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Review Article

An Updated Review on Nanoparticles Targeting Prostate Cancer

Komarala Narendra Babu[1], Vattimilli Shanmuka Sai Sumanth[2], Munnangi Sukanya[3], Ashok Thulluru[4]*

[1]*Department of Ph. Quality Assurance, Shri Vishnu College of Pharmacy (Autonomous), Bhimavaram, Andhra Pradesh, India.*
[2]*Department of Pharmaceutics, Shri Vishnu College of Pharmacy (Autonomous), Bhimavaram, Andhra Pradesh, India.*
[3]*Department of Pharmaceutics, KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada, Andhra Pradesh, India.*
[4]*Department of Pharmaceutics, Chhatrapati Shivaji Institute of Pharmacy, Durg, Chhattisgarh, India.*

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Abstract *- Prostate cancer (PC) is the leading cause of death by cancer in men. Because of the drastic decline in the survival rate of PC patients with advanced/metastatic disease, early diagnosis of the disease and therapy without toxic side effects is crucial. Chemotherapy is widely used to control the progression of PC at the later stages; however, it is associated with off-target toxicities and severe adverse effects due to the lack of specificity. Delivery of therapeutic or diagnostic agents by using targeted nanoparticles is a promising strategy to enhance the accuracy and sensitivity of PC diagnosis and increase the efficacy and specificity of therapeutic agents. In past decades, numerous efforts have been made to create nanoparticles with different architectural bases for specific delivery payloads to prostate tumors. Major PC-associated cell membrane protein markers identified as targets for such purposes include folate receptors, sigma receptors, transferrin receptors, gastrin-releasing peptide receptors, urokinase plasminogen activator receptors, and prostate-specific membrane antigens. Among these markers, prostate-specific membrane antigen has emerged as an extremely specific and sensitive targetable marker for designing targeted nanoparticle-based delivery systems for PC. This article reviews contemporary advances in the design, specificity, and efficacy of nanoparticles functionalized against PC. Whenever feasible, both diagnostic as well as therapeutic applications are discussed.*

Keywords *- Gastrin-releasing peptide receptors, Nanoparticles, Prostate cancer, Prostate-specific membrane antigens, Urokinase plasminogen activator receptor.*

1. Introduction

In emerging and underdeveloped nations, PC is among the leading causes of illness and mortality.[1] Non-skin cancer is the most common cancer in men, accounting for the second-highest death number compared to the other malignancies.[2] Depending on the severity of the malignancy, it could be localized or progressed.[3] PC can spread to the bones through the lymphatic system.[4] Radiations, chemical risks, environmental pollutants, genetics and age all appear to play a role in prostate cancer pathogenesis, although the specific mechanism remains unknown.[5] Androgens have a role in prostate development and its activities, although they can even now contribute to carcinogenesis at this time.[6] Similarly, hyperinsulinemia associated with obesity and insulin resistance has been shown to increase the risk of prostate cancer.[7] Various treatment procedures are used to lower the prostate cancer risk mentioned above, and no therapy is necessary for cancer of the benign stage.[8]Surgery can also be used to remove the lymph nodes, prostate glands and related issues when it comes to metastatic invasion.[9] Prostate cancer is also commonly treated with radiation therapy. [10]Radiation therapy for prostate cancer can be delivered in 2 ways: brachytherapy (internal radiation) and external radiation.[11]Tiny radioactive seeds are implanted within the body to provide a highly minimal optimized dosage of radiation for a relatively long time by an ultrasound-guided needle under the supervision of a physician. [12, 13]Postmenopausal hormone therapy [14] is among the most effective treatments for prostate cancer. Hormone treatment is used to reduce testosterone production. [15]The sluggish growth of cancer cells is linked to a reduction in testosterone levels. [16]To prevent testicles from generating testosterone, lutropin-releasing agonists (triptorelin, goserelin, leuprolide) are preferred. [17] In order to prevent testosterone from approaching malignant cells, anti-androgenic drugs (flutamide, bicalutamide) are required. [18]Orchiectomy could be used to remove testicles and lower testosterone levels in difficult situations. [19] Prostate tissue freezing is also used to kill cancer cells. [20] Chemotherapy using chemotherapeutic drugs such as paclitaxel and docetaxel to destroy killer and extremely invasive cancer cells can be recommended if menopausal hormone therapy does not work. [21] Unfortunately, bone mass loss, obesity, libido and erectile dysfunction are all envisioned in these therapeutic

approaches. [22] Staging, biopsy, prostate-specific antigen (PSA) testing, magnetic resonance imaging (MRI) and physical examination are some of the prostate cancer diagnosis tools that have been established. [23] The massive occurrence of gaps associated with prostate cancer's heterogeneous Nature, non-specificity, over-treatment, over-diagnosis and over-testing make prostate cancer diagnosis difficult.[24]

2. Etiology of Viral Prostate Cancer

2.1. Human Papilloma Virus (HPV)

The established etiologic factor for cancers of the anus, penis, vagina, vulva, uterus and cervix is HPV infection.[25] For its given anatomic closeness to urinary and anogenital sites, the prostate has been broadly investigated for infection of HPV. Literature studies reported, mainly in populations of the West, have varied noticeably in terms of study design and methodology. Consequently, conclusions are not homogenous, with only a few studies showing statistically essential differences in infection of HPV between patients of prostate cancer and controls. [26] Recently, studies from populations of Asian and Mediterranean suggested a link between prostate cancer and HPV, particularly high-risk sub-types 16 and 18. [27–30] Association strength alters with geography distribution [31–34]. Moreover, studies have found important positive PCa associations with sexually transmitted diseases and sexual activities, [35–37] including HPV, suggesting further that an infectious etiology may be involved in prostate carcinogenesis. HPV warrants an accurate inquiry, especially to reconcile the diversity in the results reported inside the same populations. [38–41]

2.2. Herpes Viruses

Herpes viruses are perhaps transmitted through nonsexual and sexual routes and are more common in a few populations.[42] Herpes viruses, like HHV-8 and EBV, are associated with human malignancies.[43] Infections like EBV, HHV-8, HSV-2, HSV-1, and CMV are investigated in prostate cancer.[26] A new study in Tobagomen, one of the places where mortality rates and incidence are higher due to PCa, found that HHV-8 create a latent prostate infection related to macrophage inflammation and infiltration.[44] However, a meta-analysis to explore the association between infections caused by several sexually transmitted pathogens, including CMV, HHV-8, HSV-2 and HSV-1, disclosed no significant association with increased PCa risk.[45]

2.3. Burger King Virus (BKV)

Polyomavirus BKV is commonly acquired in childhood, and the latency period is long, with the urinary tract as the primary site of latency and possibly oncogenic potential as in animal models demonstration. On paper, it is an alluring aspirant for prostate cancer viral etiology and has been identified in prostate cancer.[26] In a new study from Iran, some of the highest rates of BKV infection were announced, with 28% in prostate cancer, primarily in low Gleason scores patients, and 15% in benign prostatic hyperplasia samples.[46] Further research is required to determine how BK can exert oncogenic activity over the clinical course of the disease, especially in the initial stages of the development of prostate cancer.[47]

2.4. Xenotropic Murine Leukaemia Virus-Related Virus (XMRV)

Since its discovery in 2006, the role of the gamma retrovirus XMRV in prostate cancer has been highly argued. XMRV has been identified in prostate cancer, but high false positive rates in most published studies due to contamination of samples and laboratory reagents have brought its role as a human pathogen in prostate carcinogenesis into question. [26, 48] New studies have not found any conclusive biologic evidence of XMRV infection in prostate cancer in different populations. [49-53] Work in human cell lines has also exhibited that XMRV is not a human pathogen,[54] though it infects PCa cell lines preferentially.[55] We need to conduct further studies to know whether XMRV is clinically associated with prostate cancer onset or progression.

3. Conventional Approaches for the Treatment of Prostate Cancer

3.1. Chemotherapy

Despite the fact that surgery and radiotherapy give excellent disease control in the initial phases of prostate cancer, the clinically localized high-risk disease is linked to a high risk of recurrence following initial local therapy.[56] A number of studies have looked into the benefits of neoadjuvant and adjuvant chemotherapy for patients with early-stage cancer. In subjects with elevated localized prostate cancer (RTOG-9902), phase III research compared ADT plus radiotherapy to ADT plus radiotherapy with adjuvant combined chemotherapy(warfarin, paclitaxel, etoposide and estramustine) and found no clinical advantage for adjuvant chemotherapy.[57] Due to the highly toxic Nature of combination chemotherapy, particularly the estramustine component, the trial was prematurely terminated. In subjects with elevated localized prostate cancer, the SWOG S9921 phase III research found no difference in survival between ADT with prednisone plus mitoxantrone and ADT alone.[58] Other research of adjuvant docetaxel in elevated-risk PCa patients showed no statistically important development in PFS for the overall patient group, although the findings revealed a possible advantage for individuals with greater-risk pathology and American-African heritage.[59] Docetaxel has been shown to be highly tolerated when combination with radical prostatectomy,[60, 61] complete androgen blockade,[62] plus radiotherapy [63] in former phase II research. These findings imply that early treatment in patients with clinically confined, elevated-risk PCa may have therapeutic benefits; however, more research and extended follow-up must demonstrate an OS advantage. Improving outcomes among

subjects with elevated localized PCa remains a major therapeutic aim, and combining chemotherapies and other novel treatments with existing, well-established early-stage regimens (such as radiotherapy and ADT) is a promising approach.

3.2. Neoadjuvant Therapy

ADT is among the first cancer-specific targeted treatments (Figure 1). Two decades of trials have shown that neoadjuvant ADT, either alone or in combination with chemotherapy, may cause detectable variations in disease burden at the surgery time. A higher rate of organ-confined disease, a lower rate of extracapsular expansion, and a lower rate of positive surgical margins was among the end goals. However, these varied between trials. Decreased lymph node activity, PSA responses and testosterone levels were among the systemic endpoints influenced. Unfortunately, these studies increased local control rates could not convert into enhanced OS; granted, the bulk of these investigations was insufficient to identify statistically essential changes in biochemical relapse-free survival.

3.3. Radical Prostatectomy

The pelvic nodes, seminal vesicles (SVs) and prostate gland must be completely removed during RP. The operation's objectives are to entirely remove cancer, maintain urine continence, and bring back erectile function (EF) to the maximum extent possible, in that order. Patients in good general health with an 8-year life expectancy who have cancer that can be safely resected with a realistic likelihood of advantage through good local control or long-term cure are candidates for RP. As a result, RP can be used at any stage of clinically localized PCa (till Stage cT3aN0M0). An open radical perineal or radical retropubic approach, as well as an extraperitoneal or transperitoneal laparoscopic radical approach (LRP), whether robotic-assisted (RALP) or freehand, can be used to perform the procedure. The perineal cut is linked to fewer analgesics and quick recovery [64]. However, retropubic RP has several advantages: urologists are more familiar with the anatomy, pelvic lymphadenectomy for staging reasons is simple to perform, very few rectal injuries occur, and the vast exposure allows for great flexibility in tailoring the surgery towards each person's anatomy. It allows for more consistent neurovascular bundle preservation and a reduced positivity of surgical margins rate. The potential benefits and drawbacks of radical prostatectomy are mentioned in (Table 1).

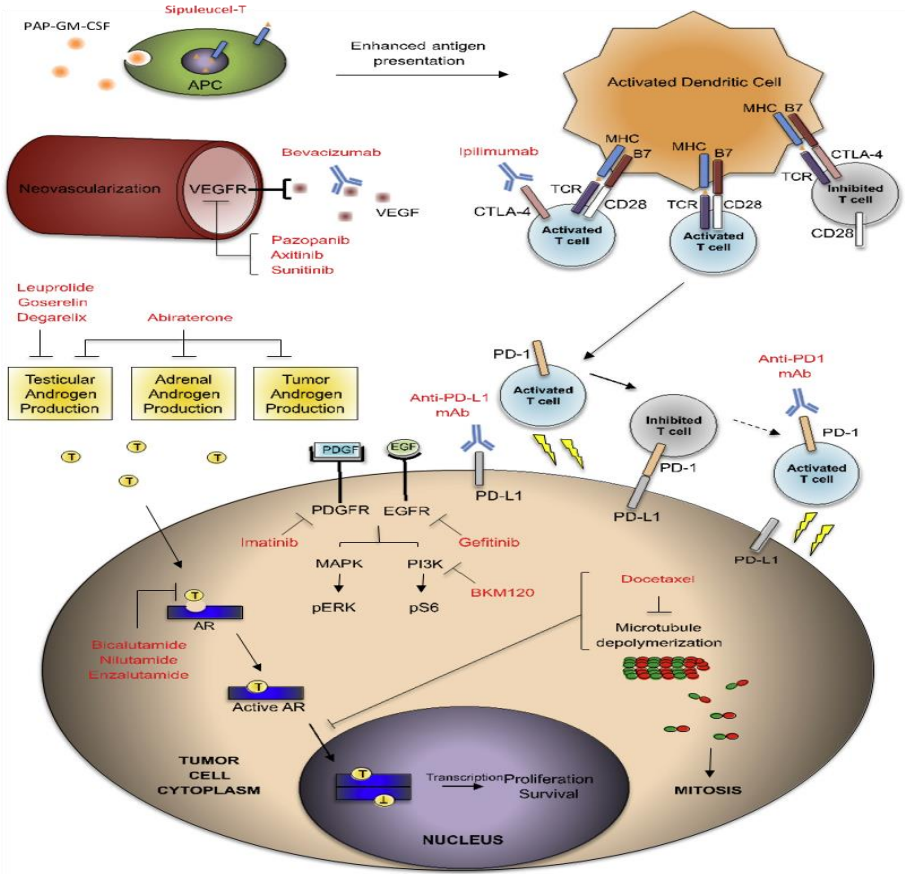

Fig. 1 Summary of action mechanisms for the treatment of prostate cancer

Table 1. Benefits and drawbacks of radical prostatectomy

Benefits	Drawbacks
Long-term control of cancer is excellent.	Excessive therapy for many malignancies that are currently detected but are low-risk.
Using modern surgical procedures, perioperative morbidity is usually transitory and minimal.	It is a technically difficult technique.
Accurate prognosis prediction based on pathologic cancer characteristics.	Death and perioperative complications are a possibility. Morbidity is delayed because of the visible incision (inguinal hernia) and time away from routine activities due to hospitalization.
Recurrences are easy to spot (using PSA testing) and locally treated (with radiotherapy).	Hospitalization, time away from usual activities, inguinal hernia (delayed morbidity), Visible incision.
Dissection of lymph nodes in the pelvis through the same incision.	There is a chance you will have an incomplete excision with positive surgical margins.
Impotence and incontinence are two major issues that can be treated.	Quality-of-life effects, retraction of penile, dry ejaculation, dysfunction of erectile and incontinence (long-term) are all possible side effects.

4. Nanoparticles Used in the Prostate Cancer Treatment

4.1. Liposomes

Thangapazhem et al. created new nanoparticles for delivering curcumin to PCa by putting these molecules within liposomes covered with prostate-specific membrane antigen (PSMA) specific antibodies. Curcumin liposome treatment of human prostate cancer cell lines resulted in substantial suppression of cell proliferation without affecting cell survival, as illustrated in (Figure 2).[65, 66]

4.2. Quantum dots (QDs)

Due to the electron energy band's quantum-restricting effect, QDs are nanoscale semiconducting structures with stronger fluorescence emission levels than typical organic fluorophores. [68, 69] QDs feature a porous structure with a large surface area, a lower electrochemical activity

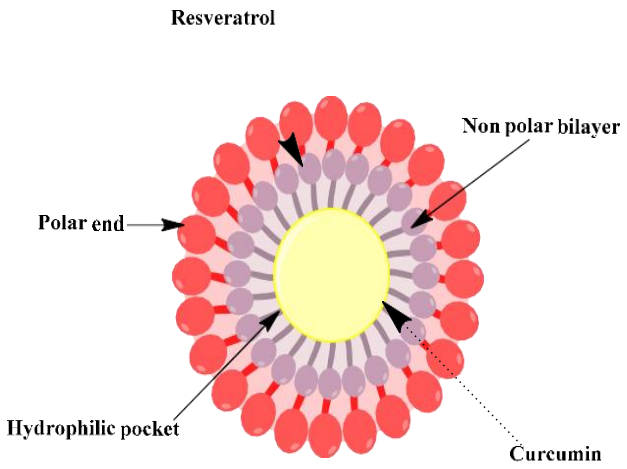

Fig. 2 Resveratrol and curcumin are co-encapsulated in liposomes for prostate cancer administration. Reproduced from [67] with permission from DeGruyter, 2017

(Greater analytical signal), a flexible structure, and a high chemical and electrical function, among other characteristics. [70, 71] QDs with these unique properties can be used to develop electrochemical biosensors. [72, 73] Ehzari et al. described an enzyme-free sandwiched immuno-sensor (Fe3O4@TMU-10 magnetic structure and cadmium-nickel quantum dots) for PSA biomarker identification. The second antibody is interlinked to a cadmium-nickel quantum dot like a non-enzymatic electro-active probe. The developed immuno-sensor demonstrated a constant range of 1 pg/mL to 100,000 pg/mL and a detection limit of 0.45 pg/mL, with adequate reliability, specificity and repeatability (Figure 3).[74]

4.3. Carbon Nanotubes (CNTs)

CNTs are hollow, cylindrical molecules with one or numerous walls and just a diameter of a nanometer.[75] They are made of carbons connected to the hexagonal structure and have a nanometer diameter. CNTs have been employed in human tissue and serum samples for electrochemical identification of PSA (prostate-specific antigen) biomarkers and have proven to be a new style of superconductor nanoparticles. [76, 77] Prostate cancer antigen 3 (PCA3) was discovered to be a considerably more accurate biomarker for PCa. Soares et al. developed the first impedance and electrochemically-established nanosensors capable of detecting PCA3 at low concentration levels like 0.128 nmol/L. Nanosensors were created using a PCA3-complementary ssDNA (single-stranded DNA) probe that was LbL (layer-by-layer) immobilized on carbon nanotubes (MWCNT) and chitosan (CHT) film (Figure 4).[78]

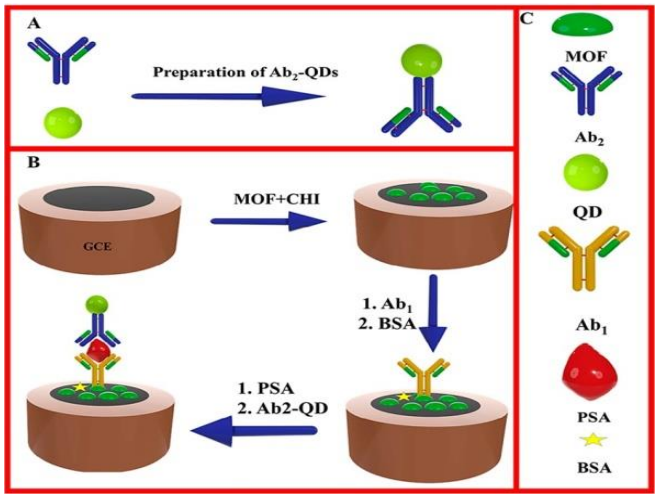

Fig. 3 PSA detection using an immunosensor which is enzyme-free, based on cadmium-nickel quantum dots and magnetic system of Fe3O4@ TMU-10 MOF. Reproduced from [74] with permission from Elsevier, 2020

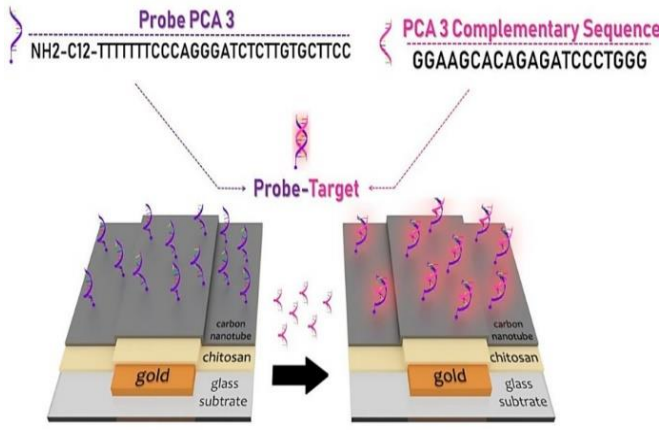

Fig. 4 For the detection of PCA3 (PC antigen 3), a biosensor manufacturing nano-platform strategy based on carbon nanotubes (MWCNT) has been developed. Reproduced from [78] with permission from the American Chemical Society, 2019.

4.4. Nanoemulsion

Different groups have developed a new technique for co-encapsulating herceptin and paclitaxel to produce a therapy for advanced prostate cancer. [79–81] Herceptin targets these cells because of the over-expression of HER2 receptors in some prostate cancer cells, herceptin targets these cells. Oil droplets in a nanoemulsion containing herceptin molecules linked to the surface can target HER2 cells, which are over-expressing, according to a study.[82] Formulation containing paclitaxel palmitate (active) and trastuzumab was tested on transgenic mice (comprising induced PCa) and prostate cancer cells.[83] During the research, no allergic reactions were detected, and the findings were superior to other published pharmacological therapies in reducing PCa cell growth.[84]

4.5. Polymeric nanoparticles with block copolymers

Sanna et al. designed and tested biodegradable, docetaxel-loaded block copolymers (PLA-PCL (poly (lactide-co-caprolactone)) and PLGAPCL (poly (lactide-co-caprolactone-co-glycolide)). The PLGA-PCL-Dtx NPs antiproliferative activity was higher in PCs cells than in the free drug in cell line research. Sawicki et al. looked into using polymeric nanoparticles for targeting cells with a diphtheria toxin gene (DT-A) produced from a promoter specific to the prostate. Injection of the DT-A gene study resulted in a significant reduction in the growth of the prostate tumour and gland, whereas direct injection had no or little effect. To target the PSMA, a carrier of drug delivery for biocompatible aptamers and polymeric nanoparticles was developed by Farokhzad and Langer. [85, 86–88] *In vivo* and *in vitro* investigations were used to examine these biocompatible polymeric NP's potential for Dtx uptake and selective administration by prostate cancer cells. As demonstrated in (Figure 5),[89] more intricate and complex Nanoparticle systems are necessary to target prostate cancer and numerous cancer disorders that incorporate diagnostic and therapeutic agents.

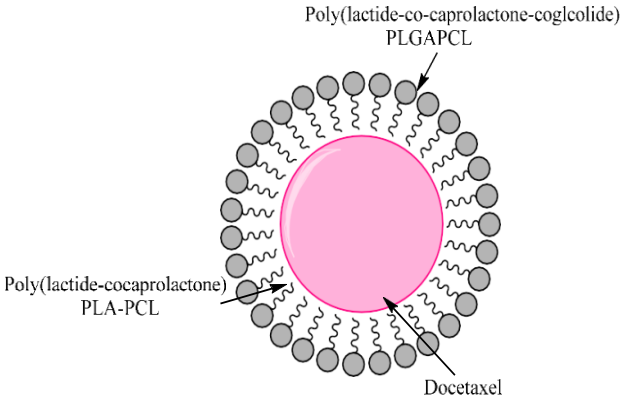

Fig. 5 Docetaxel-loaded polymeric PLA-PCL and PLGA-PCL nanoparticles which are biodegradable for PCa treatment. Reproduced from [67] with permission from DeGruyter, 2017.

4.6. Gold Nanoparticles (AuNPs)

In medical applications such as diagnostic imaging, medication delivery, phototherapy and radiation, AuNPs have been shown to be highly versatile. [90, 91] The development of gold NPs as nano-biosensors has aided surface chemistry and nano-chemistry advances. [92] The increased retention effect (EPR) and permeability of AuNPs coated using particular polymers (hydrophilic) results in good in vivo circulation and strong tumour aggregation.[93]Lue et al. coupled prostate cancer targeting antigen (PSMA-1) to AuNPs for enhanced X-ray irradiation and found that the targeting ligand boosted absorption of gold by PC3 pip cells expressing PSMA when compared with PC3 flu cells lacking PSMA receptors (Figure 6).[94]

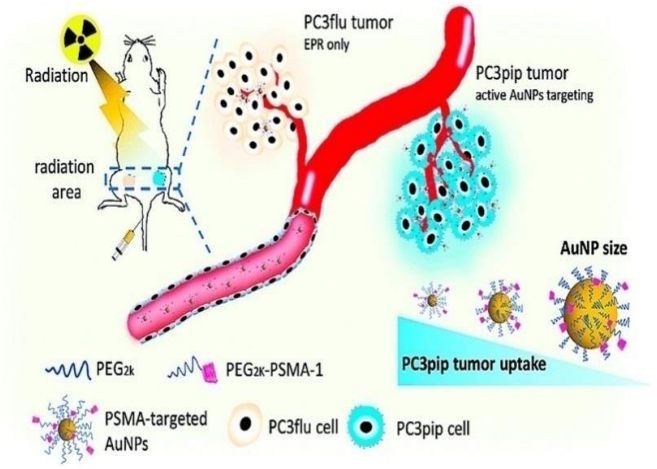

Fig. 6 PSMA-targeted gold nanoparticles of varying sizes are used in a scheme to target PC radiation. Reproduced from [94] with permission from the Royal Society of Chemistry, 2019.

4.7. Niosomes

Niosome is a cholesterol-based non-ionic bilayer surfactant system. On PCa cells, Akbarzadeh et al. employed anticancer medications and developed niosomes loaded with doxycycline as a carrier system. In vivo and in vitro studies on prostate cancer cells (PC3) revealed improved chemotherapeutic effects while normal cell lines biocompatibility increased.[95] After treating PC3 cells using niosomal formulation, the rising anticancer impact was linked to cell cycle genes.[96] These carriers can be used as an effective delivery mechanism for PCa treatment. MTT test, flow cytometry and gene expression were used to assess the anticancer activity of niosomes on PCa cell lines (PC3). [96]

4.8. Magnetic Nanoparticles (MNPs)

MNPs have been widely used due to their unique traits, such as biocompatibility, stability, physical characteristics, magnetic susceptibility and ease of processing.[97, 98] MNPs are used to identify and purify various molecular constituents, such as nucleic acids or proteins, before diagnosis.[99,100] This advancement was suggested for identifying numerous prostate cancer indicators in the bloodstream and urine.[101, 102]For detecting urine PCA3 (PCa gene-specific), Yamkamon et al. created magnetic nanoparticles Fe3O4 mixed with the streptavidin-horseradish peroxidase using a PCR technique. This approach was 1000-fold better efficiency than standard RT-PCR for detecting PCA3 at concentrations of femtogram. PCA3 expression evaluated by the developed nano-platform in PCa patients was significantly higher than in individuals having healthy controls and BPH (Figure. 7).[103]

5. Nonspecific NPs for PC Therapy

Numerous biological barriers have been discovered to obstruct the drugs response filled in nanoparticles by avoiding the nanotherapeutics accumulation at the particular tumour site, which include subsequent sequestration and opsonization by the MPS (mononuclear phagocyte system), flow in blood vessel / hemorheological limitations, cellular internalization, pressure gradients, escape from lysosomal and endosomal compartments, nonspecific distribution and pumps of drug efflux. Several target-specific Nanoparticles with numerous moieties and functions have been produced.

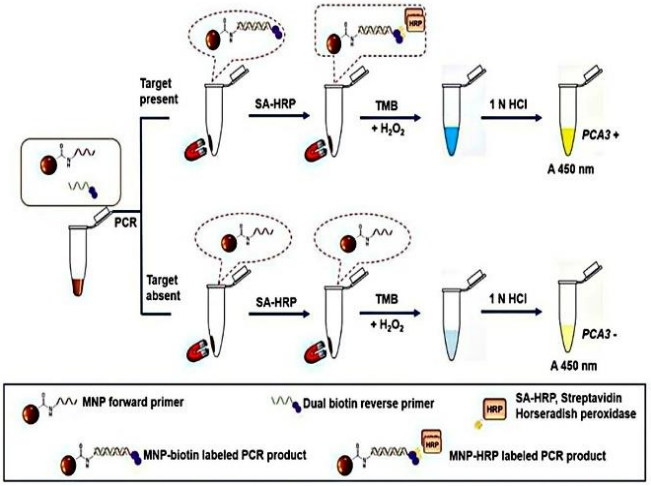

Fig. 7 The oligonucleotide combined with MNP for detection of PCA3 in sediments of urine is depicted graphically. Reproduced from [103] with permission from Leibniz Research Centre for Working Environment and Human Factors, 2020.

However, most techniques have failed to address the limitations mentioned above effectively.[104]Several ways have been used in prostate cancer treatment to counteract nanoparticle nonspecific distribution. In the PC hormone-refractory stage, for example, levels of PSMA and PSA are often quite active. Several studies have suggested that all these proteins can be used to deliver diverse functional compounds to malignant cells as therapeutic targets. It was shown that the liposome (dually modified), endowed with a PSMA-mediated liposome (multifunctional) and a PSA-response, preferentially targets PC in two ways. Surprisingly, the liposome's folate moiety, which is functionalized, is linked to positive tumours of PSMA, accompanied by PSA-responsive structures cleavage, which is common in tumour sites. Endocytosis and the polyarginine penetrating actions in liposomes allow active liposomes to be ingested by tumour cells.[105] In another investigation, the researchers also demonstrated ternary and binary compounds that successfully triggered siRNA-targeted gene silencing. The Zeta potential of the PGA-g-mPEG (polyglutamic acid-graft polyethylene glycol) layer was decreased to near neutral value of electrophoretic potential, which reduced cytotoxicity due to the excess positive charge.[106] It was established that all these complexes gave a good manner of siRNA administration to treat a variety of tumours using both in-vivo and in-vitro approaches. Simultaneously, PGA-g-mPEG coating resulted in bigger-size complexes with better

silencing efficacy than the binary complexes but without compromising the molecules' bioavailability.[106] Another study looked at the function of CD44, a multifunctional glycoprotein that has a role in intercellular communication, proliferation and cell migration. To target the CD44-positive prostate cancer cells, the researchers created nanoparticles based on hyaluronic acid that are negatively charged. This NP administered epigallocatechin-3-gallate effectively and inhibited PC development. Furthermore, it was shown that this nanoparticle binds CD44 receptors specifically and increases PC cell death in vivo.[107] Finally, a number of researches have shown how to counteract systemic-nanoparticles nonspecific distribution.

6. Target Specific NPs for PC Therapy

NPs are helpful in cancer therapy because of their many features, which include small size, a large ratio of surface-to-volume, adjustable surface chemistry and capabilities of drug encapsulation. Targeting ligand-based surface modification increases intracellular transport, and prolonged drug release is the only key advantage of utilizing NPs. [108, 109] NPs are nanoparticles with sizes below 200 nm and stimulate intracellular uptake. Encapsulation of pharmaceuticals improves the solubility of the drug while also allowing them to be delivered in a regulated manner.[110] Furthermore, the nanoparticles have low cytotoxicity and are biodegradable.[111] Using a functionalization technique, NPs can improve medication efficacy while reducing the dosage, leading to a new method for optimizing drug pharmacokinetics.[112] For various reasons, many nanoparticles are now developed for targeted medicine delivery in different diseases and malignant malignancies. For example, due to the existence of hydrogen bonding, π-π staking and hydrophobic interaction, NGO (nanographene oxide) has been popular for decades since both graphitic domains continue to be available for loading drugs.[113] Ho-Sang Jung et al. coupled NGO with HA (hyaluronic acid) biopolymer for targeted delivery to cancerous cells and epirubicin was loaded onto NGO-HA surface in another study. This led to the pH-dependent medication release and a cancer-fighting impact that was unique to the target.[114] Jhang et al. previously conjugated NGO with FA (folic acid) and employed PEG (polyethylene glycol) as a stabilizer for selective delivery to MCF-7 cells of breast cancer by targeting receptors of FA. Finally, this study showed the viability of employing graphene oxide (functionalized) as a carrier for the controlled loading, targeted distribution of several medicines, and improved therapeutic efficacy.[115] Another study exploited click chemistry towards drug administration, with NGO modified using poly (N-isopropylacrylamide) serving as a carrier for the water-insoluble aromatic camptothecin (CPT) drug, which was found to have a high potency in killing metastatic cancer skin cells (5RT3).[116] Udaya S. Toti et al. employed the IAASF (interfacial activity assisted surface functionalization) method to insert a functional group which is reactive (here it is maleimide) over the surface of the poly (D, L-lactide-co-glycolide) (PGLA) NPs before. The introduction of functional maleimide groups to connect the cRGD peptide with NPs increased NP absorption by 2 to 3-fold. This peptide targets overexpressed αvβ3 integrins in specific cancer types and tumour vasculature.[117] Changyan Liang and colleagues created biodegradable NPs against endometrial carcinoma in another work, using the truth that folate receptors are substantially over-expressed in various endometrial carcinomas.[118] Sandy and his colleagues have created LP-MSNs (mesoporous large pore nanoparticles of silica) functionalized with PLL (poly-L-lysine) as a carrier for the delivery of siRNA in osteosarcoma, which is target specific. As a result, our approach showed promise for effective gene delivery while lowering the viability of osteosarcoma cancer cells. Furthermore, up to μg/mL, low cytotoxicity and good biocompatibility were reported.[119] To summarise, targeting the tumour location with high specificity is critical. Furthermore, as previously stated, even though functionalization approaches which are target specific in nano-delivery have been developed and implemented in different types of cancers, in vitro or in vivo, there is still room to investigate different types of cancers along with prostate cancer, the possibilities of overcoming systemic nanoparticles nonspecific distribution.

7. Conclusion

The use of nanoparticles in biomedicine significantly impacted anti-neoplastic drug delivery. Active targeting strategies are either being refined or tested in the clinic. For targeting PSMA, Langer and Farokhzad and other researchers, have proposed carriers' development made from biocompatible aptamer polymers. Many other investigations resulted in the polymeric nanoparticles targeted for prostate cancer treatment involving the conversion into the clinical practice from bioconjugates. One biomarker which can be effective rarely is enough to achieve the diagnostic specificity and sensitivity needed for accurate prostate cancer risk stratification. In the next few years, experimental investigations will likely focus on the clinical evaluation and integration of various combinations of prostate cancer indicators of the next generation. As a result, the unique properties of nanomaterials can be used for increased automation, efficiency, precision and susceptibility at a lower cost. With several groundbreaking advancements in nano-diagnostic tools, cancer nanotechnology has much promise for improving prostate cancer treatment. To convert nanotechnologies into clinical use, researchers will need to test their techniques in appropriate groups of subjects adequately, define clinically appropriate limits of detection and complete clinical performance criteria evaluation in the coming years.

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