Indian Journal of Novel Drug Delivery

IJNDD

An Official Publication of Karnataka Education and Scientific Society

Review Article

# Drug Delivery and Therapeutic Approaches to Prostate Cancer

JAMEEL AHMED S MULLA*

Department of Pharmaceutics, Shree Santkrupa College of Pharmacy, Ghogaon, Tal- Karad, Dist- Satara, Maharashtra, India

**ARTICLE DETAILS**

*Article history:*
Received on 05 September 2018
Modified on 25 September 2018
Accepted on 27 September 2018

*Keywords:*
Prostate structure,
Prostate cancer,
Therapeutic approaches,
Drug delivery approaches,
Liposomes,
Nanoparticles

**ABSTRACT**

According to the global cancer statistics, prostate cancer is the second most often diagnosed cancer in males worldwide and it ranks in fifth place among cancer-related deaths. Localized prostate cancer is usually treated by surgical removal of the prostate (radical prostatectomy) or by radiation therapy. Both treatment options are frequently associated with severe side effects. Drug delivery to prostate through conventional route is associated with pharmacokinetics based and side effects related problems. This review briefly highlighted about prostate structure and its cancer. Different therapeutic approaches such as radiotherapy, chemotherapy, immunotherapy, androgen deprivation therapy (ADT), focal therapies and systemic therapies; and drug delivery approaches such as liposomes, polymeric based nanoparticles and micelles, dendrimers, gold nanoparticles, carbon based nanoparticles and magnetic nanoparticles for prostate cancer are also outlined here.



## INTRODUCTION

### Cancer

Cancer is the second leading cause of death worldwide, and is accountable for a predictable 9.6 million deaths in 2018. Globally, about 1 in 6 deaths is due to cancer. About 70% of deaths from cancer occur in low- and middle-income countries. The most common cancers are; lung (2.09 million cases), breast (2.09 million cases), colorectal (1.80 million cases), prostate (1.28 million cases), skin cancer (non-melanoma) (1.04 million cases) and stomach (1.03 million cases). Cancer arises from the transformation of normal cells into tumour cells in a multistage process that normally progresses from a pre-cancerous lesion to a malignant tumour. These changes are the consequence of the interaction between a person's genetic factors and 3 categories of external agents, including (a) physical carcinogens, such as ultraviolet and ionizing radiation (b) chemical carcinogens, such as asbestos, components of tobacco smoke, aflatoxin (a food contaminant), and arsenic (a drinking water contaminant) (c) biological carcinogens, such as infections from certain viruses, bacteria, or parasites [1].

***Author for Correspondence:***
*Email:* jameelahmed5@rediffmail.com

### Prostate

The prostate is one of the male accessory glands that contribute to the male ejaculate by producing seminal fluid. In mice, elimination of this organ reduces fertility [2]. The understanding of development, maturation and anatomy of prostate has progressed gradually throughout the past century, but it has been moderately hindered by reliance on historical anatomical descriptions [3-5]. Description of prostatic lobes has been replaced by the now widely accepted concept that the human prostate is better described as consisting of zones found within one discrete organ [6].

The prostate is an exquisitely steroid hormone sensitive organ. Considering hormone action throughout the different life stages of prostate organogenesis, puberty, and during adulthood and aging, is critical for understanding prostate anatomy and the different diseases of this organ. Certainly, most of men experience some form of prostate pathology during their lifetime. The focus has been on investigating the long-term impact of disruption of normal prostate development on structural and functional abnormalities related to specific types of prostate disease that often are not recognized until much later in life [7].

**Prostate cancer**

Prostate cancer is the most common male malignancy and remains the leading cause of death in American men, in spite of extensive efforts and recent advances in early diagnosis and surgical intervention [8].

According to the classification by the U.S. National Cancer Institute, prostate cancer can be divided into four different stages after diagnosis. In stage I, the cancer is small and confined to the prostate gland. In stage II, the cancer is larger but still limited to the prostate gland. In stage III, the cancer spreads out of the prostate gland and reaches the tissues near the prostate. The cancer may reach the seminal vesicles. In stage IV, the cancer spreads to distant organs and tissues, such as rectum, lymph nodes, bones, lung, etc. When prostate cancer spreads out of the prostate gland and metastasizes to distant parts of the body, it is called advanced prostate cancer [9]. Patients with high risk of prostate cancer progression and/or death are also considered as advanced prostate cancer [10].

Prostate cancer is the leading cancer (29% of all cancers) and the third most common cause of cancer-related death in men in the United States. It is estimated 1 in 7 men will develop prostate cancer in their lifetimes and 1 in 38 will die of prostate cancer. Although prostate cancer can be a lethal disease, most men diagnosed with prostate cancer do not die from it. Indeed, the overall 5-, 10-, and 15-year survival rates are 100%, 98%, and 95%, respectively [11].

**Detection**

Most patients with early prostate cancer are asymptomatic. In some cases, however, prostate cancer can cause local symptoms including obstructive and irritative urinary symptoms such as weak stream, increased urinary frequency, and dysuria, as well as hematuria. The presence of symptoms often suggests locally advanced disease as these can be the results of direct local invasion of the cancer into the urethra and/or bladder. Metastatic prostate cancer to the bone can cause pain and predispose patients to fractures. Although early prostate cancer typically has no signs on physical exam, abnormal digital rectal exam (DRE) such as the presence of induration or nodule in the prostate are the most common physical exam findings suggestive of prostate cancer.

Given the lack of reliable symptoms and signs to detect early prostate cancer, most cases are detected based on abnormal prostate-specific antigen (PSA). PSA is a member of the human kallikrein proteins, primarily secreted in the seminal fluid by the epithelial cells of the prostate acini. It is produced for the ejaculate and is responsible for liquifying the semen and potentially dissolving the cervical mucus allowing the free movement of sperm. PSA is present in small quantities in the serum in both bound and unbound forms that can be measured. Serum PSA levels vary with age, race, and prostate volume. In addition, prostate inflammation, infection, and cancer can cause PSA to rise. On average, 30% of patients with elevated PSA have prostate cancer diagnosed on biopsy [11]. A suspect DRE in patients with a PSA level of upto 2 ng/ml has a positive predictive value of 5–30% [12].

**Treatment**

Treatment decisions for prostate cancer are based on tumor aggressiveness (e.g., grade), stage, patient's life expectancy, and the ability of each therapy to ensure disease-free survival, maximizing quality-of-life while minimizing side effects. Localized prostate cancer is typically treated with active surveillance, radical prostatectomy, radiotherapy, or focal therapies. Metastatic prostate cancer is usually treated with systemic therapies. Given some of these therapies may interfere with fertility by either reducing or abolishing spermatogenesis and/or blocking sperm transport, some patients may be candidates for sperm banking before the initiation of treatment [11].

**THERAPEUTIC APPROACHES**

**Radiotherapy**

Radiotherapy involves the delivery of high-energy radiation to treat disease. It can be given both externally (external beam radiation) and/or internally (brachytherapy). Prior to treatment, the prostate is mapped using imaging tests (CT or MRI scan) and a treatment plan (simulation) is established. The most commonly used techniques of external beam radiation include three-dimensional conformal radiotherapy (radiation beams are then shaped and aimed at the prostate from several directions), intensity-modulated radiotherapy (the intensity of the beams is adjusted to limit the doses reaching nearby normal tissues), and proton beam radiotherapy. Brachytherapy can be delivered permanently (low-dose) by placing radioactive pellets in the prostate, or temporally (high-dose) by placing where radioactive needles in the

prostate for only a few moments and then removing them.

Androgen deprivation therapy for a few months is typically given along with radiotherapy. The most common side effects of radiotherapy for prostate cancer include radiation proctitis, radiation cystitis, urethral stricture, and erectile dysfunction. The prognosis of patients treated with radiotherapy is comparable to those treated with RP when matched by pathological stage and grade.

**Chemotherapy**

The use of cytotoxic chemotherapy is usually used in cases of metastatic disease, especially CRPC. The most commonly prescribed drugs are: docetaxel, cabazitaxel, mitoxantrone, and estramustine.

**Immunotherapy**

Several immunomodulatory agents are being investigated. Currently only Sipuleucel-T is approved for the treatment of metastatic prostate cancer. It works through activating antigen-presenting cells to stimulate T-cell immune response targeted against prostatic acid phosphatase, an antigen that is highly expressed in most prostate cancer cells.

**Androgen Deprivation Therapy (ADT)**

Androgens are required for normal growth and function of the prostate. They also stimulate prostate cancer cells growth. Lowering androgen levels or stopping them from getting into prostate cancer cells often makes prostate cancer to shrink or grow more slowly for a time. ADT is currently the initial treatment for metastatic prostate cancer. Although most tumors respond to ADT in the beginning, over the course of months to years most tumors become refractory to ADT and are called castration-resistant prostate cancer (CRPC).

**Focal Therapies**

The rationale for focal therapies of the prostate is to treat the tumor while sparing the normal prostate. Although there are several means of delivering energy to kill the tumor, the most used technique is cryotherapy. Freezing of the prostate is accomplished by using a multiprobe cryosurgical device. Multiple probes are placed percutaneously under transrectal ultrasound guidance, and the temperature is lowered to -25 to -50°C. Potential side effects include recurrence/persistence of the cancer in the untreated prostate, hematuria, urinary incontinence, erectile dysfunction, and injury to surrounding structures. Although short-term studies showed promising results, long-term oncologic results are unknown.

**Systemic Therapies**

Several systemic agents are available to treat prostate cancer. These treatments are commonly used for locally advanced and metastatic disease [11].

**DRUG DELIVERY APPROACHES**

Drug delivery system (DDS) is defined as a process of administering a pharmaceutical compound or a formulation or a device which is used to deliver the drug in the humans or animals to achieve a therapeutic effect [13].

It mainly involves the site targeting within the body and improves the efficacy of the therapeutic substance and safety by controlling the time, rate and place of release of drugs in the body.60 Targeted drug delivery (TDD) is a process which mainly integrates the dosage form and the route of administration of the drug. It involves the administration of the therapeutic product or the formulation inside the body and the release of the active ingredients by the product, and followed by the subsequent transport of the active ingredients across the biological membranes to the site of action [13, 14]. The distribution of drug to organs or tissues other than the site of action can increase the risk of toxicity [14-16].

Approaches for targeted delivery of therapeutics in cancer typically involves systemic administration of therapeutics packaged in nanocarriers (NCs) or localized delivery of therapeutics to the diseased tissue. Encapsulation of therapeutic molecules (e.g., small molecule inhibitors, chemotherapy, RNAi, etc.) in NCs can improve their solubility and bioavailability, alter their bio-distribution, and can also facilitate entry into the target cell [17].

Problems associated with oral administration may cause various bioavailability problems pertaining to the route of drug administration, including poor absorption, metabolic degradation, sub-threshold value of drug reaching the target tissue and non-specific drug distribution related side effects. In such circumstances, an alternative drug delivery route may offer advantages to circumvent some of the above mentioned hurdles of oral drug

administration. The emerging trends of using vas deferens as a local drug delivery route to prostate in conjunction with a novel concept of *in vivo* self-assembly drug carrier generated by a drug delivery system injected in the lumen of vas deferens, might be the real solution of prostate cancer prevention [18].

Nanotechnology is an advanced, emerging and promising therapeutic platform that uses nanoparticles (NPs) for the disease diagnosis to nanoparticles based drug delivery systems (DDS) that finally evade life-threatening diseases such as cancer and their treatments [19, 20]. The major advantages of using nanomaterials as a carrier for anticancer agents are the possibility of targeted delivery of the drug to the tumor site, tumor imaging, their ability to hold thousands of molecules of a drug and their ability to overcome solubility, stability and resistance issues [21-25].

NPs have the potential to provide solutions to the current difficulties in conventional cancer therapy due to their unique size, which is generally falls into a size range (1–100 nm) which is similar to basic biological materials such as DNA, proteins and other macromolecular structures found inside living cells. Nanomaterials have their unique mechanical, electronic, photonic and magnetic properties, vastly increased surface area (1000 m2/g) are projected to have a wide range of applications from drug delivery to biomedical imaging and more recently to personalized medicine [19, 26-30].

### *Liposomes*

Liposomes are a novel drug delivery system (NDDS), they are vesicular structures consisting of bilalyers which form spontaneously when phospholipids are dispersed in water. They are microscopic vesicles in which an aqueous volume is entirely enclosed by a membrane composed of lipid bilayers [31]. These structures can deliver both hydrophilic and hydrophobic drugs for cancer, antibacterial, antifungal, immunomodulation, diagnostics, ophtalmica, vaccines, enzymes and genetic elements [32].

Targeted drug delivery, using liposomal drug delivery systems, is an attractive approach to enhance the efficacy of anticancer drugs and prevent side effects, thereby potentially increasing the therapeutic index. In most preclinical prostate cancer studies, passive liposomal targeting of anticancer drugs (caused by enhanced permeability and retention of the therapeutic compound) leads to an increased antitumor efficacy and decreased side effects compared to non-targeted drugs [33].

Delivery of zinc chelator, N,N,N',N'-tetrakis(2-pyridylmethyl)- ethylenediamine using aptamer-targeted liposomes results in specific delivery to targeted cells. In vivo experiments show that TPEN-loaded, aptamer-targeted liposomes reduce tumor growth in a human prostate cancer xenograft model [34].

### *Polymeric Based Nanoparticles and Micelles*

Polymeric nanoparticles (PNPs) have attracted considerable interest over the last few years due to their unique properties and behaviors resulting from their small size [35]. Advantages of PNPs as carriers include controlled release, the ability to combine both, therapy and imaging (theranostics), protection of drug molecules and its specific targeting, facilitating improvements in the therapeutic index [36-38]. The use of biodegradable polymeric nanoparticles (NPs) for controlled drug delivery has shown significant therapeutic potential. Concurrently, targeted delivery technologies are becoming increasingly important as a scientific area of investigation. In cancer, targeted polymeric NPs can be used to deliver chemotherapies to tumor cells with greater efficacy and reduced cytotoxicity on peripheral healthy tissues [39]. Nanoparticles involve nanospheres and nanocapsules. Nanospheres are a matrix type of particle in which the drug is uniformly dispersed or dissolved in the polymer matrix, whereas nanocapsules are vesicles in which the drug core is surrounded by a polymeric film [40].

Micelles are formed by amphiphilic copolymers which self-assembled to nanosized aggregates above the critical micellar concentration. The hydrophobic moiety forms the core of micelles whereas the hydrophilic moiety forms the corona in the shell of micelles. Micelles possess a dynamic structure where the unimers of the amphiphilic copolymer are interchangeable [40].

Polymeric micelles represent an effective delivery system for poorly water-soluble anticancer drugs. With small size (10–100 nm) and hydrophilic shell of PEG, polymeric micelles exhibit prolonged circulation time in the blood and enhanced tumor accumulation [41]. Polymeric micelles are extensively studied carriers for the delivery of poorly water-soluble drugs. By enhancing the aqueous solubility and prolonging the blood half-life of chemotherapeutic agents, the anticancer agents can passively accumulate

in the tumor site through the leaky vasculature via the enhanced permeability and retention (EPR) effect [42, 43]. Compared with other drug carriers, micelles have the advantages of very small size (10–100 nm), which is critical for passive targeting to solid tumors, particularly the poorly vascularized tumors [44]. The most commonly used hydrophilic segment of micelles for drug delivery is poly (ethylene glycol) (PEG), with a molecular weight of 2–15 kDa. PEG is highly water-soluble, non-toxic and neutrally charged. PEG forms a hydrophilic corona on the surface of micelles which minimizes the nonspecific interaction with blood components and prolongs the circulation time. Besides PEG, other polymers including poly(N-vinyl pyrrolidone) (PVP) and poly(N-isopropyl acrylamide) (pNIPAM) have also been used as hydrophilic portion of micelles [45, 46].

A small molecular ligand of prostate specific membrane antigen (SMLP) conjugated poly (caprolactone) (PCL)-b-poly (ethylene glycol) (PEG) copolymers with different block lengths were synthesized to construct a satisfactory drug delivery system. Four different docetaxel-loaded polymeric micelles (DTX-PMs) were prepared by dialysis with particle sizes less than 60 nm [47]. Gao, Y et al had designed and fabricated PTX-loaded pH-sensitive polymeric micelles modified with anti-PSMA (prostate specific membrane antigen) antibody YPSMA-1 to combine active targeting to PSMA-positive prostate cancer cells with fast intracellular release of drugs. It was demonstrated that YPSMA-1-modified micelles had excellent performance featured by nano-scale size to obtain the EPR effect, a favorable pH-sensitivity to promote endo/lysosome escape and rapid drug release to kill tumor cells with effective concentration, and a higher PSMA-binding affinity to enhance the targeting to PSMA-positive tumor cells, leading to enhanced cellular uptake and cytotoxicity and thereby therapeutic efficacy of prostate cancers with negligible systemic toxicity [48].

Delivery of paclitaxel via PEG5K-embelin2 micelles leads to superior antitumor activity compared to Taxol in murine models of breast and prostate cancers [49]. Cheng et al reported A10 aptamer-functionalized PLGA–PEG NPs against prostate-specific membrane antigen (PSMA)-overexpressing LNCaP cancer cells [50]. In another case, it was used a system formed from bicalutamide loaded PLGA NPs in prostate cancer. The authors have used LNCaP and C4-2 cancer cells and it was observed that the system significantly inhibit colony formation in the two cell lines and the cell apoptosis occurs [51]. In a further study, it was investigated the *in vitro* anticancer activity of cisplatin-loaded PLGA-mPEG NPs and control (cisplatin free) on human prostate cancer LNCaP cells. It was reported an anticancer activity against LNCaP human prostate cancer cells when it was used the system formed from cisplatin-loaded PLGA-mPEG NPs [52].

### *Dendrimers*

Dendrimers (derived from the Greek “dendron,” which means tree, and “meros,” meaning part) are well- defi ned, multivalent molecules having a branched structure. These molecules were fi rst reported by Vögtle et al. as “cascade molecules,” and later Tomalia et al. named these molecules dendrimers [53, 54]. Dendrimers are nano-sized, radially symmetric molecules with well-defined, homogeneous, and monodisperse structure consisting of tree-like arms or branches [55]. These hyperbranched molecules were first discovered by Fritz Vogtle in 1978, by Donald Tomalia and co-workers in the early 1980s, and at the same time, but independently by George R. Newkome. The second group called synthesized macromolecules ‘arborols’ means, in Latin, ‘trees’. Dendrimers might also be called ‘cascade molecules’, but this term is not as much established as ‘dendrimers’ [56-58].

In 1990, Fre´chet introduced the convergent approach toward dendrimers. In convergent procedures, the synthesis is started at the periphery and elaborated to the core [59, 60]. Dendrimers are hyperbranched macromolecules with a carefully tailored architecture, the end-groups (i.e., the groups reaching the outer periphery), which can be functionalized, thus modifying their physicochemical or biological properties [61-66].

The emerging role of dendritic macromolecules for anticancer therapies and diagnostic imaging is remarkable. The advantages of these well-defined materials make them the newest class of macromolecular nano-scale delivery devices [67]. Many drug-loaded dendrimer systems have been reported with efficient uptake in prostate cancer for therapeutic treatment by taking advantage of this passive targeting mechanism [68, 69].

Recently, a G4 PAMAM dendrimer was reported as a carrier of A10 aptamer-DOX complex for prostate cancer treatment [70]. Similarly, a G5 PAMAM dendrimer conjugate with A10-3.2, a

truncated form of xPSM-A10, was reported with capability of delivering tumor suppressor genes to PSMA expressing target [71].

Curcumin has shown potential to suppress *in vitro* prostate cancer cell proliferation in both androgen-sensitive prostate cancer cell line LNCaP and androgen-independent cell line DU145 and *in vivo* tumor growth in a LNCaP xenograft mouse model [72-75]. Similar inhibitive effects have been seen for Genistein to suppress prostate cancer growth [76]. Recent evidence indicates that miR-15a and miR-16-1 act as tumor suppressor genes in prostate cancer by down-regulating the expression of survival genes such as bcl2, ccnd1, and wnt3A [77].

When functionlized with maleimide groups, a G5 PAMAM dendrimer was reported with capability to deliver thiolated miR-15a and miR-16-1into prostate cancer cells to induce the cell death [71]. Targeting Prostate-Specific Membrane Antigen (PSMA) can also be achieved by using aptamers, a class of nuclease-stabilized oligonucleotides selected by a ligand screening technology, SELEX (systematic evolution of ligands by exponential enrichment) [78-85]. Papagiannaros, et al. developed a complex formed from a PAMAM dendrimer (G4) loaded with DOX and incorporated into liposomes and this complex was tested against MCF-7 human breast carcinomas and DU145 human prostate carcinomas [86].

### *Gold Nanoparticles*

In 2004, Paciotti et al. have reported for the first time about the development of colloidal gold nanoparticle vector that targets the delivery of tumor necrosis factor (TNF) to a solid tumor growing in mice [87]. Aptamers conjugated to magnetic and gold nanoparticles are used in cancer detection and therapy [88-90].

Gold nanoparticles have potential application in various fields like physics, chemistry, material science, biology, and medicine due to their unique physical, chemical, optical, thermal, and biological properties. They remain appealing for biomedical application due to the biocompatibility, optical tunability, and easily functionalizable nature. Gold nanoparticles are generally synthesized by chemical methods which involve simple reduction of metal salts by reducing agents in a controlled fashion producing spherical nanoparticles. The most well-known synthetic procedures of gold nanoparticles include (i) the Turkevich method, (ii) the related Frens method, (iii) the Brust biphasic method, (iv) the microemulsion method and (v) the seeding method.

Gold nanoparticles are excellent carrier molecules for cancer drug delivery. Targeted drug delivery was also accomplished using gold nanoparticles. Spatially controlled drug delivery systems can be developed by conjugating nanoparticles with targeting ligands which could facilitate the preferential delivery of nanotherapeutics to the sites of interest while reducing undesired side effects elsewhere [91].

Therapeutic agents can be loaded to gold nanoparticles by covalent or noncovalent interaction. Gibson et al. have covalently conjugated paclitaxel, an anticancer drug, to gold nanoparticles of size 2 nm [92]. Stern, J. M. et al reported that laser-activated gold nanoshells can ablate human prostate cancer cells *in vitro*. This nanoparticle technology is an attractive therapeutic agent for selective tumor ablation [93]. Zhang et al had reported that both neutral gold nanoparticles (TGS-GNPs) and thioglucose-capped gold nanoparticles (Glu-GNPs) demonstrated improved radiosensitivity on DU-145 prostate cancer cells in vitro. Cell uptakes of GluGNPs were significantly increased and the cell-killing effects were enhanced compared to GNPs without glucose binding when 200 kVp X-ray was applied. These results suggest the promising clinical applications of the nanoparticles in future cancer treatment, targeting high radiation doses to metabolically active tumour cells, but sparing adjacent normal tissues [94].

### *Carbon Based Nanoparticles*

Functional carbon-based nanomaterials (CBNs) have become important due to their unique combinations of chemical and physical properties (*i.e.*, thermal and electrical conductivity, high mechanical strength, and optical properties), extensive research efforts are being made to utilize these materials for various industrial applications, such as high-strength materials and electronics [95].

Carbon-based nanoparticles such as graphene related materials (GRMs), carbon nanotubes (CNTs) and nanodiamonds (NDs) have outstanding properties making them attractive in an increasing number of applications [96-101]. Carbon nanotubes (CNT) as a class of nanomaterials holds great potential for various biomedical applications including extrinsically

activated hyperthermia for prostate cancer therapy [102]. Erdmann K et al reports revealed that carbon nanomaterials in combination with docetaxel (DTX) and mitomycin C (MMC) evoked additive to partly synergistic anti-tumor effects. Carbon nanofibers (CNFs) and carbon nanotubes (CNTs) possess the ability to sensitize cancer cells to a wide range of structurally diverse chemotherapeutics and thus represent an interesting option for the development of multimodal cancer therapies. Co-administration of chemotherapeutics with carbon nanomaterials could result in a reduction of the chemotherapeutic dosage and thus limit systemic side effects [103]. Fisher et al. demonstrated the capability of multi walled carbon nanotubes (MWNTs) coupled with laser irradiation to enhance treatment of Human prostate cancer [104]. Ghosh et al. reported DNA-encases multi walled carbon nanotubes (MWNTs) were used to safely eradicate prostate cancer *in vivo* following NIR irradiation of MWNTs [105].

### *Magnetic Nanoparticles*

Magnetic nanoparticles belong to the group of nanotechnology-based materials with an impact in fields of analytical chemistry, biosensing, and nanomedicine. It has been nearly fifteen years since Pankhurst and colleagues wrote their famous review on magnetic nanoparticles in biomedicine [106]. Applications of magnetic particles ranging from catalysis to drug delivery and remediation are only limited by their biocompatibility and immunogenicity, both of which can be controlled by proper layering and coating of particles [107]. Industrial applications of magnetic nanoparticles cover a broad spectrum of magnetic recording media and biomedical applications, for example, magnetic resonance contrast media and therapeutic agents in cancer treatment [108, 109].

For biomedical uses, the application of particles that present superparamagnetic behavior at room temperature is preferred [110-112]. Many other magnetic nanoparticle formulations are able to target prostate cancer cells and tumors by targeting folate receptors [113], secreted protein, acidic and rich in cysteine (SPARC) [114], urokinase plasminogen activator (uPAR) [115]; Mucin 1 [116, 117]; gastric-releasing peptide receptors (GRPR) [118].

## CONCLUSION

Management of prostate cancer is now being pursued by systemic delivery of anticancer drugs, but it has limitations like nonspecific distribution, decreased bioavailability and also coupled with some adverse side effects. In addition to some therapeutic approaches, these issues have been resolved by liposome and nanomedicine-based anticancer drug delivery to get better the therapeutic index with higher drug dose and reduced nonspecific distribution. Targeting prostate tumor by delivering nanomedicine through locoregional route is more effective, than the systemic delivery, which can minimize systemic exposure of the therapeutics significantly.

## REFERENCES

[1] https://www.who.int/en/news-room/fact-sheets/detail/cancer

[2] Pang, S., Chow, P., & Wong, T. (1979). The role of the seminal vesicles, coagulating glands and prostate on the fertility and fecundity of mice. Journal of Reproduction and Fertility, 56, 129–132.

[3] Tisell, L.-E., & Salander, H. (1975). The lobes of the human prostate. Scandinavian Journal of Urology and Nephrology, 9, 185.

[4] McNeal, J. E. (1980a). The anatomic heterogeneity of the prostate. In D. Coffey, D. Merchant, & G. Murphy (Eds.), Models of prostate cancer (pp. 149–160). New York: Liss.

[5] Timms, B. G. (1997). Anatomical perspectives of prostate development. In R. K. Naz (Ed.), Prostate: Basic and clinical aspects. New York: CRC Press.

[6] McNeal, J. E. (1981). The zonal anatomy of the prostate. Prostate, 2, 35–49.

[7] William A Ricke, Barry G Timms, Frederick S vom Saal. Prostate Structure. In: Michael Skinner. Encyclopedia of Reproduction, 2nd edition, Volume 1. P-315

[8] N.J. Mabjeesh, H. Zhong, J.W. Simons, Gene therapy of prostate cancer: current and future directions, Endocr. Relat. Cancer 9 (2) (2002) 115–139.

[9] J.W. Moul, H.Wu, L. Sun, D.G.McLeod, C. Amling, T. Donahue, L. Kusuda,W. Sexton, K. O'Reilly, J. Hernandez, A. Chung, D. Soderdahl, Early versus delayed hormonal therapy for prostate specific antigen only recurrence of prostate cancer after radical prostatectomy, J. Urol. 171 (3) (2004) 1141–1147.

[10] J.W.Moul, The evolving definition of advanced prostate cancer, Rev. Urol. 6 (Suppl. 8) (2004) S10–S17.
[11] Daniel M Moreira and Michael R Abern. Prostate Cancer: Overview, Detection, Treatment. In: Michael Skinner. Encyclopedia of Reproduction 2nd Edition. Volume 4. P-474-7.
[12] M. R. Cooperberg, J. W. Moul, and P. R. Carroll, The Changing Face of Prostate Cancer. *J. Clin. Oncol.* 23(2), 8146 - **8151** (2005).
[13] K. K. Jain, *Methods Mol. Biol.* 437, 1 (2008).
[14] G. Tiwari, R. Tiwari, B. Sriwastawa, L. Bhati, S. Pandey, P. Pandey, and S. K. Bannerjee, *Int. J. Pharm. Investig.* 2, 2 (2012).
[15] D. Paolino, P. Sinha, M. Fresta, and M. Ferrari, Encyclopedia of Medical Devices and Instrumentation, 2nd edn., Wiley & Sons, Hoboken, New Jersey, USA (2006).
[16] R. Ravichandran, *Advances in Nanoparticles* 2, 51 (2013).
[17] Rosenblum D, Joshi N, Tao W, Karp JM, Peer D. Progress and challenges towards targeted delivery of cancer therapeutics. Nat Commun. 2018 Apr 12;9(1):1410.
[18] Jha PK, Jha R, kumar GS, Gupta S and Hossain M. Localized Drug Delivery in Prostate Cancer Treatment. SM J Reprod Health Infertil. 2016;1(1):1003.
[19] Sanna V, Sechi M. Nanoparticle therapeutics for prostate cancer treatment. Maturitas 2012; 73(1): 27-32.
[20] Wang AZ, Langer R, Farokhzad OC. Nanoparticle delivery of cancer drugs. Annu Rev Med 2012; 63: 185-98.
[21] Ferrari M. Cancer nanotechnology: Opportunities and challenges. Nat Rev Cancer, 2005; 5: 161-71.
[22] Kumari P, Ghosh B, Biswas S. Nanocarriers for cancer-targeted drug delivery. J Drug Target 2016; 24(3): 179-91.
[23] Bamrungsap S, Zhao Z, Chen T, *et al.* Nanotechnology in therapeutics: A focus on nanoparticles as a drug delivery system. Nanomedicine 2012; 7(8): 1253-71.
[24] Nehoff H, Parayath NN, Domanovitch L, Taurin S, Greish K. Nanomedicine for drug targeting: strategies beyond the enhanced permeability and retention effect. Int J Nanomed 2014; 9: 2539-55.
[25] Moghimi SM, Hunter AC, Murray JC. Long-circulating and target specific nanoparticles: Theory to practice. Pharmacol Rev 2001; 53(2): 283-318.
[26] M. Ferrari, *Nat. Rev. Cancer* 5, 161 (2005).
[27] H. S. Nalwa (ed.), Encyclopedia of Nanoscience and Nanotechnology, American Scientific Publishers, Los Angeles, CA (2004), p. 1.
[28] H. S. Nalwa (ed.), *J. Biomed. Nanotechnol.* 10, 2421 (2014).
[29] H. S. Nalwa (ed.), *J. Biomed. Nanotechnol.* 10, 1635 (2014).
[30] P. Kumari, B. Ghosh, and S. Biswas, *J. Drug Target.* 24, 179 (2016).
[31] Yadav D, Sandeep K, Pandey D, Dutta RK (2017) Liposomes for Drug Delivery. J Biotechnol Biomater 7: 276. doi: 10.4172/2155-952X.1000276.
[32] Mehran Alavi, Naser Karimi, and Mohsen Safaei. Application of Various Types of Liposomes in Drug Delivery Systems. Adv Pharm Bull. 2017 Apr; 7(1): 3–9.
[33] Kroon J, Metselaar JM, Storm G, van der Pluijm G. Liposomal nanomedicines in the treatment of prostate cancer. Cancer Treat Rev. 2014 May;40(4):578-84.
[34] Stuart, C. H., Singh, R., Smith, T. L., D'Agostino, R., Caudell, D., Balaji, K., & Gmeiner, W. H. (2016). Prostate-specific membrane antigen-targeted liposomes specifically deliver the Zn2+ chelator TPEN inducing oxidative stress in prostate cancer cells. Nanomedicine, 11(10), 1207–1222
[35] O.C. Farokhzad, R. Langer, Impact of nanotechnology on drug delivery, ACS Nano 3 (2009) 16–20.
[36] Y. Zhong, F. Meng, C. Deng, Z. Zhong, Ligand-directed active tumor-targeting polymeric nanoparticles for cancer chemotherapy, Biomacromolecules 2014 (1955-1969) 15.
[37] N. Kamaly, Z. Xiao, P.M. Valencia, A.F. Radovic-Moreno, O.C. Farokhzad, Targeted polymeric therapeutic nanoparticles: design, development and clinical translation, Chem. Soc. Rev. 41 (2012) 2971–3010.
[38] T. Krasia-Christoforou, T.K. Georgiou, Polymeric theranostics: using polymer-based systems for simultaneous imaging and therapy, J. Mater. Chem. B 1 (2013) 3002–3025.
[39] Chan JM, Valencia PM, Zhang L, Langer R, Farokhzad OC. Polymeric nanoparticles for drug delivery. Methods Mol Biol. 2010;624:163-75.
[40] Plapied L, Duhem N, des Rieux A, Preat V. Fate of polymeric nanocarriers for oral

drug delivery. Curr Opin Colloid Interface Sci 2011;16:228-37.

[41] Yifei Zhang,1 Yixian Huang,1 and Song Li1,2. Polymeric Micelles: Nanocarriers for Cancer-Targeted Drug Delivery. AAPS PharmSciTech, Vol. 15, No. 4, August 2014.

[42] Nie S, Xing Y, Kim GJ, Simons JW. Nanotechnology applications in cancer. Annu Rev Biomed Eng. 2007;9:257–88.

[43] Gao Z, Lukyanov AN, Singhal A, Torchilin VP. Diacyllipidpolymer micelles as nanocarriers for poorly soluble anticancer drugs. Nano Lett. 2002;2(9):979–82.

[44] Davis ME, Chen Z, Shin DM. Nanoparticle therapeutics: an emerging treatment modality for cancer. Nat Rev Drug Discov. 2008;7(9):771–82.

[45] Benahmed A, Ranger M, Leroux JC. Novel polymeric micelles based on the amphiphilic diblock copolymer poly(N-vinyl-2- pyrrolidone)-block-poly(D, L-lactide). Pharm Res. 2001;18(3):323–8.

[46] Chung JE, Yokoyama M, Aoyagi T, Sakurai Y, Okano T. Effect of molecular architecture of hydrophobically modified poly(Nisopropylacrylamide) on the formation of thermoresponsive core-shell micellar drug carriers. J Control Release. 1998;53(1– 3):119–30

[47] Jin J, Sui B, Gou J, Liu J, Tang X, Xu H, et al. (2014) PSMA Ligand Conjugated PCL-PEG Polymeric Micelles Targeted to Prostate Cancer Cells. PLoS ONE 9(11): e112200.

[48] Gao, Y., Li, Y., Li, Y., Yuan, L., Zhou, Y., Li, J., … Liu, Y. (2015). PSMA-mediated endosome escape-accelerating polymeric micelles for targeted therapy of prostate cancer and the real time tracing of their intracellular trafficking. Nanoscale, 7(2), 597–612.

[49] Lu J, Huang Y, Zhao W, Marquez RT, Meng X, Li J, et al. PEGderivatized embelin as a nanomicellar carrier for delivery of paclitaxel to breast and prostate cancers. Biomaterials. 2013;34(5):1591–600.

[50] Cheng J, Teply BA, Sherifi I, et al. Formulation of functionalized PLGA-PEG nanoparticles for in vivo targeted drug delivery. Biomaterials. 2007;28(5):869–876.

[51] Guo J, Wu SH, Ren WG, Wang XL, Yang AQ (2015) Anticancer activity of bicalutamide-loaded PLGA nanoparticles in prostate cancers. Exp Ther Med 10: 2305-2310.

[52] Gryparis EC, Hatziapostolou M, Papadimitriou E, Avgoustakis K (2007) Anticancer activity of cisplatin-loaded PLGA-mPEG nanoparticles on LNCaP prostate cancer cells. Eur J Pharm Biopharm 67: 1-8.

[53] Buhleier , E. , Wehner , W.and Vögtle , F.( 1978 ) “ Cascade”- and “Nonskid-Chain-like” Syntheses of Molecular Cavity Topologies . Synthesis , 1978 , 155 , 158 .

[54] Tomalia , D.A. , Baker , H. , Dewald , J. , Hall , M. , Kallos , G. , et al . ( 1985 ) A new class of polymers: starburstdendritic macromolecules . Polym J , 17 , 117 – 32.

[55] Srinivasa-Gopalan S, Yarema KJ. Nanotechnologies for the Life Sciences: Dendrimers in Cancer Treatment and Diagnosis, Volume 7. New York: Wiley; 2007.

[56] Klajnert B, Bryszewska M. Dendrimers: properties and applications. Acta Biochim Pol. 2001;9:199–208.

[57] Tomalia DA, Frechet JMJ. Discovery of dendrimers and dendritic polymers: a brief historical perspective. J Polym Sci A Polym Chem. 2002;9:2719–2728.

[58] Tomalia DA. The dendritic state. Mater Today. 2005;9:34–36.

[59] Hawker, C. J.; Fre´chet, J. M. J. J. Am. Chem. Soc. 1990, 112, 7638-7647.

[60] Hawker, C. J.; Fre´chet, J. M. J. J. Chem. Soc., Chem. Commun. 1990, 1010-1013

[61] Bosman AW, Meijer EW. About dendrimers: structure, physical properties, and applications. Chem Rev. 1999;9:1665–1688.

[62] Gilles ER, Frechet JMJ. Dendrimers and dendritic polymers in drug delivery. Drug Discov Today. 2005;9:35–43.

[63] Tomalia DA, Baker H, Dewald JR, Hall M, Kallos G, Martin S, Roeck J, Ryder J, Smith P. Dendrimers II: architecture, nanostructure and supramolecular chemistry. Macromolecules. 1986;9:2466.

[64] Kim Y, Zimmerman SC. Applications of dendrimers in bio-organic chemistry. Curr Opin Chem Biol. 1998;9:733–742.

[65] Smith DK, Diederich F. Functional dendrimers: unique biological mimics. Chem Eur J. 1998;9:1353–1361.

[66] Stiriba S-E, Frey H, Haag R. Dendritic polymers in biomedical applications: from potential to clinical use in diagnostics and therapy. Angew Chem Int Ed. 2002;9:1329–1334.

[67] Wolinsky JB, Grinstaff MW. Therapeutic and diagnostic applications of dendrimers

for cancer treatment. Adv Drug Deliv Rev. 2008;9:1037–1055.

[68] Lim J, Lo ST, Hill S, Pavan GM, Sun X, Simanek EE. Antitumor activity and molecular dynamics simulations of paclitaxel-laden triazine dendrimers. Mol. Pharm. 2012;9(3):404–412.

[69] Lo ST, Stern S, Clogston JD, Zheng J, Adiseshaiah PP, Dobrovolskaia M, Lim J, Patri AK, Sun X, Simanek EE. Biological assessment of triazine dendrimer: toxicological profiles, solution behavior, biodistribution, drug release and efficacy in a PEGylated, paclitaxel construct. Mol. Phar.m. 2010;7(4):993–1006.

[70] Lee IH, An S, Yu MK, Kwon HK, Im SH, Jon S. Targeted chemoimmunotherapy using drug-loaded aptamer-dendrimer bioconjugates. J. Controlled Release. 2011;155(3):435–441.

[71] Wu X, Ding B, Gao J, Wang H, Fan W, Wang X, Zhang W, Wang X, Ye L, Zhang M, Ding X, Liu J, Zhu Q, Gao S. Second-generation aptamer-conjugated PSMA-targeted delivery system for prostate cancer therapy. Int. J. Nanomed. 2011;6:1747–1756.

[72] Mukhopadhyay A, Bueso-Ramos C, Chatterjee D, Pantazis P, Aggarwal BB. Curcumin downregulates cell survival mechanisms in human prostate cancer cell lines. Oncogene. 2001;20(52):7597–7609.

[73] Dorai T, Cao YC, Dorai B, Buttyan R, Katz AE. Therapeutic potential of curcumin in human prostate cancer. III. Curcumin inhibits proliferation, induces apoptosis, and inhibits angiogenesis of LNCaP prostate cancer cells in vivo. Prostate. 2001;47(4):293–303.

[74] Dorai T, Gehani N, Katz A. Therapeutic potential of curcumin in human prostate cancer-I. curcumin induces apoptosis in both androgen-dependent and androgen-independent prostate cancer cells. Prostate Cancer Prostatic. Dis. 2000;3(2):84–93.

[75] Dorai T, Gehani N, Katz A. Therapeutic potential of curcumin in human prostate cancer. II. Curcumin inhibits tyrosine kinase activity of epidermal growth factor receptor and depletes the protein. Mol. Urol. 2000;4(1):1–6.

[76] Davis JN, Muqim N, Bhuiyan M, Kucuk O, Pienta KJ, Sarkar FH. Inhibition of prostate specific antigen expression by genistein in prostate cancer cells. Int. J. Oncol. 2000;16(6):1091–1097.

[77] Bonci D, Coppola V, Musumeci M, Addario A, Giuffrida R, Memeo L, D'Urso L, Pagliuca A, Biffoni M, Labbaye C, Bartucci M, Muto G, Peschle C, De Maria R. The miR-15a-miR-16-1 cluster controls prostate cancer by targeting multiple oncogenic activities. Nat. Med. 2008;14(11):1271–1277.

[78] Brody, E. N.; Gold, L. Aptamers as therapeutic and diagnostic agents. J. Biotechnol. 2000, 74 (1), 5–13.

[79] Brody, E. N.; Willis, M. C.; Smith, J. D.; Jayasena, S.; Zichi, D.; Gold, L. The use of aptamers in large arrays for molecular diagnostics. Mol. Diagn. 1999, 4 (4), 381–388.

[80] Ellington, A. D.; Szostak, J. W. In vitro selection of RNA molecules that bind specific ligands. Nature 1990, 346 (6287), 818– 822.

[81] Ellington, A. D.; Szostak, J. W. Selection in vitro of singlestranded DNA molecules that fold into specific ligand-binding structures. Nature 1992, 355 (6363), 850–852.

[82] Gander, T. R.; Brody, E. N.; Mehler, R. E.; Heilig, J. S.; Singer, B. S.; Gold, L. Driving forces in cancer diagnostics. Med. Lab. Obs. 2003, 35 (1), 10–16.

[83] Gold, L.; Singer, B.; He, Y. Y.; Brody, E. SELEX and the evolution of genomes. Curr. Opin. Genet. Dev. 1997, 7 (6), 848–851.

[84] Irvine, D.; Tuerk, C.; Gold, L. SELEXION. Systematic evolution of ligands by exponential enrichment with integrated optimization by non-linear analysis. J. Mol. Biol. 1991, 222 (3), 739–761.

[85] Tuerk, C.; Gold, L. Systematic evolution of ligands by exponential enrichment: RNA ligands to bacteriophage T4 DNA polymerase. Science 1990, 249 (4968), 505–510.

[86] Papagiannaros A, Dimas K, Papaioannou GT, Demetzos C (2005) Doxorubicin-PAMAM dendrimer complex attached to liposomes: Cytotoxic studies against human cancer cell lines. Int J Pharm 302: 29-38.

[87] Paciotti GF, Myer L, Weinreich D, Goia D, Pavel N, McLaughlin RE, et al. Colloidal gold: a novel nanoparticle vector for tumor directed drug delivery. Drug Deliv 2004;11(3):169-83.

[88] Huang YF, Chang HT, Tan W. Cancer cell targeting using multiple aptamers conjugated on nanorods. Anal Chem 2008;80(3):567-72.

[89] Huang YF, Sefah K, Bamrungsap S, Chang HT, Tan W. Selective photothermal therapy for mixed cancer cells using aptamer-conjugated nanorods. Langmuir 2008;24(20):11860-5.
[90] Potyrailo RA, Conrad RC, Ellington AD, Hieftje GM. Adapting selected nucleic acid ligands (aptamers) to biosensors. Anal Chem 2008;70(16):3419-25.
[91] Chandran, P. R., & Thomas, R. T. (2015). Gold Nanoparticles in Cancer Drug Delivery. Nanotechnology Applications for Tissue Engineering, 221–237.
[92] Gibson JD, Khanal BP, Zubarev ER. Paclitaxel-functionalized gold nanoparticles. J Am Chem Soc 2007;129(37):11653-61.
[93] Stern, J. M., Stanfield, J., Lotan, Y., Park, S., Hsieh, J.-T., & Cadeddu, J. A. (2007). Efficacy of Laser-Activated Gold Nanoshells in Ablating Prostate Cancer Cells in Vitro. Journal of Endourology, 21(8), 939–943.
[94] Zhang, X., Xing, J., Chen, J., Ko, L., Amanie, J.O., Gulavita, S.P., Pervez, N., Yee, D., Moore, R.M., & Roa, W. (2008). Enhanced radiation sensitivity in prostate cancer by gold-nanoparticles. *Clinical and investigative medicine. Medecine clinique et experimentale, 31 3*, E160-7.
[95] Cha C, Shin SR, Annabi N, Dokmeci MR, Khademhosseini A. Carbon-based nanomaterials: multifunctional materials for biomedical engineering. ACS Nano. 2013 Apr 23;7(4):2891-7.
[96] M.S. Mauter, M. Elimelech, Environmental applications of carbon-based nanomaterials, Environ. Sci. Technol. 42 (16) (2008) 5843-5859.
[97] Q. Wang, B. Arash, A review on applications of carbon nanotubes and graphenes as nano-resonator sensors, Comput. Mater. Sci. 82 (2014) 350-360.
[98] B. Zhang, Y. Wang, G. Zhai, Biomedical applications of the graphene-based materials, Mater. Sci. Eng. C 61 (2016) 953e964.
[99] C. Zhu, D. Du, Y. Lin, Graphene-like 2D nanomaterial-based biointerfaces for biosensing applications, Biosens. Bioelectron. 89 (2017) 43-55.
[100] M. Zhou, Z. Wang, X. Wang, Carbon Nanotubes for Sensing Applications, Elsevier Inc., 2017.
[101] D. Gon Lim, R. Ena Prim, K. Hyun Kim, E. Kang, K. Park, S. Hoon Jeong, Combinatorial nanodiamond in pharmaceutical and biomedical applications, Int. J. Pharm. 514 (2016) 41-51.
[102] Wang W, Chen G, Chen Y (2013) Nanotechnology as a Platform for Thermal Therapy of Prostate Cancer. J Mol Biomark Diagn 4:e117. doi:10.4172/2155-9929.1000e117
[103] Erdmann K, Ringel J, Hampel S, Wirth MP, Fuessel S. Carbon nanomaterials sensitize prostate cancer cells to docetaxel and mitomycin C via induction of apoptosis and inhibition of proliferation. Beilstein J Nanotechnol. 2017 Jun 23;8:1307-1317.
[104] Fisher JW, Sarkar S, Buchanan CF, Szot CS, Whitney J, et al. (2010) Photothermal Response of Human and Murine Cancer Cells to Multiwalled Carbon Nanotubes after Laser Irradiation. Cancer Res 70: 9855-9864.
[105] Ghosh S, Dutta S, Gomes E, Carroll D, Agostino RD, et al. (2009) Increased Heating Efficiency and Selective Thermal Ablation of Malignant Tissue with DNA-Encased Multiwalled Carbon Nanotubes. ACS Nano 3: 2667-2673,.
[106] Pankhurst, Q.A.; Connolly, J.; Jones, S.K.; Dobson, J. Applications of magnetic nanoparticles in biomedicine. J. Phys. D Appl. Phys. 2003, 36, 167–181.
[107] Saha, S.; Loo, S.C.J. Application-driven multi-layered particles—The role of polymers in the architectural design of particles. Polymer 2015, 71, A1–A11.
[108] Philipse AP, van Bruggen MP, Pathmamanoharan C. The preparation of magnetite nanoparicles for biomedical. Langmuir. 1994;10:92.
[109] Garcell L, Morales MP, Andres-Verges M, Tartaj P, Serna CJ. a significant enhancement in the *colloidal* properties, such. J Colloid Interface Sci. 1998;205:470.
[110] Cabuil V. Dekker Encyclopedia of Nanoscience and Nanotechnology, Chapter 119 Magnetic Nanoparticles:Preparation and Properties. Roldan group puplications. 2004.
[111] Morcos SK. Nephrogenic systemic fibrosis following the administration of extracellular gadolinium based contrast agents: is the stability of the contrast agent molecule an important factor in the pathogenesis of this condition? Br J Radiol. 2007;80(950):73–76.
[112] Ersoy H, Rybicki FJ. Biochemical safety profiles of gadolinium-based extracellular contrast agents and nephrogenic systemic

fibrosis. J Magn Reson Imaging. 2007;26(5):1190–1197.
[113] An Q, et al. Peroxidase-like activity of Fe3O4@carbon nanoparticles enhances ascorbic acidinduced oxidative stress and selective damage to PC-3 prostate cancer cells. ACS Appl Mater Interfaces. 2013; 5(24):13248–13257.
[114] Ghosh D, et al. M13-templated magnetic nanoparticles for targeted in vivo imaging of prostate cancer. Nat Nanotechnol. 2012; 7(10):677–682.
[115] Abdalla MO, et al. Enhanced noscapine delivery using uPAR-targeted optical-MR imaging trackable nanoparticles for prostate cancer therapy. J Control Release. 2011; 149(3):314–322.
[116] Shahbazi-Gahrouei D, Abdolahi M. Detection of MUC1-expressing ovarian cancer by C595 monoclonal antibody-conjugated SPIONs using MR imaging. ScientificWorldJournal. 2013; 2013:609151.
[117] Guo F, et al. Enhancement of Thermal Damage to Adenocarcinoma Cells by Iron Nanoparticles Modified with MUC1 Aptamer. J Nanosci Nanotechnol. 2016; 16(3):2246–2253.
[118] Lee CM, et al. Prostate cancer-targeted imaging using magnetofluorescent polymeric nanoparticles functionalized with bombesin. Pharm Res. 2010; 27(4):712–721.