability and Retention Effect.

Introduction

Today's solid cancer treatments are increasingly more individualized for each patient and their particular tumor kind. Nowadays, tumor markers are frequently utilized to determine a patient's appropriateness for a certain medical treatment. Additionally, surgery has evolved to be more specialized and cautious overall. Modern imaging methods provide precise mapping of lesions, enhancing patient selection and preoperative planning. However, because current imaging methods use non-specific contrast agents, there are substantial restrictions. For instance, contrast materials based on iodine that are used in computed tomography (CT) can be extremely hazardous. Legislation tightly regulates the use of radioisotopes for nuclear imaging, which results in radiation exposure for patients and healthcare personnel as well as low spatial resolution. One way to get over some of these restrictions might be through nanotechnology.

Nobel laureate Richard Feynman initially proposed nanotechnology in 1959 [1]. The production of materials and technologies at the atomic, molecular, and supramolecular levels is included in this quickly expanding discipline. A nanometer is one billionth of a meter in the metric system. Structures with sizes ranging from 1 to 100 nm are called nanoparticles. The physical and chemical characteristics of

nanoparticles vary depending on their size and can be optical, magnetic, catalytic, thermodynamic, or electrochemical [2]. The National Institute of Health (Bethesda, MD, USA) has referred to this field as "nanomedicine" because of the significant potential for therapeutic application of these particles. In 2009, the National Institutes of Health funded nanotechnology with $1.5 billion, bringing attention to the field of nanomedicine. Within the next ten years, the global nanotechnology market is predicted to reach $1 trillion.

Nanoparticles with short blood circulation periods and a hydrodynamic diameter of less than 5 nm easily extravasate across the endothelium. Nanoparticles that are less than 6 nm are removed by the kidneys and filtered by the glomerulus. Over 8 nm nanoparticles and those with particular surface characteristics, like charge and hydrophobicity, are phagocytosed by liver Kupffer cells and eliminated through the biliary system [3]. Certain tiny nanoparticles can be big enough to be kept in the systemic circulation and avoid being opsonized by the reticulo-endothelial system (RES). These attributes cause these particles to circulate in the body for longer periods due to their enhanced permeability and retention effect (EPR), which Maeda proved in 2001 [4]. The tumor's synthesis of vascular endothelial growth factor (VEGF) is what causes EPR. VEGF induces disordered angiogenesis, which results in the creation of blood vessels with permeable walls that are "leaky'' [5]. There is insufficient lymphatic drainage in many cancers. These two elements cause 10–100 nm-sized nanoparticles to be retained and accumulated at the tumor location.

Because of their vast surface area, nanoparticles may tolerate several functional groups on their surface. Dual or multifunctional nanoparticles that can perform both treatment and diagnosis at the same time can be created by conjugating distinct functional groups, such as therapeutic (chemo) and diagnostic (magnetic) agents, onto the same particle [6].

Prior attempts have been made to integrate imaging with treatment. Although radio-immunoconjugates were taken into consideration, it was discovered that they exposed patients and medical staff to ionizing radiation, had minimal tumor uptake, and had dose-limiting toxicity [7]. Nowadays, a new area of interdisciplinary research spanning the scientific domains of biology, chemistry, engineering, and medicine is developing around cancer nanotechnology. It is probably going to develop into a brand-new area of clinical nanotechnology for diagnosis and treatment.

Advantages of Nanotechnology

The following are some benefits that drug delivery systems using nanoparticles have over those using more traditional drug delivery methods:

- By including nanoreceptors on their surface, pharmaceutical substances can be directed to a particular region of the human body. Target tissues are particularly recognized by these receptors, which then attach to them and release the medication molecules [8-10].
- As a result, the drug's cytotoxic actions do not harm healthy tissues.
- Nanoparticle coatings can be used to encapsulate drugs to prevent them from degrading [11].
- Because they are so tiny, nanoparticles are easily absorbed by impacted cells and can pass through smaller capillaries. Drug accumulation at the target locations is facilitated by this.
- The application of biodegradable nanoparticles permits long-term, sustained medication release at the target location [12].
- Therefore, better performance and increased efficacy result from nanosystems with improved drug delivery and target selectivity.

Disadvantages of Nanotechnology

In addition to the previously listed benefits of nanotechnology in medicine, particularly in cancer treatment, several unfavorable side effects prevent nanostructures from being used widely. Our earlier research indicates that living things are becoming increasingly exposed to nanoparticles due to misuse. Lipid peroxidation and oxidative stress are two ways that iron oxide nanoparticles might accelerate the rate of cell death. Zinc oxide, gold, and silver nanoparticle exposure can cause cell death by altered gene expression patterns, aberrant protein expression in cells, and mitochondrial dysfunction, respectively. Similarly, by decreasing membrane fluidity and damaging cell membranes, carbon nanotubes can raise the rate of cell death. Every employed nanostructure has both known and undiscovered toxicity to every living being [13].

Passive and Active Targeting Strategies

Passive Targeting

The process of drug-loaded nanocarriers being passively targeted and accumulating in tumor tissue is reliant on their size. The pathologic features of the tumor arteries, such as a leaky vasculature and inadequate lymphatic drainage, lead to passive targeting. The term increased permeation and retention (EPR) effect refers to the extravasation of particulate materials into the tumor tissue and their retention. Matsumura and Maeda were the first to propose this concept [14]. However, the reticuloendothelial system's cells (the mononuclear phagocyte system, or MPS) may

opsonize these particles since they are perceived as foreign entities, which would decrease the drug's availability at the necessary location. Effectively engineered nanocarriers, including those coated with polyethylene glycol (a process known as PEGylation), can elude detection by the MPS. These drug delivery methods are called "stealth" systems [15]. PEG coatings on the surface of the majority of passive-targeting nanosystems provide biocompatibility and "stealth" qualities. To adjust for differences in chain length and molecular weight, a range of PEGs is employed to regulate both the grafting efficiency and coating thickness. Compared to short-chain PEGs, longer chains provide a more steric effect surrounding the nanocarrier [16]. Another way to modify the surface of nanocarriers is to use PEG derivatives, like block copolymers of the poloxamer kind [17]. One such product on the market is Genexol-PM, a micellar formulation made of PEG-based block copolymers (GenexolPM was approved in 2007 in Korea and marketed in Europe).

Aiming at a Target: Active Drug Targeting

Drug delivery within the tumor cells is not guaranteed by the EPR effect, despite the drug's buildup in the tumor tissue due to membrane-specific mechanisms that are necessary for cellular internalization. As a result, a lot of work is being done to create nano-delivery systems that optimize accumulation at target locations using alternative techniques including receptor-mediated endocytosis. By attaching a ligand to overexpressed receptors on the tumor cell surface and internalizing the receptor-bound complex through phagocytosis/endocytosis processes, site-specific targeting and entrance inside the tumor cell can be accomplished [17]. Drug release and complicated lysosomal breakdown result in an enhanced therapeutic impact. The receptor for transferrin [18-21] and the overexpressed folic acid receptor seen in many cancer types are candidates for active medication delivery [22,23]. Transferrin is a glycoprotein that is attached to cell membranes and is involved in controlling cell development as well as cellular iron uptake. Through the internalization of iron-loaded transferrin mediated by the transferrin receptor, iron absorption takes place. Similarly, for tumor-specific medication delivery, the folic acid receptor is likewise a valuable target. It is well known that when the cancer's grade worsens, the density of folate receptors rises. Active targeting can also be achieved by taking advantage of processes necessary for the formation of tumors, including neoangiogenesis, or by focusing on biomarkers unique to a tumor. One such biomarker for ovarian cancer is CA-125, which is expressed in over 85% of patients with the disease [24,25].

Using the endothelial growth factor receptor (EGFR) as a target to improve the delivery of anticancer medicines to tumors overexpressing EGFR is another potential strategy in active targeting. Normal cell functions, including growth, proliferation, and survival, are mostly regulated by EGFR. The advancement of cancer has been linked to upregulation. Consequently, anti-EGFR therapeutic approaches have now gained clinical approval, including receptor-blocking monoclonal antibodies (Cetuximab) [26]. Another strategy involves combining a nanovehicle with an EGFR-binding ligand, like natural EGF, to enable internalization and delivery of the nanovehicle to targeted tumor cells. A 53-amino acid protein measuring 6 kDa is called EGF. EGF is a desirable option for targeting moiety due to its smaller size than antibodies. Despite widespread recognition of active targeting's advantages, this technique has only produced a small number of clinically proven nanoproducts thus far.

Nanoparticles in Drug Delivery

Over the past ten years, there has been a notable advancement in the creation of nanoparticles as efficient drug-delivery vehicles. The following are the many kinds of nanoparticles that are presently being researched for use as drug-delivery systems [27]:

(A)polymeric biodegradable nanoparticles that include

- nanospheres
- nanocapsules

(B)ceramic nanoparticles

(C)polymeric micelles

(D)dendrimer

(E)liposomes.

These nanoparticles can be structurally associated with particular biological molecules, such as enzymes, hormones, antibodies, and pharmaceutical medicines, to make them efficient drug delivery vehicles.

Polymeric Biodegradable Nanoparticles in Drug Delivery

These are colloidal, solid particles made up of macromolecules with sizes ranging from 10 nm to 1000 nm [28]. Depending on how things are prepared Tsapis N, et al. [29,30]. There are two types of nanoparticles: nanospheres and nanocapsules. The properties and release characteristics of the medication enclosed in these nanostructures are entirely different.

A matrix system is a nanosphere. Sahoo SK, et al. [31] where the medication is evenly and physically distributed; on the other hand, nanocapsules are vesicular systems where the medication is contained within a cavity that is encircled by a distinct polymer membrane. By hydrolyzing, these drug deliverers break down into substances that are acceptable to the body, allowing the encapsulated drugs to reach the intended tissues.

This erosion process might take place at the polymer's surface, where the release rate is proportional to its surface area, or in bulk, where the matrix breaks down uniformly. The polymer undergoes degradation into lactic and glycolic acids, which are subsequently reduced by the Krebs cycle to carbon dioxide and water. Previous studies concentrated on employing naturally existing polymers as biodegradable systems, such as cellulose and collagen [32,33]. The emphasis presently is on creating biodegradable polymers with enhanced properties through chemical synthesis. Polyanhydrides, polyacrylic acids, polyesters, polyurethanes, and poly(methyl methacrylates) are a few examples. Polymeric nanospheres based on DL-lactide diblock copolymers and methoxy poly(ethylene glycol) have been synthesized by another set of researchers [34]. The results of the cytotoxicity tests indicated that the nanospheres did not harm cells and displayed continuous drug release.

Ceramic Nanoparticles

Alumina, titanium, silica, or calcium phosphate are the materials used to make ceramic nanoparticles. A few benefits of these ceramic nanoparticles are their ultra-low size (less than 50 nm), great biocompatibility, ease of preparation, and good dimensional stability [35]. These particles successfully shield the doped drug molecules from denaturation brought on by temperature and pH variations outside. To target them to specific areas, their surfaces can be readily changed with various functional groups and coupled with a range of ligands or monoclonal antibodies [36]. It is possible to produce these nanoparticles with the required porosity, shape, and size. A ceramic nanoparticle is not affected by changes in its surroundings in terms of swelling or porosity. Insulin administration via parenteral means has been tested using self-assembling ceramic nanoparticles [37,38]. The insulin was carried by calcium phosphate nanoparticle cores, which were characterized and investigated in vivo. When the effectiveness of the conventional pig insulin solution was compared with the in vivo performance of this drug delivery method, the findings were better.

Polymeric Micelles

These supramolecular networks self-assemble in an aqueous media and are made up of cross-linked mixtures of hydrophobic and hydrophilic ligands. Because the diameter of these copolymers is only a few tens of nanometers, they are perfect for encasing individual drug molecules [39]. There are two forms of copolymer micelles: random and block, based on their structural structure. These drug carriers' small size allows them to bypass the reticuloendothelial system (RES) and renal exclusion, which improves the absorption by tumor cells. While administering medication, its hydrophilic outer shell shields the core and its contents from the surrounding aqueous medium in the human body. These can be injected and are especially helpful in delivering medications that are insoluble in water. These drug carriers' dispersion is mostly determined by their size and surface characteristics. Micelles that have sugar-group ligands affixed to their surface, for instance, have been demonstrated to selectively target glucose receptors found in cell membranes. The majority of delivery methods based on micelles are composed of poly (ethylene dioxide) triblock networks or along with a polypeptide combination [40].

Dendrimers

The discovery of dendrimers occurred in the early 1980s. These monomers have an inner core surrounded by several branches [41]. The benefits of polymeric micelles are shared by these compounds. It is simple to synthesize dendrimers at the nanoscale level. Moreover, they feature a special globular form with interior chambers that allow medication molecules to be properly stored while being shielded from the elements by the hydrophobic outer surface [31]. Divergent synthesis, or the bottom-up strategy, can be used to construct these from the center to the periphery Ihre H, et al. [42,43] Alternatively, it is known as convergent synthesis (top-down technique) [43,44]. Medication molecules have two options: they can be securely encased inside the interior cavities or adhered to the exterior.

Liposomes

1968 saw the first description of liposomes [45]. These are tiny synthetic spherical vesicles composed of cholesterol and phospholipids that are found in nature and are not harmful [31]. Because of their hydrophobicity, biocompatibility, small size, and simplicity of manufacture, liposomes are a promising drug delivery method. To increase the bloodstream's circulation time, polyethylene glycol units (PEG) might be attached to their surfaces. For increased target specificity, liposomes can also be coupled with ligands or antibodies.

Nanotechnology in Cancer Treatment

Finding cancer early in the carcinogenesis process is essential to cancer treatment. The scientific community is being encouraged by the outcomes of nanotechnology research to develop novel, non-invasive instruments at the nanoscale level for these kinds of applications. Cantilevers at the nanoscale Wee KW, et al. [46] as well as quantum dots Voura EB, et al. [47,48] are being investigated for cellular cancer detection. Treatment strategies should be developed to eliminate cancer cells without endangering healthy cells if the tumor is discovered later rather than during its early stages. To target tumor cells and administer anticarcinogenic

drugs in a regulated manner, a multitude of scientific studies are being carried out to investigate the usage of polymeric micelles, magnetic nanoparticles, and colloid gold nanoparticles as drug delivery systems [49-51]. By covering them with antibodies, peptides, sugars, hormones, and anti-carcinogenic medications, among other substances, that are particular to tumors, these nanoparticle-based drug delivery systems can be used to identify where in tumor cells they are located.

Magnetic Nanoparticles

Iron oxide particles covered in sugar molecules are known as magnetic nanoparticles [52]. Thus, the immune system does not recognize these. Without harming the nearby healthy tissues, these particles heat up and kill tumor cells when they come into contact with an external magnetic field. Researchers have used organic polymers and nanosized magnetites to create biodegradable magnetic nanoparticles [53].

Following the characterization investigations, the magnetic nanoparticles were guided to the designated area of the experimental setup using an external magnetic field. These research findings support the idea of employing an external magnetic field to direct magnetic nanoparticles to particular parts of the human body.

To deliver therapeutic medicines, for example, to specific brain cells without randomly infecting the entire brain, iron oxide nanoparticles can also be coated with amino groups. A study on the interaction between brain cells and functionalized superparamagnetic iron oxide nanoparticles has illustrated this idea [54].

Functionalizing iron oxide nanoparticles with glycoproteins such as lactoferrin and ceruloplasmin has been investigated as a means of directing them to particular cell receptors [55]. The majority of luteinizing hormone release hormone (LHRH) receptors are expressed in breast cancer tissue. Therefore, the iron oxide nanoparticles can be coupled with luteinizing hormone-releasing hormone to localize them to the malignant breast tissue. Such a strategy Zhou J, et al. [56] has shown that iron oxide nanoparticles are target-selective when used to treat breast cancer. These methods demonstrate how magnetic nanoparticles can be functionalized with appropriate moieties to target tumor cells exclusively.

Colloid Gold Nanoparticles

Present research is being done on colloidal gold nanoparticles as a possible medication delivery method for cancer treatment. Numerous therapeutic strategies are being proposed, and in-depth investigations are being conducted to examine the effects of these strategies. One such technique is the delivery of the anticancer protein tumor necrosis factor (TNF) via gold colloid nanoparticles. Colloidal gold nanoparticles have been evaluated in a developing tumor in mice as TNF medication delivery vehicles [57]. While TNF has been used to treat cancer, there have been side effects such as hypotension and even fatal cases of organ failure. Recent studies, however, have demonstrated that therapeutic doses of TNF can be effectively administered to eradicate tumor cells in animals when combined with colloid gold particles [58]. The use of a laser to destroy the tumor cells in human breast cancer tissue has been described by a technique of selective nanothermolysis of self-assembling gold nanoparticles [59]. Secondary Ab goat anti-mouse IgG was coated on these gold nanoparticles. This particular structural arrangement demonstrated targeted localization in the primary Ab-targeted adenocarcinomatous breast cells.

Polymeric Micelles

Because polymeric micelles have a specific target and release hydrophobic anticancer medicines in a controlled manner, they are a unique drug delivery mechanism [60]. Effective drug delivery of cytotoxic drugs to cancer cells using polymeric micelles has been demonstrated by conjugating Doxorubicin with poly (ethylene glycol)-poly (α,β-aspartic acid) block copolymer [61]. Doxorubicin also known as Adriamycin was physically entrapped and chemically bound to the core of a polymeric micelle. This drug carrier's bloodstream circulation period was lengthened because of the RES's decreased absorption. Linking polymeric micelles to monoclonal antibodies, sugars, biotin, or peptides specific to tumors can help localize the micelles to the cancer cell [62].

Ceramic Nanoparticles and Photodynamic Therapy

An earlier study report described the use of ultrafine silica-based nanoparticles containing photosensitive anti-carcinogenic medications [63]. It has been investigated if these ceramic nanoparticles and photodynamic treatment can be used to specifically target and kill tumor cells. The medication releases singlet oxygen upon activation at a wavelength of 650 nm, which causes the tumor cells to necrotize. An earlier study demonstrated the idea of employing platforms made of silica nanoparticles to adhere to the outside of tumor cells and deliver singlet oxygen [64].

Advances in Nanotechnology Research

The following is only an incomplete summary of advances in nanotechnology:

- In frozen slices of prostate tumor tissue, a nanotechnology-based device that looks for thioredoxin-interacting protein partners was able to tell apart the stromal tissue linked to benign prostatic hyperplasia (BPH) from that linked to prostate cancer.
- b. An oral formulation of green tea's active component encapsulated in nanoparticles demonstrated a higher level of therapeutic efficacy against prostate cancer xenografts in mice in preclinical research compared to a non-encapsulated control formulation.

The ability of luteolin, a naturally occurring compound found in green vegetables, to inhibit the growth of human lung cancer and head and neck cancer cells in cell culture and mice was enhanced when the compound was encapsulated in a water-soluble polymer to form nanoparticles. This suggests that the delivery of similar naturally occurring dietary agents in the form of nanoparticles may have potential applications for chemoprevention.

A single polymer can create a multifunctional nanomedicine platform with a wide range of clinically relevant applications, including improved imaging sensitivity, effective drug delivery to tumors, and the conversion of light to heat inside tumors (photothermal treatment) [65,66].

Future Directions

Nanotechnology is now a key enabler for predictive oncology, which uses genetic and/or molecular markers to predict disease development, progression, and clinical outcomes, as well as personalized oncology, which bases cancer detection, diagnosis, and treatment on each patient's unique tumor molecular profile. The US National Cancer Institute has recently sponsored eight national Centers of Cancer Nanotechnology Excellence in acknowledgment of its potential influence on cancer research.

Future research in several areas appears very promising, but success will need to come from a concentrated effort. The creation of nanoparticles with a single or many functionalities is the first step.

Nanoparticles have demonstrated they have a bright future as a new generation of cancer treatments, offering the potential for developing and tweaking features that are not achievable with existing types of therapeutic medicines. Moreover, the creation of multifunctional nanoparticles may someday enable them to simultaneously identify and eliminate cancer cells.

More clinical data will undoubtedly lead to a more logical design of optimized nanoparticles with improved selectivity, efficacy, and safety as nanotechnology advances, even though there are still many unanswered questions and challenges in the clinical development of nanoparticles. However, we currently know too little about the safety of nanocarriers. A comprehensive study is necessary to understand the pharmacokinetic behavior of various nanoparticle kinds, and a database listing the potential health concerns connected with each form of nanoparticle should be established. To determine the dangers of using nanoparticles, preliminary and supplementary animal research should be done, paying close attention to the removal procedures. Moreover, the effects on the environment and the possible health risks to individuals who produce these particles have received relatively little consideration. The government must create safety guidelines immediately given the myriad of ways that nanoparticles might be used in the medical field, especially in cancer research. Researchers and funding organizations' enthusiasm for the technology is evident in the rise of Nanotechnology Research Centers, some of which are financed by the National Science Foundation and the National Institutes of Health. Many uses of nanotechnology will become standard in medical practice within the next few years. Ironically, these advances may occasionally be too tiny to be observed because they will be gradual and initially stem from continual "wet science" rather than from scaled-down machining and computation.

Conclusion

The research reports on using various nanostructures in oncology are methodically provided in this review article. This article claims that nanotechnology has powerful and advantageous applications in medicine and that these applications have given rise to a new science known as nanomedicine. Treatments for diseases, particularly cancer, can be achieved with nanomedicine. Nanoparticles, nanorods, carbon nanotubes, liposomes, and other nanostructures offer a significant deal of promise to replace the active ingredients now employed in cancer treatments. These drugs can also be used to treat infectious disorders that are linked to cancer. Thus, nanotechnology has created new opportunities for medical research, particularly for studies concerning novel cancer therapy strategies. More research in this area is needed because the negative side effects of nanostructures have restricted their widespread use.

References

1. Feynman RP (1959) There's plenty of room at the bottom. In: 1st (Edn.), Caltech Engineering and Science, California Institute of Technology, Pasadena, CA, pp: 22-36.

2. Sanvicens N, Marco MP (2008) Multifunctional nanoparticles— properties and prospects for their use

in human medicine. Trends Biotechnol 26(8): 425-433.

3. Longmire M, Choyke PL, Kobayashi H (2008) Clearance properties of nano-sized particles and molecules as imaging agents: considerations and caveats. Nanomed 3(5): 703-717.

4. Maeda H (2001) The enhanced permeability and retention(EPR) effect in tumor vasculature: the key role of tumor-selective macromolecular drug targeting. Adv Enzyme Regul 41: 189-207.

5. Jain RK (2008) Lessons from multidisciplinary translational trials on anti-angiogenic therapy of cancer. Nat Rev Cancer 8(4): 309-316.

6. Yezhelyev MV, Gao X, Xing Y, Al-Hajj A, Nie S, et al. (2006) Emerging use of nanoparticles in diagnosis and treatment of breast cancer. Lancet Oncol 7(8): 657-667.

7. Loo C, Lowery A, Halas N, West J, Drezek R (2005) Immunotargeted nanoshells for integrated cancer imaging and therapy. Nano Lett 5(4): 709-711.

8. Gelperina S, Kisich K, Iseman MD, Heifets L (2005) The potential advantages of nanoparticle drug delivery systems in chemotherapy of tuberculosis. Am J Resp Crit Care Med 172(12): 1487-1490.

9. Dinauer NB, Sabine W, Carolin K, Jorg L, Klaus BH (2005) Selective targeting of antibody-conjugated nanoparticles to leukemic cells and primary T-lymphocytes. Biomaterials 26(29): 5898-5906.

10. Gupta AK, Berry C, Gupta M, Curtis A (2003) Receptor-mediated targeting of magnetic nanoparticles using insulin as a surface ligand to prevent endocytosis. Trans Nanobiosci 2(4): 255-261.

11. Pandey R, Ahmad Z, Sharma S, Khuller GK (2005) Nano-encapsulation of azole antifungals: potential applications to improve oral drug delivery. Int J Pharm 301(1-2): 268-276.

12. Yoo HS, Oh JE, Lee KH, Park TG (1999) Biodegradable nanoparticles containing doxorubicin-PLGA conjugate for sustained release. Pharm Res 16(7): 1114-1118.

13. Soleymani S (2013) A Review of Toxicity of Some Conventional Nanomaterials. Journal of Pharmaceutical and Health Sciences 2(1): 51-56.

14. Matsumura Y, Maeda H (1986) A new concept for macromolecular therapeutics in cancer chemotherapy: mechanism of tumor tropic accumulation of proteins and the antitumor agent semantics. Cancer Res 46(12): 6387-6392.

15. Danhier F, Feron O, Preat V (2010) To exploit the tumor microenvironment; passive and active targeting of nanocarriers for anticancer drug delivery. J Control Release 148(2): 135-146.

16. Gref R, Domb A, Quellec P, Blunk T, Muller RH, et al. (1995) The controlled intravenous delivery of drugs using PEG-coated sterically stabilized nanospheres. Adv Drug Deliv Rev 16(2-3): 215-233.

17. Torchilin VP (2007) Targeted pharmaceutical nanocarriers for cancer therapy and imaging. AAPS J 9(2): 128-147.

18. Suzuki R, Takizawa T, Kuwata Y (2008) Effective anti-tumor activity of oxaliplatin encapsulated in transferrinePEG-liposome. Int J Pharm 346(1-2): 143-150.

19. Gaspar MM, Radomska A, Gobbo AL, Bakowsky U, Radomsky MW, et al. (2012) Targeted delivery of transferrin conjugated liposomes to an orthotopic model of lung cancer in nude mouse. J Aerosol Med Pulm Drug Deliv 25(6): 310-318.

20. Vandana Soni V, Jain SK, Kohli DV (2005) The potential of transferrin and transferrin conjugates of liposomes in drug delivery and targeting. Am J Drug Deliv 3(3): 155-170.

21. Daniels TR, Bernabeu E, Rodrigueez JA (2012) Transferrin receptors and the targeted delivery of therapeutic agents against cancer. Biochim Biophys Acta 1820(3): 291-317.

22. Lu Y, Low PS (2012) Folate-mediated delivery of macromolecular anticancer therapeutic agents. Adv Drug Deliv Rev 54(5): 675-693.

23. Andrew R, Hilgenbrink LPS (2005) Folate receptor-mediated drug targeting: from therapeutics to diagnostics. J Pharm Sci 94(10): 2135-2146.

24. Bast RC, Feeney M, Lazaus H, Nadler LM, Colvin RB, et al. (1981) Reactivity of a monoclonal antibody with human ovarian carcinoma. J Clin Investig 68(5): 1331-1337.

25. Moor RG, MacLaughlan S (2010) Current clinical use of biomarkers for epithelial ovarian cancer. Curr Opin Oncol 22(5): 492-497.

26. Wong SF (2005) Cetuximab: an epidermal growth factor receptor monoclonal antibody for the treatment of colorectal cancer. Clin Ther 27(6): 684-694.

27. Yih TC, Al-Fandi M (2006) Engineered nanoparticles as precise drug delivery systems. J Cell Biochem 97(6):

1184-1190.

28. Brigger I, Dubernet C, Couvreur P (2002) Nanoparticles in cancer therapy and diagnosis. Adv Drug Deliver Rev 54(5): 631-651.

29. Tsapis N, Bennett D, Jackson B, Weitz DA, Edwards DA (2002) Trojan particles: large porous carriers of nanoparticles for drug delivery. P Natl Acad Sci 99(19): 12001-12005.

30. Si PZ, Zhang ZD, Geng YD, You CY, Zhao XG, et al. (2003) Synthesis and characteristics of carbon-coated iron and nickel nanocapsules produced by arc discharge in ethanol vapor. Carbon 41(2): 247-251.

31. Sahoo SK, Labhasetwar V (2003) Nanotech approaches to drug delivery and imaging. Drug Discov 8(24): 1112-1120.

32. Fujioka K, Takada Y, Sato S, Miyata T (1995) Novel delivery system for proteins using collagen as a carrier material: the minipellet. J Control Release 33: 307-315.

33. Pereswetoff-Morath L, Edman P (1996) Immunological consequences of nasal drug delivery in dextran microspheres and ethyl (hydroxyethyl) cellulose in rats. Int J Pharm 128: 23-28.

34. Kim YS, Shin IG, Lee YM (1998) Preparation and characterization of biodegradable nanospheres composed of methoxy poly (ethylene glycol) and DL-lactide block copolymer as novel drug carriers. J Control Release 56(1-3): 197-208.

35. Vollath DD, Szabo V, Haubelt J (1997) Synthesis and properties of ceramic nanoparticles and nanocomposites. J Eur Ceram Soc 17(11): 1317-1324.

36. Douglas SJ, Davis SS, Illum L (1987) Nanoparticles in drug delivery. Crit Rev Ther Drug Carr Syst 3(3): 233-261.

37. Cherian AK, Rana AC, Jain SK (2000) Self-assembled carbohydrate-stabilized ceramic nanoparticles for the parenteral delivery of insulin. Drug Dev Ind Pharm 26(4): 459-463.

38. Corkery K (2000) Inhalable drugs for systemic therapy. Resp. Care 45(7): 831-835.

39. Jones MC, Leroux JC (1999) Polymeric micelles – a new generation of colloidal drug carriers. Eur J Pharm Biopharm 48(2): 101-111.

40. Vogelson CT (2001) Innovative pharmaceutical treatments require innovative methods of administration. Modern Drug Discovery 4(4): 49-50.

41. Tomalia DA, Baker H, Dewald GR, Hall M, Kallos G, et al. (1985) A new class of polymers: starburst-dendritic macromolecules. Polym J 17(1): 117-132.

42. Ihre H, Padilla De Jesus OL, Frechet JM (2001) Fast and convenient divergent synthesis of aliphatic ester dendrimers by anhydride coupling. J Am Chem Soc 123(25): 5908-5917.

43. Zwiorek K, Kloeckner J, Wagner E, Coester C (2005) Gelatin nanoparticles as a new and simple gene delivery system. J Pharm Pharm Sci 7(4): 22-8.

44. Onitsuka K, Fujimoto M, Kitajima H, Ohshiro N, Takei F, et al. (2004) Convergent synthesis of platinum-acetylide dendrimers. Chem–Eur J 10(24): 6433-6446.

45. Weissmann G, Troll W, Van Duuren BL, Sessa G (1968) Studies on lysosomes – X: effects of tumor-promoting agents upon biological and artificial membrane systems. Biochem 17(12): 2421-2434.

46. Wee KW, Kang GY, Park J, Kang JY, Yoon DS, et al. (2005) Novel electrical detection of label-free disease marker proteins using piezoresistive self-sensing micro-cantilevers. Biosens Bioelectron 20(10): 1932-1938.

47. Voura EB, Jaiswal JK, Mattoussi H, Simon SM (2004) Tracking metastatic tumor cell extravasation with quantum dot nanocrystals and fluorescence emission-scanning microscopy. Nat Med 10(9): 993-998.

48. Kaul Z, Yaguchi T, Kaul SC, Hirano T, Wadhwa R, et al. (2003) Mortalin imaging in normal and cancer cells with quantum dot immuno-conjugates. Cell Res 13(6): 503-507.

49. Ito A, Shinkai M, Honda H, Kobayashi T (2005) Medical application of functionalized magnetic nanoparticles. J Biosci Bioeng 100(1): 1-11.

50. El-Sayed IH, Huang X, El-Sayed MA (2005) Surface plasmon resonance scattering and absorption of anti-EGFR antibody conjugated gold nanoparticles in cancer diagnostics: applications in oral cancer. Nano Lett 5(5): 829-834.

51. Wang J, Mongayt D, Torchilin VP (2005) Polymeric micelles for delivery of poorly soluble drugs: preparation and anticancer activity in vitro of paclitaxel incorporated into mixed micelles based on poly (ethylene glycol)-lipid conjugate and positively charged lipids. J Drug Targ 13(1): 73-80.

52. Pankhurst QA, Connolly J, Jones SK, Dobson J (2003)

Applications of magnetic nanoparticles in biomedicine. J Phys D Appl Phys 36(13): 167-181.

53. Asmatulu R, Zalich MA, Claus RO, Riffle JS (2005) Synthesis, characterization and targeting of biodegradable magnetic nanocomposite particles by external magnetic fields. J Magn Magn Mater 292: 108-119.

54. Juillerat-Jeanneret L, Cengelli F, Maysinger D, Tschuddi-Monnet F, Hofmann H (2005) Interaction of functionalized superparamagnetic iron oxide nanoparticles with the brain. Eur Cells Mater 10(5): 3.

55. Gupta AK, Curtis ASG (2004) Lactoferrin and ceruloplasmin derivatized superparamagnetic iron oxide nanoparticles for targeting cell surface receptors. Biomaterials 25(15): 3029-3040.

56. Zhou J, Leuschner C, Kumar C, Hormes JF, Soboyejo WO (2006) Sub-cellular accumulation of magnetic nanoparticles in breast tumors and metastases. Biomaterials 27(9): 2001-2008.

57. Paciotti GF, Myer L, Weinreich D, Goia D, Pavel N, et al. (2004) Colloidal gold: a novel nanoparticle vector for tumor directed drug delivery. Drug Deliv 11(3): 169-183.

58. Colloid Gold Nanoparticles Deliver Cancer-Fighting Drugs.

59. Zharov VP, Galitovskaya EN, Johnson C, Kelly T (2005) Synergistic enhancement of selective nanophotothermolysis with gold nanoclusters: potential cancer therapy. Laser Surg Med 37(3): 219-226.

60. Kwon GS, Okano T (1996) Polymeric micelles as new drug carriers. Adv Drug Deliver Rev 21: 2: 107-116.

61. Yokoyama M, Miyauchi M, Yamada N, Okano T, Sakurai Y, et al. (1990) Characterization and anticancer activity of the micelle-forming polymeric anticancer drug adriamycin-conjugated poly (ethylene glycol)-poly (aspartic acid) block copolymer. Cancer Res 50(6): 1693-1700.

62. Gregoriadis G, Florence AT (1993) Recent advances in drug targeting. Trends Biotechnol 11(11): 440-442.

63. Roy I, Ohulchanskyy T, Pudavar H, Bergey E, Oseroff A, et al. (2003) Ceramic-based nanoparticles entrapping water-insoluble photosensitizing anticancer drugs: a novel drug-carrier system for photodynamic therapy. J Am Chem Soc 125(26): 7860-7865.

64. Yan F, Kopelman R (2003) The embedding of meta-tetra (hydroxyphenyl)-chlorin into silica nanoparticle platforms for photodynamic therapy and their singlet oxygen production and pH-dependent optical properties. Photochem. Photobiol 78(6): 587-591.

65. Nanotech News: An online resource for news about cancer nanotechnology research.

66. Alliance for Nanotechnology in Cancer Fact Sheet: Provides an overview of the Alliance programs, awardees, accomplishments, and future goals: National Cancer Institute publication, USA.