Indian J. L. Sci. 7 (1): 1-7, 2017 Review Article ISSN: 2277-1743 (Print)
ISSN: 2278-7879 (Online)

NANOTECHNOLOGY APPLICATIONS IN CANCER TREATMENT: AN OVERVIEW

Nidhi Mishra and Rashmi Srivastava[1]

Department of Zoology, University of Allahabad, Allahabad-211002, Uttar Pradesh, India
E-mail: srivastavarashmi@yahoo.com

ABSTRACT

Cancer remains one of the most dreaded and enigmatic diseases, with current treatment methods primarily limited to surgery, radiation, and chemotherapy. Ironically, these conventional approaches often pose significant risks, including damage to healthy tissues and the possibility of cancer recurrence due to incomplete eradication of malignant cells. Nanotechnology has emerged as a promising field with the potential to revolutionize cancer diagnosis and therapy. It offers an innovative means of targeting cancerous cells directly and selectively. Advances in materials science have led to the development of novel nanoscale targeting strategies that may offer new hope to cancer patients. Several therapeutic nanocarriers have already been developed and approved for clinical use, incorporating molecules that selectively bind to and target cancer cells. This review provides an overview of the application of nanotechnology in oncology, focusing on the types of nanoscale particles, the potential of nanocarriers and targeting molecules in cancer diagnosis and treatment, and the emerging possibilities of destroying malignant tumors with minimal damage to healthy tissues and organs.

KEYWORDS: Cancer; Nanotechnology; Nanocarriers; Disease diagnostics; Therapy

Nanotechnology is the science of manipulating matter at the nanoscale, typically ranging from 1 to 100 nanometers. The idea was first proposed by physicist Richard Feynman in 1959 and later named by Norio Taniguchi in 1974. In the 1980s, K. Eric Drexler expanded on the concept, envisioning nanoscale machines capable of precise atomic-level construction. The field advanced rapidly with tools like the scanning tunneling microscope, which allowed scientists to observe individual atoms (Filipponi and Sutherland, 2013).

Nanomaterials, including solids and semi-solids like hydrogels, differ from larger-scale materials due to their unique size-related properties. They are categorized based on dimensions: zero-dimensional (e.g., nanoparticles, quantum dots), one-dimensional (e.g., nanotubes, nanowires), and two-dimensional (e.g., thin films, coatings). Many natural structures, like DNA (2.5 nm in diameter), viruses, and red blood cells, also exist at the nanoscale (Kawadkar et al., 2011).

Nanoparticles are especially valuable for their unique properties, such as quantum effects and high surface-to-volume ratios. They can be made from a variety of materials and come in different shapes, making them suitable for diverse applications across chemistry, biology, physics, and medicine. In particular, nanotechnology offers powerful tools for diagnosing and treating diseases like cancer, neurological and cardiovascular conditions, and infections. The main aim is to develop nanoparticles that can target specific molecules within diseased cells under laboratory and clinical settings (Kawadkar et al., 2011). This review focuses on the applications of nanotechnology in cancer diagnosis and therapy.

Cancer and characteristic features of cancerous tissues

Cancer remains one of the most complex and challenging diseases to prevent, diagnose, and treat. It arises from tissues where cells exhibit abnormal growth and division compared to healthy cells. Fundamentally, cancer is a genetic disease involving two major types of cellular dysfunction: (i) permanent activation of cell replication due to mutations, chromosomal translocations, or gene amplifications (genetic instability), and (ii) disabling of programmed cell death mechanisms (apoptosis) caused by genetic alterations (Souhami et al., 2004; Fu et al., 2005; Srivastava and Ahn., 2016, Srivastava et al., 2016).

The result is a growing mass of undifferentiated cells, which can stimulate the formation of abnormal blood vessels by releasing angiogenic signals. These tumor-induced vessels are often leaky and disorganized, damaging nearby tissues and lymphatic networks (Lammers et al., 2008; Schroeder et al., 2012; Chapman et al., 2013). Such a mass is referred to as a malignant tumor, which competes with healthy tissues for nutrients and space. As the tumor expands, some cells may enter the bloodstream and establish secondary tumors in distant organs—a process known as metastasis, which is typically life-threatening (Mansoor et al., 2007).

Tumor blood vessels differ from those in normal tissues, expressing specific protein markers associated with tumor angiogenesis. These markers may be found in endothelial cells, pericytes, or the extracellular matrix (Ruoslahti, 2002). Similarly, lymphatic vessels within tumors often exhibit unique features distinct from those in healthy tissues (Laakkonen et al., 2002). Additionally, cancer cells often show molecular alterations, including

[1]**Corresponding author**

distinct cell surface receptors that can serve as potential diagnostic or therapeutic targets (Alexis et al., 2008).

Application of Nanotechnology in Cancer Treatment

Traditional cancer treatments like surgery, radiation, and chemotherapy have limitations, including damage to normal tissues and risk of recurrence. Nanotechnology offers promising advances for more precise cancer diagnosis and therapy by targeting cancer cells directly. Several therapeutic nanocarriers containing molecules that selectively bind to cancer cells have been clinically approved. These nanoparticles enable rapid tumor detection and destruction while minimizing harm to healthy tissues. They can also enhance the efficacy of existing chemotherapy and radiation treatments (Kalev et al., 2008). Such nanomedicines are multifunctional carriers designed to improve targeting, drug delivery, controlled release, stability, and biocompatibility (Peer et al., 2007; Schnieber et al., 2010; Jaishree and Gupta, 2012). Various nanoformulations combining carriers and drugs have been developed for cancer diagnosis and therapy (Cheng et al., 2010; Kelkar and Reineke, 2011; Hollis et al., 2014).

Cancer Diagnosis

Early detection of cancer requires minimal tissue, ongoing monitoring, and selective cancer cell targeting. Nanomaterials such as liposomes, nanoshells, carbon nanotubes, quantum dots, and superparamagnetic nanoparticles have improved detection methods (Jaishree and Gupta, 2012). These are engineered to recognize tumor-specific markers, receptors, and enzymes, facilitating targeted uptake and enhanced identification of cancer cells (Koning and Krijger, 2007; Alexis et al., 2008). Nanoparticles conjugated with antibodies can selectively bind tumor cells (e.g., HER-2 in breast cancer), improving diagnostic sensitivity (Loo et al., 2005). Gold and iron oxide nanoparticles act as effective imaging contrast agents for MRI, ultrasound, and nuclear medicine (Smith et al., 2014). Superparamagnetic iron oxide nanoparticles (50–100 nm) provide superior MRI contrast and have been used to detect metastatic breast cancer by differentiating healthy from diseased tissue (Cuenca et al., 2006; Subramanian et al., 2015). Quantum dots enhance fluorescence emission up to 100-fold compared to organic dyes, aiding sensitive detection (Kosaka et al., 2012). Their physicochemical properties, biocompatibility, and efficient excretion make nanoparticles ideal for biomarker detection and imaging (Loo et al., 2005; Nune et al., 2009).

Cancer Treatment

Since the introduction of drug-loaded liposomes in the 1970s, nanomedicine has progressed through various nanomaterials including gold nanoparticles, polymeric nanoparticles, quantum dots, and fullerenes, culminating in clinically approved nanomedicines for chemotherapy (Rani et al., 2012) (Table 1).

Nanoparticles usually form the core of nano-biomaterials. The surface of nanoparticles can be decorated with various molecules to avoid recognition by the immune system, enabling them to reach their targets more efficiently. Due to their smaller size, higher efficacy, specificity, low toxicity, bioavailability, and higher surface-to-volume ratio, nanoparticles can penetrate various biological barriers and efficiently target metastatic tumors compared to conventional drugs (Lammers et al., 2008; Ventola, 2012). Their small size allows nanoparticles to reach the leaky tumor vasculature and accumulate easily in the tumor microenvironment through the enhanced permeation and retention (EPR) effect (Peer et al., 2007; Schroeder et al., 2012; Chapman et al., 2013). However, it has been found that EPR-mediated targeting is advantageous only for solid tumors but not for circulating tumor cells (CTCs) and micrometastatic tumors (Li et al., 2014).

Nanocarriers target cancerous cells or tissues either passively or actively. Passive targeting exploits the EPR effect. Passively targeted nanocarriers first reached clinical trials in the mid-1980s, and the first products based on liposomes and polymer–protein conjugates were marketed in the mid-1990s. Subsequently, therapeutic nanocarriers based on this strategy were approved for wider use. Active targeting, on the other hand, involves conjugating nanocarriers containing chemotherapeutics with molecules that bind to overexpressed antigens or receptors on target cells (Peer et al., 2007). The conjugation of tumor-specific ligands onto the surface of nanoparticles promotes active targeting, increases specificity, and enables effective delivery of chemotherapeutic drugs to tumors (Sanna et al., 2014). Nanocarriers offer several advantages over free drugs: they protect the drug from premature degradation, prevent premature interaction of the drug with the biological environment, enhance drug absorption into selected tissues (such as solid tumors), control pharmacokinetics and tissue distribution, and improve intracellular penetration (Jaishree and Gupta, 2012).

Other nanocarriers

A wide range of nanocarriers have been synthesized for drug delivery, including liposomes, micelles, carbon nanotubes, quantum dots, gold nanoparticles, dendrimers, nanoemulsions, nanospheres, nanoshells, polymersomes, peptide nanoparticles,

polymer–drug conjugates, and polymeric nanoparticles. A few of these are discussed below, highlighting their properties and functional mechanisms:

(i) Liposomes

Liposomes are self-assembled nanoparticles formed by phospholipid bilayers, with hydrophilic heads facing outward and hydrophobic tails inward. Their aqueous core can carry water-soluble drugs, while the bilayer holds hydrophobic drugs (Dianzani et al., 2014). Liposomal doxorubicin (Doxil), modified with polyethylene glycol (PEG), was the first widely used liposomal chemotherapy (Aslan et al., 2013; Wang and Tepper, 2014).

Table 1: Some of the approved nanocarrier-based anticancer drugs used in different types of cancers.

Name of compound	Nanocarrier	Type of Cancer	References
Abraxane/paclitaxel	Albumin-bound paclitaxel	Metastatic breast cancer	Gradishar et al. (2005)
Bexxar/anti-CD20 conjugated to iodine-131	Radio-immunoconjugate	Relapsed or refractory, low-grade, follicular, or transformed non-Hodgkin lymphoma	Peer et al. (2007)
DaunoXome/ daunorubicin	Liposome	Kaposi's sarcoma	Gabizon (2001a)
Doxil/doxorubicin	PEG-Liposome	Refractory Kaposi's sarcoma, recurrent breast cancer, ovarian cancer	Safra et al. (2000), Gabizon (2001a), Merle et al. (2006) Schütz et al. (2013)
Myoset/doxorubicin	Liposome	Combination therapy for recurrent breast cancer, ovarian cancer, Kaposi's sarcoma	Gabizon(2001b)
Oncaspar/PEG-L-asparaginase	Polymer-protein conjugate	Acute lymphoblastic leukemia	Pasut and Veronese (2009)
Ontak/IL-2 fused to diphtheria toxin	Immunotoxic fusion protein	Cutaneous T-cell lymphoma	Peer et al. (2007)
Styrene maleic anhydride-neocarzinostatin (SMANCS)/ zinostatin	Polymer-protein conjugate	Hepatocellular carcinoma	Peer et al. (2007)
Zevalin/anti-CD20 conjugated to yttrium-90	Radio-immunoconjugate	Relapsed or refractory, low-grade, follicular, or transformed non-Hodgkin's lymphoma	Peer et al. (2007)
Zoladex/goserelin acetate	Polymer rods	Prostate cancer	Tsukagoshi (2002)

(ii) Gold Nanoparticles

Gold nanoparticles (AuNPs) are used in drug delivery due to their unique physicochemical and optical properties. Their shapes (spheres, rods, tubes) affect their therapeutic and imaging roles (Xie et al., 2010). Gold nanomaterials easily conjugate with antibodies and have higher absorption efficiency than conventional dyes, allowing photothermal cancer therapy by inducing thermal cell destruction (Jain et al., 2007; Hirsch et al., 2003; Loo et al., 2004).

(iii) Quantum Dots

Quantum dots are semiconductor particles consisting of small fluorescent nanocrystals that absorb a broad spectrum of electromagnetic waves and emit light in the near-infrared range (Hervaultab and Thanh, 2014). Examples include cadmium selenide, cadmium telluride, zinc selenide, zinc sulphide, and zinc telluride. These are increasingly used as imaging and labeling probes in cancer therapeutics (Bruchez et al., 1998; Seydel, 2003; Gao et al., 2004; Clift and Stone, 2012). Quantum dots have a central core made of a metal or metalloid that can be encapsulated by biocompatible materials such as ZnS and silica to prevent their premature elimination from the body before reaching cancer cells (Jin and Hildebrandt, 2012).

Quantum dots can also be used to track drug delivery by other nanoparticles, enabling the detection of metabolites, proteins, and other biomarkers produced by tumors. They are becoming an important class of theranostic agents due to their unique optical properties, such as high quantum yield, resistance to chemical modification, and intrinsic fluorescence emission

spectra. These properties make quantum dots highly effective for sensing and releasing anticancer drugs at the desired site.

(iv) Carbon Nanotubes

Carbon nanotubes are cylindrical graphite sheets with electrical and physical properties useful for biosensing, drug delivery, and cancer therapy. Multi-walled and single-walled types have been used to detect cancer biomarkers and target tumor cells, including human breast cancer cells (Zhang et al., 2014; Madan et al., 2012).

(v) Composite Nanoparticles

Composite nanoparticles combine multiple functional blocks into multifunctional systems for cancer therapy. For example, tamoxifen-loaded magnetite/poly (l-lactic acid) nanoparticles and curcumin-loaded tripolymeric composites show promising in vitro activity against breast and HeLa cancer cells (Hu et al., 2006; Das et al., 2010).

(vi) Dendrimers

Dendrimers are highly branched macromolecules suitable for delivering both water-soluble and insoluble drugs simultaneously. For instance, generation 5 poly(propyleneimine) dendrimers co-encapsulate hydrophobic methotrexate and hydrophilic all-trans retinoic acid for cancer therapy (Tekade et al., 2009).

(vii) Metallic Nanoparticles

Metallic nanoparticles, including superparamagnetic iron oxide particles, serve as theranostic agents for imaging (MRI) and magnetically targeted drug delivery (Berry and Curtis, 2003; Alexiou et al., 2005). Their biocompatibility allows metabolism and recycling in the body (McNeil, 2005). Conjugation with monoclonal antibodies enhances targeting of cancer cells (Remsen et al., 1996). Drugs like doxorubicin and paclitaxel are delivered using these nanoparticles (Kohler et al., 2006; Jain et al., 2008).

(viii) Nanofibers

Nanofibers, composed of organic/inorganic materials with diameters below 1000 nm, have been explored for drug delivery and hyperthermia cancer therapy. Magnetic nanoparticle-containing nanofibers can release doxorubicin under an alternating magnetic field, killing up to 70% of melanoma cells in vitro (Kim et al., 2013). Further studies are needed to evaluate their full potential (Diaz and Vivas-Mejia, 2013; Lee et al., 2015).

(ix) Additional Nanoparticles

Nanoemulsions improve bioavailability of poorly water-soluble drugs and are used in bioimaging (Lu and Park, 2013; Balducci et al., 2013). Protein nanoparticles like Abraxane® (albumin-bound paclitaxel) are clinically approved for metastatic breast cancer, showing better response and fewer side effects than traditional paclitaxel (Gradishar et al., 2005; Alexis et al., 2010). Protein-bound IgG antibodies demonstrate prolonged tumor retention, aiding targeted therapy (Wen et al., 2013).

Conclusion

Although several promising novel nanotechnology-based treatment methods are under development, much work remains to be done. Nanotechnology can be applied both in preventive strategies and during active disease treatment to combat cancer. As techniques improve to engineer more sophisticated nanodevices equipped with effective targeting mechanisms for biomolecules, nanoparticles will significantly enhance our ability to treat various types of cancer more effectively.

Conflicts of Interest: The authors declare no conflicts of interest.

REFERENCES

Alexiou, C., Jurgons, R., Schmid, R., Hilpertb, A., Bergemannc, C., Parakd, F., Iroa, H. (2005). In vitro and in vivo investigations of targeted chemotherapy with magnetic nanoparticles. J.Magn. Magn. Mater. **293**, 389-93.

Alexis, F., Pridgen, E.M., Langer, R., Farokhzad, O.C. (2010). Nanoparticle Technologies for Cancer Therapy.Scha¨fer-Korting, M. (ed.) In: Drug Delivery, Handbook of Experimental Pharmacology 197, Springer-Verlag, Berlin Heidelberg, 55–86 pp.

Alexis, F., Rhee, J.W., Richie, J.P., Radovic-Moreno, A.F., Langer, R., Farokhzad, O.C. (2008). New frontiers in nanotechnology for cancer treatment. Urol. Oncol. **26**, 74–85.

Aslan, B., Ozpolat, B., Sood, A.K., Lopez-Berestein, G. 2013. Nanotechnology in cancer therapy. J. Drug Targeting **21**, 904–913.

Balducci, A., Wen, Y., Zhang, Y., Helfer, B.M., Hitchens, T.K., Meng, W.S., Wesa, A.K.,Janjic, J.M. (2013). A novel probe for the non-invasive detection of tumor-associated inflammation. Oncoimmunology **2**, e23034.

Berry, C.C., Curtis, A.S.G. (2003). Functionalization of magnetic nanoparticle for application in

biomedicine. J. Phys. Appl. Phys. **36**, R198-R206.

Bruchez, M., Moronne, M.J., Gin, P., Weiss, S.A. (1998). Semiconductor nanocrystals as fluorescent biological labels. Science, **25**, 2013-16.

Chapman, S., Dobrovolskaia, M., Farahani, K., Goodwin, A., Joshi, A., Lee, H., Meade, T., Pomper, M., Ptak, K., Rao, J., Singh, R., Sridhar, S., Stern, S., Wang, A., Weaver, J.B., Woloschak, G., Yang, L. (2013).Nanoparticles for cancer imaging: The good, the bad, and the promise. Nano Today **8**, 454-460.

Cheng, H., Kastrup, C.J., Ramanathan, R., Siegwart, D.J., Ma, M., Bogatyrev, S.R., Xu, Q., Whitehead, K.A., Langer, R., Anderson, D.G. (2010). Nanoparticulate cellular patches for cell-mediated tumoritropic delivery. ACS Nano **4**, 625–631.

Clift, M.J., Stone, V. (2012). Quantum dots: an insight and perspective of their biological interaction and how this relates to their relevance for clinicaluse. Theranostics **2**(7), 668–680.

Cuenca, A.G., Jiang, H., Hochwald, S.N., Delano, M., Cance, W.G., Grobmyer, S.R. (2006). Emerging implications of nanotechnology on cancer diagnostics and therapeutics. Cancer **107**(3), 459-466.

Das,R.K., Kasoju, N., Bora, U. (2010). Encapsulation of curcumin in alginate- Chitosan-pluronic composite nanoparticles for delivery to cancer cells. Nanomedicine **6**(1), 153-60.

Diaz, M.R., Vivas-Mejia, P.E. (2013). Nanoparticles as Drug Delivery Systems in Cancer Medicine: Emphasis on RNAi-Containing Nanoliposomes. Pharmaceuticals **6**, 1361–1380.

Dianzani, C., Zara, G.P., Maina, G., Pettazzoni, P., Pizzimenti, S., Rossi, F., Gigliotti, C.L., Ciamporcero, E.S., Daga, M., Barrera, G. (2014). Drug delivery nanoparticles in skin cancers. BioMed. Res. Int.2014, 895986.

Filipponi, L., Sutherland, D. (2013). NANOTECHNOLOGIES: Principles, Applications, Implications and Hands-on Activities. (Ed.) European Commission Directorate-General for Research and Innovation Industrial technologies (NMP) programme, European Commission, Brussels.

Fu, X.S., Hu, C.A., Chen, J., Wang, J., Liu, K.J.R. (2005). Cancer genomic, proteomics and clinic applications. In: Dougherty, E., Shmulevich, I., Chen, J., Wang, J. (Eds.) Genomic Signal Processing and Statistics, European Applied Signal Processing Inc., Hindawi Publishing Corporation, New York, NY, 267-408 pp.

Gabizon, A.A. (2001a). Pegylated liposomal doxorubicin: metamorphosis of an old drug into a new form of chemotherapy. Cancer Invest. **19**, 424–436.

Gabizon, A. A. (2001b). Stealth liposomes and tumor targeting: one step further in the quest for the magic bullet. Clin. Cancer Res. **7**, 223–225.

Gao, X., Cui, Y., Levenson, R.M., Chung, L.W., Nie, S. (2004). In vivo Cancer targeting and imaging with semiconductor quantum dots. Nat. Biotechnol. **22**, 969-76.

Gradishar, W.J., Tjulandin, S., Davidson, N., Shaw, H., Desai, N., Bhar, P., Hawkins, M., Shaughnessy, J. O'. (2005). Superior efficacy of albumin-bound paclitaxel, ABI-007, compared with polyethylated castor oil-based paclitaxel in women with metastatic breast cancer: results of a phase III trial. J. Clin. Oncol. **23**, 7794-7803.

Hervaultab, A., Thanh, N.T.K. (2014). Magnetic nanoparticle-based therapeutic agents for thermo-chemotherapy treatment of cancer. Nanoscale **6**, 11553-11573.

Hirsch, L.R., Stafford, R.J., Bankson, J.A., Sershen, S.R., Rivera, B., Price, R.E., Hazle, J.D., Halas, N.J., West, J.L. (2003). Nanoshell-mediated near-infrared thermal therapy of tumours under magnetic resonance guidance. Proc. Natl. Acad. Sci. USA **100**, 13549-54.

Hollis, C.P., Weiss, H.L., Leggas, M., Evers, B.M., Gemeinhart, R.A., Li, T. (2013). Biodistribution and bioimaging studies of hybrid paclitaxel nanocrystals: lessons learned of the EPR effect and image-guided drug delivery. J. Control Release **172**(1), 12-21.

Hu, F.X., Neoh, K.G., Kang, E.T. (2006). Synthesis and in vitro anti-cancer evaluation of tamoxifen-loaded magnetite/PLLA composite nanoparticles. Biomaterials **27**(33), 5725-33.

Jain, P.K., El-Sayed, I.H., El-Sayed, M.A. (2007). Au nanoparticles target cancer. Nanotoday **2**, 18-29.

Jain, T.K., Richey, J., Strand, M., Leslie-Pelecky, D.L., Flask, C.A., Labhasetwar, V. (2008). Magnetic nanoparticles with dual functional properties: Drug delivery and magnetic resonance imaging. Biomaterials **29**, 4012-21.

Jaishree, V., Gupta, P.D. (2012). Nanotechnology: A Revolution in Cancer Diagnosis. Ind. J. Clin. Biochem. **27**(3), 214–220.

Jason, R.M., Ralph, W. (2008). Multifunctional magnetic nanoparticle for targeted imaging and therapy. Adv. Drug Deliv. Rev. **60**, 1241-51.

Jin, Z., Hildebrandt, N. (2012). Semiconductor quantum dots for in vitro diagnostics and cellular imaging. Trends Biotechnol. **30**, 394–403.

Kalevi, K., Paola, E., Kim, B., Ernest, K.J., Pauwels. (2008). Nanoparticles in Cancer. Current Radiopharmaceuticals **1**, 30-36.

Kawadkar, J., Chauhan, M.K., Maharana, M. (2011). Nanobiotechnology: application of nanotechnology in diagnosis, drug discovery and drug development. Asian J. Pharmaceut. Clin. Res. **4**(1), 23-28.

Kelkar, S.S., Reineke, T.M. (2011). Theranostics: combining imaging and therapy. Bioconjug. Chem. **22**, 1879-903.

Kim, Y.J., Ebara, M., Aoyagi, T. (2013).A Smart Hyperthermia Nanofiber with Switchable Drug Release for Inducing Cancer Apoptosis. Adv. Funct. Mater.**23**, 5753–5761.

Kohler, N., Sun, C., Fichtenholtz, A., Gunn, J., Fang, C., Zhang, M. (2006). Methotrexate-immobilized poly (ethylene glycol) magnetic nanoparticles for MR imaging and drug delivery. Small **2**, 785-92.

Koning, G.A., Krijger, G.C. (2007). Targeted multifunctional lipid-based nanocarriers for image-guided drug delivery. Anticancer Agents Med. Chem. **7**, 425–40.

Kosaka, N., Bernardo, M., Mitsunaga, M., Choyke, P.L., Kobayashi, H. (2012). MR and optical imaging of early micrometastases in lymph nodes: triple labeling with nano-sized agents yielding distinct signals. Contrast Media and Mol. Imaging **7**, 247–253.

Laakkonen, P., Porkka, K., Hoffman, J.A., Ruoslahti, E. (2002). A tumor-homing peptide with a targeting specificity related to lymphatic vessels. Nat. Med. **8**, 751–755.

Lammers, T., Hennink, W.E., Storm, G. **2008**. Tumour-targeted nanomedicines: principles and practice. Br. J. Cancer **99**(3), 392–397.

Li, J., Cheng, D., Yin, T., Chen, W., Lin, Y., Chen, J., Li, R., Shuai, X. (2014). Copolymer of poly(ethylene glycol) and poly(l-lysine) grafting polyethylenimine through a reducible disulfide linkage for siRNA delivery. Nanoscale **6**, 1732–1740.

Lee, H.-J., Lee, S., Uthaman, S., Thomas, R., Hyun, H., Jeong, Y., Cho, C.- S., Park, I.-K. (2015). Biomedical Applications of Magnetically Functionalized Organic/Inorganic Hybrid Nanofibers. Int. J. Mol. Sci., **16**, 13661-13677.

Loo, C., Lin, A., Hirsch, L., Lee, M.H., Barton, J., Halas, N., West, J., Drezek, R. (2004). Nanoshell-enabled photonics-based imaging and therapy of cancer.Technol. Cancer Res. Treat. **3**(1), 33-40.

Loo, C., Lowery, A., Halas, N., West, J., Drezek, R. (2005). Immunotargetednanoshells for integrated cancer imaging and therapy. Nano. Lett. **5**(4), 709–11.

Lu, Y., Park, K. (2013) Polymeric micelles and alternative nanonized delivery vehicles for poorly soluble drugs. Int. J. Pharm. **453**, 198–214.

Madani, S.Y., Tan, A., Dwek, M., Seifalian, A.M. (2012). Functionalization of single-walled carbon nanotubes and their binding to cancer cells. Int. J. Nanomedicine **7**, 905-14.

Masoori, G.A., Mohazzabi, P., McCormack, P., Jabbari, S. (2007). Nanotechnology in cancer prevention, detection and treatment: bright future lies ahead. World Review of Science, Technology and Sustainable Development **2/3**(4), 226-257.

McNeil, S.E. (2005). Nanotechnology for the biologist. J.Leukoc.Biol. **78**, 585-94.

Merle, P., Ahmed, S.S., Habersetzer, F., Abergel, A., Taieb, J., Bonyhay, L., Costantini, D., Dufour-Lamartinie, J., Trepo, C. 2006. Phase 1 study of intra-arterial hepatic (IAH) delivery of doxorubicin-transdrug (DT) for patients with advanced hepatocellular carcinoma (HCC). J. Clin. Oncol. **24**, 14094.

Nune, S.K., Chanda, N., Shukla, R., Katti, K., Kulkarni, R.R., Thilakavathy, S., Mekapothula, S., Kannan, R., Katti, K.V. (2009). Green nanotechnology from tea: phytochemicals in tea as building blocks for production of biocompatible gold nanoparticles. J. Mater. Chem. **19**, 2912–2920.

Pasut, G., Veronese, F.M. (2009). PEG conjugates in clinical development or use as anticancer agents: an overview. Adv. Drug Deliv. Rev. **61**, 1177–1188.

Peer, D., Karp, J.M., Hong, S., Farokhzad, O. C. ,Margalit, R., Langer, R. (2007). Nanocarriers as an emerging platform for cancer therapy. Nat. Nanotechnol. **2**, 751–60.

Rani,D., Somasundaram, H.V., Nair, S., Koyakutty, M. (2012). Advances in cancer nanomedicine. J. Indian Inst. Sci. **92**(2), 187-218.

Remsen, L.G., McCormick, C.I., Roman-Goldstein, S., Nilaver, G., Weissleder, R., Bogdanov, A., Hellström, I., Kroll, R.A., Neuwelt, E.A. (1996). MR of carcinoma-specific monoclonal antibody conjugated to monocrystallineiron oxide nanoparticles: The potential for noninvasive diagnosis. AJNR Am. J.Neuroradiol. **17**, 411-8.

Ruoslahti, E. (2002). Specialization of tumour vasculature. Nat. Rev. Cancer **2**, 83–90.

Safra, T., Muggia, F., Jeffers, S., Tsao-Wei, D.D., Groshen, S., Lyass, O., Henderson, R., Berry, G., Gabizon, A. (2000). Pegylated liposomal doxorubicin (doxil): reduced clinical cardiotoxicity in patients reaching or exceeding cumulative doses of 500 mg/m2. Ann. Oncol. **11**, 1029–1033

Sanna, V., Pala, N., Sechi, M. (2014).Targeted therapy using nanotechnology: Focus on cancer. Int. Nanomedicine **9**, 467–483.

Scheinber, D.A., Villa, C.H., Escorcia, F.E., Mcdevitt, M.R. (2010). Conscripts of the infinite armada: systemic cancer therapy using nanomaterials. Nature Rev. **7**, 266-276.

Schroeder, A., Heller, D. A., Winslow, M. M., Dahlman, J. E., Pratt, G. W., Langer, R., Jacks, T., Anderson, D.G. (2012). Treating metastatic cancer with nanotechnology. Nat. Rev. Cancer **12**, 39–50.

Schütz, C.A., Juillerat-Jeanneret, L., Mueller, H., Lynch, I., Riediker M. (2013). Therapeutic nanoparticles in clinics and under clinical evaluation Nanomedicine **8**, 449–467.

Seydel, C. (2003). Quantum dots get wet. Science, **300**, 80-91.

Smith, B.R., Eid, E., Ghosn, B., Rallapalli, H., Prescher, J. A., Larson, T., Herzenberg, L.A., Gambhir, S.S. (2014). Selective uptake of single-walled carbon nanotubes by circulating monocytes for enhanced tumour delivery. Nature Nanotech. **9**, 481–487.

Souhami, R.L., Tannok, I., Hohernberger, P., Horiot, J-C. 2004. Oxford Textbook of Oncology, (2002); Benjamin Lewin, Genes VIII, Prentice-Hall, p.889.

Srivastava, R., & Ahn, S. H. (2015). Modifications of RNA polymerase II CTD: Connections to the histone code and cellular function. Biotechnology advances, **33**(6), 856-872

Srivastava, R., Mishra, N., Singh, U. M., & Srivastava, R. (2016). Genotoxicity: Mechanisms and its impact on human diseases. Octa Journal of Biosciences, **4**, 67-70

Subramanian, A., Manigandan, A., Sivashankari, A., Sethuraman, S. (2015). Development of nanotheranostics against metastatic breast cancer – a focus on the biology & mechanistic approaches. Biotechnol. Adv. **33**, 1897-1911

Tekade, R.K., Dutta, T., Gajbhiye, V., Jain, N.K. (2009). Exploring dendrimer towards dual drug delivery: pH responsive simultaneous drug-release kinetics. J. Microencap. **26**(4), 287–296.

Tsukagoshi, S. (2002). A new LH-RH agonist for treatment of prostate cancer, 3-month controlled-release formulation of goserelin acetate (Zoladex LA 10. 8 mg depot). Outline of pre-clinical and clinical studies. GanTo Kagaku.Ryoho. **29**, 1675–1687.

Ventola, C.L. (2012). The Nanomedicine Revolution: Part 1: Emerging Concepts. P. T. **37**(9), 512-525.

Wang,A.Z., Tepper, J.E. 2014. Nanotechnology in radiation oncology. J. Clin. Oncol. **32**, 2879–2885.

Wen, Y., Kolonich, H.R., Kruszewski, K.M., Giannoukakis, N., Gawalt, E. S., Meng, W.S. (2013). Retaining antibodies in tumors with a self-assembling injectable system. Mol. Pharma. **10**, 1035–1044.

Xie, J., Lee, S., Chen, X. (2010). Nanoparticle-based theranostic agents. Adv.Drug.Deliv. Rev. **62**(11), 1064-79.

Zhang, Y., Gao, G., Liu, H., Fu, H., Fan, J., Wang, K., Chen, Y., Li, B., Zhang, C., Zhi, X., He, L., Cui, D. (2014). Identification of Volatile Biomarkers of Gastric Cancer Cells and Ultrasensitive Electrochemical Detection based on Sensing Interface of Au-Ag Alloy coated MWCNTs. Theranostics **4**(2), 154-162.