International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 07-01-2024, Accepted: 22-01-2024, Published: 06-02-2024
Volume 9, Issue 1, 2024, Page No. 38-46

Recent perspective in medication of prostate cancer

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Abstract
The Prostate cancer is a prevalent malignancy affecting the male population globally. This disease starts in the prostate gland and usually progresses slowly, although it can also occasionally be aggressive and fatal. Multiple factors, including as genetic susceptibility, hormonal effects, and environmental circumstances, play a role in its etiology. Development of tumors as a result of abnormal cell proliferation within the prostate gland is a characteristic of prostate cancer. It can be pathologically benign or aggressive, and it presents as an adenocarcinoma. The prognosis varies greatly, from aggressive varieties that cause metastasis and mortality to indolent growth that has no effect on life expectancy. There are several different forms and categories of prostate cancer, such as castration-resistant prostate cancer (CRPC), locally progressed, metastatic, and localized prostate cancer. Each of them needs a different approach to treatment.
The accuracy of the traditional diagnostic techniques for prostate cancer, such as Transrectal ultrasonography (TRUS)-guided biopsy, PSA testing, and a digital rectal examination (DRE), is limited. Multiparametric magnetic resonance imaging (mpMRI) has demonstrated encouraging outcomes in terms of identifying prostatic lesions. A variety of therapies are available for treating prostate cancer, including surgery (orchiectomy/castration), hormonal therapy, chemotherapy, immunotherapy, radiation therapy and more recent targeted therapies. The dosage types used to treat prostate cancer vary greatly and include IV infusions, implants, injections, and oral drugs. The strength of the dosage is adjusted based on the specific condition of each patient, varying from low maintenance dosages to greater concentrations for more aggressive diseases.
Recently the novel drug delivery strategies are being investigated to increase treatment effectiveness and minimize negative effects. Nanotechnology, liposomal formulations, and targeted drug administration with nanoparticles are examples of novel drug delivery techniques. Precision surgeries and treatments benefit from the use of robotics, which makes the processes more precise and less invasive.

Keywords: Prostate cancer, Prostate-specific antigen, Androgen-deprivation therapy, Androgen receptor, Dihydrotestosterone, Androgen Independence.

Introduction
The second most prevalent cause of mortality for males diagnosed with cancer in the United States is prostate cancer, behind skin cancer. [1] Over the course of the last 20 years or more, prostate cancer has evolved from a late-stage illness with localized progression & advanced stages to one that is often detected by chance or during screening. This is both an amazing and difficult development. [2]
Androgens, or male sex hormones, particularly Dihydrotestosterone (DHT) and testosterone, bind to AR and are essential for the proliferation of prostate cells. [3] Although castration limits serum androgen to <50 ng/dL or 1.7 nmol/L, CRPC is typically marked by an increase in PSA levels as the cancer advances. [4]
There are several clinical states that are used to diagnose and treat prostate cancer. The first state is localized illness, which is followed by non-castrate -W0 increasing prostate-specific antigen (PSA) state and non-castrate metastatic disease. Lastly, the majority of men die in the castration-resistant states. [5] Prostate-specific antigen (PSA) rises are the clinical marker for castration-resistant prostate cancer (CRPC). This is often understood to be three consecutive increases in blood testosterone levels after antiandrogen withdrawal for a minimum of four weeks, even in the face of subsequent hormonal changes and/or radiologic progression. [6]

1. Hormonal treatments that either block AR signaling & translocation (Bicalutamide and Flutamide) or target the enzyme CYP17A1, which is involved in the manufacture of adrenal steroids (Abiraterone acetate). [7]
2. Chemotherapy employing medications such as Cabazitaxel, Docetaxel, and Mitoxantrone which target microtubule depolymerization & cell division, resulting in cell cycle arrest. [8]
3. Immunotherapy (Sipuleucel T, Provenge ®) that activates T cells to trigger an immune response. [9]
4. Radiopharmaceuticals, such as Strontium-89 chloride, Samarium-153, Rhenium-186, And Radium- 223 chloride, are used in radiation therapy. [10]

About the Disease
The human prostate exhibits a pseudostratified epithelium having three distinct types of epithelial cells at the histological level: luminal, basal, and neuroendocrine. The luminal epithelial cells create an uninterrupted layer of polarized columnar cells which express high levels of AR, secrete proteins, and exhibit distinguishing markers such cytokeratin's 8 and 18. Underneath the luminal epithelium, basal cells show low or undetectable amounts of AR but high molecular weight cytokeratin's 5 and 14, as well as p63. Lastly, uncommon cells with an unclear function that

show endocrine markers like synaptophysin and chromogranin-A but are AR-negative are known as neuroendocrine cells. [11] Prostate epithelial stem cells' tissue distribution is crucial for determining the potential cell type or types that gave rise to the prostate. A cell or cell type found in normal, untransformed tissue is referred to as the cell of origin since it has the potential to undergo oncogenetic transformation and become a cancer.

The complex interactions between acquired somatic gene changes, germline vulnerability, and macro-environment & micro-environmental variables are associated with the development of prostate cancer. Multiple foci with distinct genetic changes, varying capacities for metastatic seeding, and innate resistance to treatment are common features of localized prostate cancer. [12] Numerous lines of evidence indicate that inflammation is a regular occurrence in the adult prostate. According to the National Institutes of Health (NIH) standard classification, prostatitis is a complex and heterogeneous phenomenon that is also known as chronic pelvic pain syndrome (CPPS) or chronic prostatitis. The four categories that make up CPPS are (I) acute bacterial prostatitis; (II) chronic bacterial prostatitis; (III) chronic prostatitis ⁄ CPPS; and (IV) asymptomatic inflammatory prostatitis. The first three of these categories deal with males who exhibit symptoms of the disease. Only 5–10% of prostatitis occurrences are thought to be caused by bacteria, with Escherichia coli (E. coli) and Enterococcus spp (being the most frequently implicated pathogens. [13]

Adult men's prostates frequently exhibit both short- and long-term prostatic inflammation (as much as to 80–90% exhibit some degree of inflammation). Prostatic immune cell counts rise above the levels of resident cells, which are apparently normal in these cases. Despite being widespread, this enhanced invasion of inflammatory cells in the prostate has been suggested to be harmful & may be the cause of many often-identified prostate disorders. In fact, all of the primary disorders of the human prostate, such as BPH, prostatitis syndromes, and prostate cancer, have been related to prostatic inflammation. Acute inflammation is typified by neutrophils, while chronic inflammation is characterized by mononuclear cells, which are primarily lymphocytes and macrophages. Prostatic inflammation can also occur in a variety of patterns depending on the site (stromal, intraepithelial, or luminal) [14]

Since patients who present with low to grade primary tumors may have very outcomes, such as indolent prostate cancer which can be monitored without or highly disease that necessitates, the cell of origin model is particularly in the case of prostate cancer. Still, classifying histopathological or genetic subgroups of prostate cancer which differ in the outcomes of patients has proven extraordinarily challenging. Therefore, research on the cell of origin may be very beneficial if the cell of origin as a model of prostate cancer holds true, since it may lead to the discovery of biomarkers that might be significant in predicting prognosis or that could help prevent overtreatment and direct the right kind of therapy. [15]

PCa develops from an accumulation of inherited genetic and epigenetic changes, similar to many other malignancies. There are now just three known risk factors for prostate neoplasia development: age, ethnicity, and a family history of prostate cancer. The geographic variation in PCa incidence and mortality—with rates substantially lower in Southeast and East Asia than in the US and Western Europe—may be partially explained by these genetic features. On the other hand, the higher incidence of PCa seen in Chinese and Japanese men within a generation of their migration to the West suggests that environmental factors—especially lifestyle factors like diet—also play a role in the development of PCa. Chronic inflammation is one possible mediator between environmental stressors and PCa development. [16]

Several developmental signalling pathways, such as the Wnt, fibroblast growth factor (FGF), and Hedgehog pathways, have been implicated in mediating epithelial–mesenchymal interactions during prostate organogenesis in more recent studies. [17] Molecular and cytogenetic analyses reveal that multiple metastases in an individual are clonally related, indicating that advanced prostate cancer is monoclonal. These results imply that the selective advantage of particular clones during cancer progression may give rise to metastatic prostate cancer; however, this clonal evolution process could also be the result of therapeutic interventions like androgen deprivation, which could target cells with different levels of malignant potential. [18]

Risk Factors

1. Age, race, and geography [19]

Once a person reaches the age of more than 40 Prostate cancer frequency is rises quickly, and peaks between those aged of 65 and 74 years old. Prostate cancer that can be clinically detected seldom develops before that point. Compared to White or Hispanic males, Black men are more likely to get prostate cancer; this difference may be caused by a combination of inherited and/or dietary variables.

2. Familial and genetic factors [20]

Prostate cancer is associated with strong hereditary factors. Men who have a family record of prostate cancer on one or the other side of the gene are more likely to develop the disease themselves, particularly if a member of their direct family has been diagnosed around age 65. A family history of other hereditary malignancies (e.g. Breast, ovarian, colorectal, and pancreatic, cancer) may further increase an individual's risk of developing prostate cancer detected before the age of 50, as well as melanoma). Men are more likely to develop prostate cancer if they have close relatives who have had prostate cancer.

3. Urinary Tract Infection [21]

Prostate cancer and reported gonorrhoea (or sexually transmitted infections in general, because gonorrhoea represents a substantial portion of reported STIs) were found to be positively correlated in many, but not all, cases. Prostatic inflammation is typically caused by an unknown factor. The initial inciting event may have been caused by a direct infection, a chemical and physical trauma that causes reflux, dietary variables, estrogen, or any combination of factors. Moreover, numerous pathogenic organisms have been shown to be able to spread through the prostate and trigger an inflammatory response. These comprise sexually transmitted species such as Neisseria gonorrhoea, Chlamydia trachomatis, Trichomonas vaginalis, and Treponema pallidum, as well as non-sexually transmitted bacteria such as Propionibacterium acnes.

4. Smoking [22]

In addition to increasing the risk of developing prostate cancer in the future, cigarette smoking may have an impact on the prognosis of the disease once it has been diagnosed. Race is another possible complicating factor. The majority of research on smoking's role as a prostate cancer risk factor has been done on White people. Smoking, however, seems to affect African Americans far more.

Histology of prostate cancer [23]

McNeal first put up the idea of the prostate's zonal structure in 1968. Usually found anteriorly, these tumors are not perceptible and are found by coincidence after the removal of a benign obstructive adenoma. Stage B tumors are positioned posteriorly, next to the prostate's rectal surface, and are palpable. 91% of the patients with stage A cancer who had their Transurethral resection of the prostate (TURP) and radical prostatectomy specimens analysed exhibited residual cancer of peripheral zone origin, whereas only seventy-nine percent of them had solely transition zone (TZ) cancer in their TURP specimens. The cancer in the peripheral zone (PZ) comprised 56% of the residual disease and had a considerably higher grade (median Gleason score) compared to the cancer found in the TURP specimen.

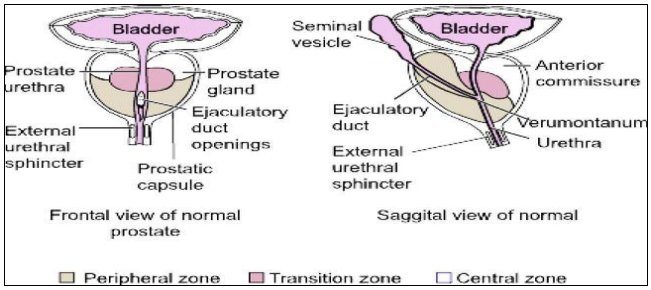

Fig 1: Frontal view and Saggital View of normal prostate.

Pattern of disease spread [24]

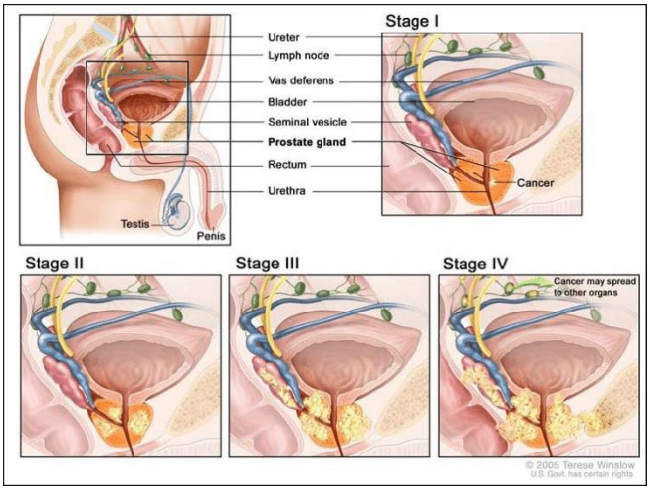

Fig 2: pattern of prostate cancer spread from stage I to IV

T1 stage: Indicates that the cancer is neither tactile nor visible in a clinical sense using imaging techniques.

T2 stage: Indicates that the tumor is identifiable but contained inside the prostate.

T3 stage: Indicates that the tumor has penetrated the prostatic capsule.

T4 stage: Indicates that other than seminal vesicles, the tumor is either fixed or has progressed to surrounding structures such as the pelvic wall, rectum, bladder, levator muscles, and external sphincter.

The clinical course of the disease is included in the nodal stages (N0–N1) and metastatic stages (M0–M1c). The lymph nodes (N1) and bones are the most prevalent sites for metastases (M1).

TNM Classification of prostate cancer [25]

Table 1: TNM Classification of prostate cancer

Primary tumour (T)		
TX	clinical Primary tumour cannot be assessed	
T0	Absence of a primary tumor	
T1	T1-Clinically inapparent tumour neither palpable nor visible by imaging	
	T1a	Tumour incidental histological discovery in ≤ 5% of tissue resected
	T1b	Tumour incidental histological finding in >5% of tissue resected
	T1c	Needle biopsy revealed the tumour (e.g. due of high PSA)
T2	T2-Cancer restricted to the prostate	
	T2a	Tumour involves ≤ 50% of one lobe
	T2b	Tumour involves > 50% of one lobe but not both lobes
	T2c	Tumour involves both lobes
T3	T3-Tumour extends through the prostate capsule	
	T3a	Extracapsular extension (unilateral or bilateral)
	T3b	Tumour invades seminal vesicle(s)
T4	The tumor is either stationary or spreads to nearby structures, such as the pelvic wall, rectum, bladder, levator muscles, and external sphincter, in addition to seminal vesicles.	
Regional lymph nodes (N)		
NX	clinical regional lymph nodes were not assessed	
N0	No regional lymph node metastasis	
N1	Metastases in regional lymph node(s)	
Distant metastasis (M)		
M0	No distant metastasis	
M1	Distant metastasis	
M1a	Non-regional lymph node(s)	
M1b	Bone(s)	
M1c	Different location, either with or without bone illness	

Screening for Prostate Cancer [26]

Acid phosphatase (AP) [orthophosphoric monoester phosphohydrolase, EC 3.1.3.2.] and digital rectal examination (DRE) are commonly employed in the diagnosis and surveillance of prostate cancer. Diseases other than prostate cancer may also induce high serum AP activity since AP is found in red blood cells, leukocytes, platelets, and organs such the liver, spleen, and kidneys in addition to the prostate. Assessment by solitary radial immuno-diffusion. Subsequently, Cooper and Foti created a number of immunoassays for the identification of PAP; PAP is typically tested using either enzyme immunoassay (EIA) or radioimmunoassay (RIA). Different from PAP, another tumor marker for prostate cancer has long been researched. In 1979, Wang *et al*. discovered and isolated the prostate-specific antigen (PSA) from human prostates to homogeneity.

Identification Techniques in Prostate cancer: [27]

- Digital Rectal Examination (DRE)
- PSA Screening
- Trans-rectal ultrasonography (TRUS) and ultrasound-guided biopsy
- CT scanning

- MRI – using multi parametric technology
- Bone scanning
- Choline positron emission tomography (PET)/CT scanning
- Detection of biomarkers in serum (e.g., Kallikrein proteins) or in urine (e.g., PCA3 or TMPRSS–ERG fusions).

Mechanisms of Androgen Resistance [28]

During the androgen-dependent stage of the disease, prostate cancer cells primarily depend on the androgen receptor for growth and survival. Upon entering the cell, testosterone is converted by the enzyme 5 alpha reductase into its active metabolite, Dihydrotestosterone (DHT). DHT enters the nucleus after interacting with androgen receptors in the cytoplasm, where it binds to androgen-responsive DNA sequences to activate genes involved in cell proliferation. During androgen-independent development, prostate cancer cells adopt a variety of cellular mechanisms to survive and flourish in the androgen-depleted environment.

Possible Pathways to Androgen Independence:

1. The androgen receptor (AR) gets phosphorylated by either the AKT (protein kinase B) pathway or the mitogen-activated protein kinase (MAPK) pathway in the outlaw pathway, resulting in a ligand-independent AR. This process involves the activation of receptor tyrosine kinases (RTKs).
2. The promiscuous pathway broadens the AR's specificity, enabling it to be triggered by nonandrogenic steroids that are typically found in the bloodstream.
3. The hypersensitive pathway encompasses three main methods: either heightened sensitivity of AR to offset low androgen levels, greater synthesis of AR (usually by gene amplification), or elevated the breakdown of the hormone testosterone by 5 α reductase to a more active androgen, Dihydrotestosterone.
4. Because the bypass pathway parallels other survival pathways, like the one containing the antiapoptotic protein B-cell lymphoma 2 (BCL), AR and its ligand are not necessary.
5. Through the process of stem-cell repopulation, androgen-independent stem cells from cancer multiply, become resistant to therapy, and ultimately take over as the predominant population within the tumor.

Therapeutic classes and agents approved for prostate cancer [29]

Table 2: Therapeutic classes and agents approved for prostate cancer

Class	Target	Agent	Mechanism of action	Indication(s)	Notable S/E
Non-steroidal androgen receptor antagonist (1st generation)	Androgen receptor	Nilutamide Bicalutamide, Flutamide,	Competitively and reversibly prevent Dihydrotestosterone & testosterone from attaching to the androgen receptor's ligand binding domain.	Used alongside GnRH agonists in the treatment of metastatic cancer	Abdominal pain Hot flashes, Pain, infection,
Non-steroidal androgen receptor antagonist (2nd generation)	Androgen receptor	DarolutamideEnzalutamide Apalutamide	Competitively and reversibly prevent DHT and testosterone from attaching to the androgen receptor's ligand binding site.	CRPC, mCSPC, nmCRPC (in combination with ADTc)	Fatigue, Hypertension, Nausea, Seizures, Arthralgia, Hot flashes
Androgen biosynthesis inhibitor	Steroidal enzyme CYP17A1	Abiraterone	Abiraterone suppresses the expression of CYP17A1 in prostate, testicles, and adrenal tumors.	mCRPC, mCSPC	Hypokalemia, Edema, Hypertension, Hepatotoxicity
GnRH antagonists	GnRH receptor	Relugolix Degarelix	Competitively & reversibly inhibit the pituitary glands GnRH receptors, preventing the release of the hormones FSH and LH.	Advanced prostate cancer	Hot flashes, Fatigue, Weight Gain, Hepatotoxicity
GnRH agonists	GnRH receptor	Leuprolide Goserelin Triptorelin Histrelin	Constant activation of the GnRH receptor causes a first spike in FSH, LH, testosterone, and DHT, which is then followed by reductions.	Advanced prostate cancer (including mCRPC)	General pain, Hot flashes, Sweating, Gastrointestinal disorders

1. Hormonal therapy [30]

Men with recently discovered metastatic prostate cancer respond quickly to castration, either surgically or medically. They experience a reduction in serum prostate specific antigen (PSA) levels, a resolution of bone pain, and a regression of soft tissue metastases. However, the majority of individuals experience a tumor that becomes androgen-independent within a median of 18 to 24 months following castration.

- **Hormonal Agents for the Treatment of Prostate Cancer**

1. Estrogen

a. Drug: Diethylstilbestrol

b. Mechanism/action: Suppresses LH-RH secretion, Decreases LH level, increases T level

c. Major side effects: Cardiovascular events, loss of libido, impotence

2. LH-RH agonists

a. Drug: Leuprolide, Goserelin

b. Mechanism/action: Suppress LH-RH secretion, Decreases LH level, increases T level

c. Major side effects: ‘‘Flare’’ phenomenon, hot flashes, loss of libido, impotence

3. LH-RH antagonists

a. Drug: Abarelix

b. Mechanism/action: Antagonizes LH-RH receptor, Decreases LH level, increases T level

c. Major side effects: Histamine release, loss of libido, impotence, hot flashes

4. Steroidal antiandrogens

a. Drug: Cyproterone acetate, Megestrol acetate

b. Mechanism/action: Antagonize AR in target tissues, suppress LH-RH secretion, Decreases LH level, increases T level

c. Major side effects: Cardiovascular events, fluid retention, gynecomastia, impotence

5. Non-steroidal antiandrogens

a. Drug: Flutamide, Nilutamide, Bicalutamide

b. Mechanism/action: Antagonize AR in target tissues, increases T level

c. Major side effects: Gynecomastia, hepatotoxicity (flutamide), visual and respiratory disturbances and alcohol intolerance (nilutamide), GI problems

6. 5 α -reductase inhibitors

a. Drug: Finasteride, Benzoquinoline

b. Mechanism/action: Inhibits type II 5 α -reductase, Decreases LH level, increses T level Inhibits types I/II 5 α -reductase, Decreases LH level, increses T level

c. Major side effects: Decreased libido, impotence.

7. Adrenal androgen inhibitors

a. Drug: Corticosteroids, Ketoconazole

b. Mechanism/action: Reduces the production of ACTH prevents the synthesis of adrenal and testicular steroids by inhibiting P450 hydroxylase, Decreases T level

c. Major side effects: Mood changes, Adrenal insufficiency, fatigue, GI problems

2. Chemotherapy

a. Docetaxel [31]

After two historic phase III trials, the first drug to show improvement in mCRPC was docetaxel therapy. The taxanes, which include docetaxel and paclitaxel, are anticancer medications that stabilize microtubules and promote microtubule polymerization at high levels. (All taxanes attach to the same taxoid-binding site on tubulin, which is found on the microtubule's inner surface, or to an overlapping location. By attaching to microtubules and reducing microtubule dynamics during the especially sensitive mitotic stage of the cell cycle, taxanes along with other microtubule-targeting medications prevent the growth of cancer cells without appreciably changing the mass or structure of microtubules. Cell death, a reduction in cell proliferation, and mitotic arrest result from stabilization of the microtubule dynamics of the mitotic spindle. It is recommended to deliver docetaxel intravenously every three weeks for ten cycles.

b. Cabazitaxel [32]

There are about 450 molecules from 10-deacetylbaccatin-III were utilized in a preclinical screen to locate a novel second-generation semisynthetic taxane called cabacizataxel (Jevtana®, Sanofi), which could be used as a treatment for both taxane-sensitive and taxane-resistant tumors. 2010 saw the approval of using cabazitaxel in addition to prednisone to treat patients with hormone-refractory metastatic prostate cancer who had previously had docetaxel-based therapy.

c. Mitoxantrone [33]

The U.S. Food and Drug Administration (FDA) approved mitoxantrone in 1996 for the treatment of metastatic castrate-resistant prostate cancer (mCRPC) due to its palliative benefits, which included an improvement in bone pain and an effect on the usage of analgesics. Mitoxantrone may cause gastrointestinal distress, myelosuppression, fever, pain, and, less frequently, acute myelogenous leukemia and congestive heart failure (CHF), despite its alleged palliative benefits.

Table 3: Recently FDA Approved Chemotherapeutic agents. [34]

Drug	Target	Effect
Enzalutamide	AR	AR antagonism, prevents signalling
Denosumab	RANKL	Reduces the resorption of bone
Zoledronic acid	Osteoclasts	Osteoclasts Decreases bone resorption
Galeterone (TOK-001)	CYP17A1	Antagonist
Apalutamide	androgen receptor	selective androgen receptor inhibitor

3. Immunotherapy [35]

Table 4: Recently FDA Approved immunotherapeutic agents.

Drug	Target	Effect
Sipuleucel-T	Activation of PBMCs ex *vivo* with GM-CSF and PAP	Activation of T cells
Prostvac-VF	Transmission of PSA transgene	Activation of T cells enhances median survival
Ipilimumab	CTLA-4	Activation of T cells
GVAX	Activation of T cells	Activation of T cells

4. Radiation therapy by using Radiopharmaceuticals: [36, 37]

- **Strontium-89 chloride**

Pure β-emitter strontium-89 (Sr-89) has an estimated half-life of 50.5 days. A cationic calcium mimic was Sr-89. It is more readily absorbed into bone metastases where bone turnover is higher. After using this medication, the locations of bone metastases show the highest level of activity. Since the β particle range in bone tissues is limited to 3 mm, Sr-89 is linked to certain hematological toxicity.

- **Samarium-153 lexidronam**

With an atomic number of 62, samarium belongs to the lanthanide series. Neutron capture of ^{152}Sm 2O3.28 yields Sm-153; only trace amounts of Eu-152 and Eu-154 byproduct are produced in this high yielding (>99%) process. With a maximum energy of 810 keV, Sm-153 releases an electron, a beta particle that is effective against cancerous cells. Sm-153 has a brief half-life of 46.7 hours, which enables quick removal.

- **Rhenium-186 etidronate**

In the late 1980s, Re-1, 1-hydroxyethylidene-diphosphonate (HEDP) was identified as a possible radiotherapeutic agent for the treatment of bone metastases. Re^{186}'s safety and effectiveness were investigated in a few of the early phase I/II trials. The majority of hematological toxicities were minor and temporary. Three patients experienced 1-2 weeks of grade-2 thrombocytopenia, while three patients experienced grade-2 leukopenia.

- **Radium-223 chloride**

The FDA authorized radium-223 in 2013. It is an alpha ray emitter radiopharmaceutical that uses α (alpha) particles to specifically target bone metastases. Because radium is a "calcium mimetic," it preferentially accumulates in bone areas due to rising turnover, such as osteoblastic metastasis. Within 100 lm of the target region, the radiation from the released alpha particle breaks DNA double-strand strands, selectively affecting that area without causing harm to the surrounding tissue.

Current marketed prepapration and dose

1. Abiraterone acetate [38]

In the case of metastatic castration-resistant prostate cancer in adults:

- **Zytiga:** Take 1 g (two 500 mg tablets or four 250 mg tablets) orally once day in addition to 5 mg of prednisone taken orally every 12 hours (twice daily) to offset the deleterious effects of CYP17 inhibition.

- **Yonsa:** take 500 mg (four 125 mg tablets) orally once day in addition to 4 mg of methylprednisolone orally twice day to counteract the adverse effects of CYP17 suppression. Adult dosage in metastatic high-risk castration-sensitive prostate cancer:

2. Enzalutamide [39]

- **Dosing Information:** Four 40 mg capsules, or 160 mg, taken orally once a day, is the recommended dosage of XTANDI. You can take XTANDI with or without meals. Take the capsules whole. Never dissolve, chew, or open the capsules.

- **Usage and Indications:** XTANDI® is recommended for the treatment of individuals suffering from castration-resistant prostate cancer (CRPC).

- **The Dosage Forms and Strengths:** XTANDI 40 mg capsules are soft gelatine capsules that are rectangular and white to off-white in colour. ENZ is embossed in black ink on them.

3. Sipuleucel-T [40]

For the treatment of metastatic castration-resistant prostate cancer (mCRPC) that is either asymptomatic or very symptomatic, sipuleucel-T is recommended.

- **Indication**

A minimum amount of 50 million activated autologous CD54+ cells suspended within 250 millilitres of Lactated Ringer's solution are used in each dosage of the immunotherapy. It is advised to administer three dosages, spaced about two weeks apart.

Missing an infusion on time necessitates an additional leukapheresis operation for the patient.

It is advised to take an oral pretreatment (30 minutes before the infusion) including acetaminophen & an antihistamine to reduce infusion-related side effects like fever and/or chills.

Novel Approaches for Delivering the Drug in Prostate Cancer

1. Nano carriers [41]

Another extensively researched field of cancer therapy is Nano carriers. These synthetic non-bioactive nonviral vectors offer a productive means of delivering medication to cells. This strategy has the special benefits of being less poisonous, less immunogenic, and adaptable to chemical changes. But this method's main drawback is its comparatively low transfection efficiency. Biodegradable materials are usually used in the creation of nano-vectors, such as nanoparticles or nanocapsules. These 10–100 nm particles encapsulate or adsorb genetic elements to produce a nano complex. The exceptional capacity of nanomaterials to adsorb, concentrate, and preserve genetic materials stems from their versatility in chemical alteration. There are two categories of these nanovectors: the inorganic ones, which are made of gold nanoparticles, iron oxide, and silica, and the polymeric ones, which are made of PLGA, lipids, dendrimers, and chitosan. Endocytosis is believed to be the main mode of delivery.

2. Cancer stem cell therapy [42]

Tumor initiation, development, metastasis, and recurrence are all caused by the self-renewal and proliferation of cancer stem cells (CSCs). Thus far, CSC has been identified in a broad range of solid tumors, such as melanoma and cancers of the lung, colon, prostate, ovary, and brain. The main causes of therapy failure in multiple malignancies are chemotherapeutic drug resistance and lack of selectivity.

Additionally, compared to non-CSC populations, CSC populations have greater resistance to conventional chemotherapy. Eliminating CSC is therefore essential to the treatment of cancer. Different targets of contemporary cancer therapy strategies have been reported by Chen *et al*. Surface marker are having two possible targets, along with signalling pathway involves ABC superfamily, anti-apoptotic factors, detoxifying enzymes, DNA repair enzymes, and specific oncogenic factors are among the several possible CSC therapeutic targets.

3. Magnetic Nanoparticles (MNP) [43]

Widder *et al*. were the first to use magnetic microspheres for directing anticancer drugs to tumor tissue by using an external magnetic field. With time, magnetism-assisted therapy has developed into a sophisticated theranostic approach that integrates diagnosis and therapy. Magnetic nanoparticles (MNPs) are adaptable systems with a range of modifications available for use in medical and diagnostic settings. MNP been shown to be superior MRI (magnetic resonance imaging) contrast agents because of their super paramagnetic properties. These substances are well tolerated and biocompatible. Because of this, some MNPs are approved as MRI contrast agents or are undergoing clinical trials to help identify different types of cancer. In order to create MNPs, minerals like magnetite (Fe3O4), maghemite (γFe2O3), and iron-based metal oxides are frequently utilized.

Future Therapies

5. Nano carriers [44]

Nanocarriers are colloidal Nano scale systems that carry anticancer agents, like macromolecules like genes or proteins or small molecular weight drugs. This allows the anticancer agents to accumulate in tumors and avoid normal tissues, achieving a cytotoxic concentration that is several times higher in the tumors than in the rest of the body when compared to free drugs. Furthermore, the medication is shielded from degradation by Nano carriers, which also lengthen the drug's half-life in the circulation, decrease renal clearance, increase the cargo of cytotoxic drugs, enable control over the anticancer agent's release kinetics, and enhance the solubility of insoluble drugs.

6. Polymer therapeutics [45]

These structures, which comprise polymer–drug conjugates and polymer–protein conjugates among others, are

characterized as Nano scale linear, water-soluble polymeric macromolecular conjugated to small molecule anticancer drugs or anti-tumor proteins through cleavable linkers that remain stable during the cytotoxic component's transportation and release the anticancer drug within the tumor. Anticancer proteins' covalent bond with polymers lengthens their blood circulation time, boosts their stability, and decreases their immunogenicity.

7. Carbon nanotubes [46]

With a diameter of 1-4 nm (based on the number of grapheme layers), a length of 1-100 lm, and special structural, electrical, optical, and mechanical capabilities, carbon nanotubes contain tubular hydrophobic networks of carbon atoms. Even so, chemical modifications to the structure of carbon nanotubes turn them into water-soluble carriers, improving their biocompatibility and lowering their toxicity. Because of their extremely high surface area, many anticancer medications can be incorporated into their surface or inner cavity, resulting in a high payload. These innovative carriers can penetrate the plasma membrane and Enter malignant cells (by endocytosis or needle-like penetration), regardless of the kind of cancer cells or the functionalization of the nanotubes.

Conclusion

In conclusion, this article provides a comprehensive overview of Prostate Cancer disease, encompassing its pathology, pathophysiology, prognosis, causes, types, and classification. It also give insight into medicines and treatment used for treatment of prostate cancer, exploring classes of drugs which are used to treat the prostate cancer, their targets, agents, mechanisms of action, and notable side effects. Additionally, it focuses on the current therapies and treatment options, including Drug & its dosage forms along with its Route of Administration. Furthermore, it explores the innovative realm of drug delivery methods, incorporating novel drug delivery systems for enhanced medical interventions.

Conflict of Interest

All Authors declared that there is no conflict of interest.

Abbreviations

CRPC: Castration: Resistant Prostate Cancer	nmCRPC: non: metastatic Castration: Resistant Prostate Cancer
TRUS: Trans Rectal UltraSonography	mCSPC: metastatic Castration Sensitive Prostate Cancer
PSA: Prostate Specific Antigen	GnRH: Gonadotropin Hormone: Releasing Hormone
DRE: Digital Rectal Examination	LH: Luteinizing Hormone
mpMRI: Multiparametric magnetic resonance imaging	LH: RH: Luteinizing Hormone: Releasing Hormone
IV: Intravenous	T: Testosterone
AR: Androgen Receptor	5α DHT: 5α Dihydrotestosterone
ADT: Androgen: Deprivation Therapy	ACTH: Adrenocorticotropic hormone
NIH: National Institutes of Health	GI: Gastrointestinal
CPPS: Chronic Pelvic Pain Syndrome or chronic prostatitis.	DNA: Deoxyribonucleic acid
BPH: Benign Prostatic Hyperplasia	USFDA: U.S. Food and Drug Administration
PCa: Prostate Cancer	CHF: Congestive Heart Failure
FGF: Fibroblast Growth Factor	GM: CSF: Granulocyte: Macrophage Colony: Stimulating Factor
STIs: Sexually Transmitted Infections	PAP: Prostatic Acid Phosphatase
PCPT: Prostate Cancer Prevention Trial	PBMC: Peripheral Blood Mononucleated Cell
SELECT: Selenium and Vitamin E Cancer Prevention Trial	RANKL: Receptor Activator of Nuclear κB Ligand.
TURP: Transurethral resection of the prostate	CTLA: 4 = Cytotoxic T: lymphocyte associated protein 4
TZ: Transition Zone	mAb – monoclonal Antibody
PZ: Peripheral Zone	PSMA: prostate: specific membrane antigen
ISUP: International Society of Urological Pathology	LNCaP cells: Lymph Node Carcinoma of the Prostate
AP: Acid Phosphatase	DTPA: Diethylenetriamine pentaacetate
EIA: Enzyme Immunoassay	GRPr: Gastrin: Releasing Peptide receptors
RIA: Radioimmunoassay	BBN: Bombesin
CT: Computed Tomography	NMB: Neuromedin B
PET: Positron Emission Tomography	CSC: Cancer stem cells
DHT: Dihydrotestosterone	MNP: Magnetic Nanoparticles
MAPK: Mitogen: Activated Protein Kinase	RTKs: Receptor Tyrosine Kinases

Acknowledgement

I would like to give heartfelt thanks to Management and Principal, SVPM College of Pharmacy, Malegaon (Bk II), Baramati, Pune for providing all facilities required for the completion of this review work.

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