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RESEARCH PAPER

Synergistic Effects of Hydrogel Nanoparticles and Docetaxel for Prostate Cancer: A Review

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ABSTRACT

Prostate cancer remains one of the most prevalent malignancies affecting men worldwide, necessitating continuous advancements in therapeutic strategies to improve clinical outcomes. Docetaxel, a microtubule-stabilizing chemotherapeutic agent, has demonstrated significant efficacy in managing metastatic castration-resistant prostate cancer. However, its clinical utility is frequently compromised by dose-dependent toxicity, suboptimal bioavailability, and the emergence of drug resistance. Nanotechnology-based drug delivery systems have gained attention for their ability to enhance therapeutic precision, improve drug solubility, and reduce systemic side effects. Hydrogel nanoparticles offer a promising platform for encapsulating docetaxel, providing controlled and sustained drug release, improved tumor selectivity, and enhanced intracellular drug accumulation. This review examines the synergistic potential of hydrogel nanoparticles and docetaxel in prostate cancer therapy, highlighting mechanistic insights into improved drug delivery efficiency, apoptotic induction, and resistance mitigation. By integrating hydrogel nanoparticle-based formulations, the therapeutic index of docetaxel can be optimized, contributing to more effective and personalized prostate cancer treatment approaches.

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INTRODUCTION

Prostate cancer remains a significant global health concern, with its incidence continuing to rise due to aging populations and lifestyle-associated risk factors. While localized prostate cancer is often managed through surgical intervention, radiation therapy, or androgen deprivation therapy, advanced or metastatic forms of the disease pose substantial therapeutic challenges [1]. Castration-resistant prostate cancer, characterized by its ability to progress despite androgen depletion, necessitates the use of systemic chemotherapeutic agents such as docetaxel [2]. Docetaxel has emerged as a cornerstone in the management of metastatic prostate cancer, exerting its therapeutic effects by stabilizing microtubules, impairing mitotic spindle function, and inducing apoptosis in proliferative tumor cells. Despite its efficacy, docetaxel treatment is associated with various limitations, including poor solubility, rapid systemic clearance, multidrug resistance, and significant hematological and gastrointestinal toxicities [3].

Nanotechnology has gained considerable interest in cancer therapy due to its potential to improve drug delivery efficiency and therapeutic specificity. Nanoparticle-based formulations provide enhanced drug stability, controlled release kinetics, and improved tumor selectivity through passive and active targeting mechanisms [4]. Among various nanoparticle platforms, hydrogel nanoparticles offer unique advantages due to their hydrophilic and tunable network structure, which facilitates sustained drug release and minimizes off-target toxicity [5]. Hydrogel nanoparticles can encapsulate docetaxel, protecting it from premature degradation and improving its accumulation within prostate tumor tissues [6].

This review aims to explore the synergistic effects of hydrogel nanoparticles and docetaxel, emphasizing their combined impact on apoptosis induction, resistance mitigation, and drug delivery optimization. By integrating hydrogel-based nanocarriers with conventional chemotherapy, innovative approaches can be developed to enhance docetaxel's therapeutic index while reducing its systemic side effects. The application of hydrogel nanoparticles in prostate cancer therapy introduces novel perspectives in precision medicine, paving the way for more effective, targeted, and personalized treatment strategies.

DOCETAXEL: PHARMACOLOGICAL PROFILE AND LIMITATIONS

Mechanism of Action as a Microtubule Stabilizer

Docetaxel is a second-generation taxane derivative that exerts its cytotoxic effects by interfering with microtubule dynamics, a critical component of cell division. As a microtubule stabilizer, docetaxel promotes the assembly of microtubules and prevents their depolymerization, leading to cell cycle arrest and apoptosis in proliferative tumor cells [7]. Microtubules are dynamic structures composed of α- and β-tubulin subunits that play an essential role in mitotic spindle formation during cell division. Their polymerization and depolymerization are tightly regulated processes that enable chromosome segregation and cellular replication [8]. Docetaxel binds to β-tubulin within microtubules, stabilizing their structure and inhibiting dynamic instability. This stabilization prevents proper mitotic spindle formation, leading to mitotic arrest at the G2/M phase of the cell cycle. As a result, cells are unable to progress through mitosis, triggering apoptotic cell death due to prolonged spindle dysfunction and accumulation of cellular stress [9]. Apart from its primary microtubule-stabilizing effects, docetaxel also induces cellular apoptosis through secondary mechanisms. Disruption of microtubule dynamics influences intracellular trafficking, impairing the transport of essential molecules such as growth factors and survival signals [10]. Docetaxel further modulates signaling pathways involved in apoptosis, including the BCL-2 family of proteins. By downregulating anti-apoptotic proteins such as BCL-2 and upregulating pro-apoptotic factors such as BAX and BAK, docetaxel enhances mitochondrial permeability transition, leading to cytochrome c release and activation of caspases [11].

Therapeutic Efficacy and Resistance Mechanisms

Docetaxel is widely used as a frontline chemotherapeutic agent for metastatic castration-resistant prostate cancer due to its potent cytotoxic effects and ability to improve overall survival [12]. Have demonstrated that docetaxel-based chemotherapy provides significant benefits in patients with progressive disease, leading to tumor regression and prolonged progression-free survival. However, its long-term therapeutic efficacy is often hindered by drug resistance mechanisms, which reduce treatment sensitivity

and limit clinical response [13]. Resistance to docetaxel occurs through multiple molecular adaptations, primarily involving alterations in microtubule dynamics, drug efflux mechanisms, and activation of compensatory survival pathways [14]. One major mechanism of docetaxel resistance involves the overexpression of β-tubulin isotypes that exhibit reduced drug binding affinity. Tumor cells undergoing prolonged docetaxel exposure frequently upregulate β-III tubulin, a tubulin isoform associated with diminished taxane binding. This adaptation allows microtubules to retain their dynamic properties despite docetaxel treatment, leading to reduced therapeutic efficacy [15]. Another resistance mechanism involves the upregulation of ATP-binding cassette transporters such as P-glycoprotein, which function as drug efflux pumps. These transporters actively remove docetaxel from cancer cells, lowering intracellular drug concentrations and preventing cytotoxic effects. Increased P-glycoprotein expression is commonly observed in chemoresistant tumors, contributing to treatment failure and disease progression [16]. Docetaxel resistance is also mediated by the activation of compensatory signaling pathways that counteract apoptosis. The phosphoinositide 3-kinase and mitogen-activated protein kinase cascades promote survival and proliferation, enabling tumor cells to evade docetaxel-induced cytotoxicity [17].

The emergence of resistance necessitates alternative strategies to improve docetaxel efficacy in prostate cancer treatment. Nanoparticle-based drug delivery platforms, including hydrogel nanoparticles, offer potential solutions by improving drug solubility, enhancing intracellular retention, and reducing efflux-mediated resistance [18]. The controlled release properties of hydrogel nanoparticles allow for sustained docetaxel exposure, preventing rapid clearance and maintaining therapeutic concentrations within tumor cells. Functionalized nanoparticles can be designed to target resistant tumor populations, overcoming drug efflux mechanisms and enhancing apoptosis induction [6].

HYDROGEL NANOPARTICLES: PROPERTIES AND DRUG DELIVERY POTENTIAL

Composition and Structural Characteristics of Hydrogel Nanoparticles

Hydrogel nanoparticles are an advanced class of nanoscale drug delivery systems that utilize hydrophilic polymeric networks to encapsulate therapeutic agents while ensuring controlled release. These nanoparticles are composed of interconnected polymeric chains that exhibit a high degree of water retention, providing flexibility and tunability in biomedical applications [19]. Their structure allows them to undergo reversible swelling and deswelling depending on environmental conditions, making them particularly useful for sustained and stimuli-responsive drug release [20]. Hydrogel nanoparticles are classified based on their polymer composition, which determines their physicochemical properties, stability, and interactions with biological tissues. Naturally derived hydrogel-forming polymers include chitosan, alginate, gelatin, hyaluronic acid, and collagen, which exhibit superior biocompatibility, biodegradability, and minimal toxicity [21]. These natural polymers interact favorably with physiological systems, reducing immune activation and facilitating sustained drug exposure. Synthetic hydrogel polymers such as polyvinyl alcohol, polyacrylamide, polyethylene glycol, and poly(N-isopropylacrylamide) provide mechanical stability and allow for precise control over nanoparticle swelling behavior and drug diffusion properties [22].

The architecture of hydrogel nanoparticles depends on several factors, including cross-linking density, polymer composition, and hydrophilic-hydrophobic balance. The degree of cross-linking determines nanoparticle porosity, influencing drug encapsulation efficiency and release kinetics [23]. Highly cross-linked networks provide slower drug diffusion, whereas loosely cross-linked networks allow faster drug permeation. Stimuli-responsive hydrogel nanoparticles can be engineered to react to physiological triggers such as changes in pH, temperature, or enzymatic activity, enabling selective drug release at tumor sites [24]. Tumor microenvironments often exhibit acidic conditions and elevated enzymatic activity, making pH-sensitive or enzyme-degradable hydrogels an effective approach for targeted therapy [25].

Biocompatibility and Controlled Drug Release Mechanisms

Biocompatibility is a critical feature of hydrogel nanoparticles, ensuring minimal systemic toxicity and favorable biological interactions. The hydrophilic nature of hydrogel matrices prevents excessive protein adsorption, reducing immune

system recognition and lowering the risk of inflammatory responses. Biodegradable polymers allow hydrogel nanoparticles to degrade into non-toxic byproducts over time, reducing long-term accumulation and potential adverse effects [26]. Hydrogel nanoparticles offer controlled drug release through diffusion, swelling-induced release, degradation-mediated release, and stimuli-triggered release mechanisms. Diffusion-controlled release occurs when drug molecules migrate through hydrogel pores due to concentration gradients. Swelling-induced release is regulated by changes in hydrogel hydration, where nanoparticle expansion facilitates drug diffusion. Degradation-mediated release relies on polymer breakdown, allowing encapsulated drugs to gradually escape as the network decomposes [27]. Stimuli-responsive hydrogels introduce an additional layer of drug delivery precision by utilizing physiological triggers to regulate drug release. pH-sensitive hydrogels can respond to acidic tumor environments, releasing drugs selectively at malignant sites while avoiding exposure to healthy tissues [20].

SYNERGISTIC EFFECTS OF HYDROGEL NANOPARTICLES AND DOCETAXEL

Improved Drug Solubility and Bioavailability

Docetaxel is a hydrophobic drug with poor water solubility, requiring formulation with organic solvents such as polysorbate 80 and ethanol for intravenous administration. These excipients contribute to hypersensitivity reactions, hemolysis, and hepatotoxicity, limiting the clinical tolerability of docetaxel-based therapies. The encapsulation of docetaxel within hydrogel nanoparticles addresses this challenge by providing a biocompatible delivery system that enhances drug solubility while eliminating the need for toxic solubilizing agents[28]. Hydrogel nanoparticles consist of hydrophilic polymeric networks capable of encapsulating poorly soluble drugs, effectively dispersing docetaxel within aqueous media. This improved solubility facilitates systemic distribution, ensuring enhanced drug bioavailability without necessitating aggressive solvent-based formulations [29]. Bioavailability is significantly enhanced due to the nanoscale dimensions of hydrogel nanoparticles, which optimize drug dispersion and tissue penetration. Hydrogel nanoparticles range between 50 and 200 nanometers, allowing efficient accumulation within tumors via the enhanced permeability and retention effect associated with aberrant tumor vasculature. This preferential accumulation enhances drug distribution in malignant tissues, improving therapeutic action while reducing systemic toxicity [30]. The integration of hydrogel nanoparticles into docetaxel formulations results in sustained therapeutic concentrations, ensuring prolonged drug exposure within prostate cancer cells. This sustained availability maximizes microtubule-targeting efficacy, reinforcing docetaxel-mediated mitotic arrest and apoptotic induction. The combination of improved solubility, prolonged circulation time, and selective tumor accumulation establishes hydrogel nanoparticles as an essential platform for optimizing docetaxel delivery [31].

Enhanced Intracellular Accumulation and Retention

One of the primary limitations of conventional docetaxel therapy is its poor intracellular retention, as many cancer cells actively expel chemotherapeutic agents through drug efflux mechanisms. ATP-binding cassette transporters, particularly P-glycoprotein and multidrug resistance proteins, significantly reduce intracellular docetaxel concentrations, resulting in therapeutic failure and disease progression [16, 32]. Hydrogel nanoparticle-based delivery systems circumvent these resistance mechanisms by improving intracellular drug retention, preventing rapid efflux, and ensuring sustained exposure to cytotoxic concentrations [33]. The nanoparticle surface properties and size influence intracellular accumulation. Hydrogel nanoparticles are designed to exhibit optimal surface chemistry, allowing enhanced interaction with cellular membranes and facilitating receptor-mediated uptake [34]. Tumor-targeting strategies involve functionalizing hydrogel nanoparticles with ligands such as folic acid or transferrin, enabling selective uptake by cancer cells with overexpressed receptors. This receptor-mediated endocytosis ensures efficient internalization of docetaxel-loaded nanoparticles, significantly improving intracellular drug concentration [35]. The sustained drug release kinetics of hydrogel nanoparticles further contribute to enhanced intracellular retention. Unlike free docetaxel, which is rapidly cleared from cells, hydrogel nanoparticles enable gradual release over extended periods, maintaining

therapeutic drug levels within the cytoplasm [36].

Hydrogel nanoparticles reduce the expression of efflux transporters, diminishing active drug removal mechanisms. This effect is mediated by intracellular oxidative stress and metabolic alterations induced by nanoparticle exposure, sensitizing prostate cancer cells to docetaxel-induced apoptosis [37].

Reduction of Systemic Toxicity and Improved Therapeutic

The dose-dependent toxicity of docetaxel poses significant challenges in prostate cancer therapy, as high systemic concentrations lead to severe hematological toxicity, neurotoxicity, and gastrointestinal complications [38]. Hydrogel nanoparticle-based docetaxel delivery systems optimize therapeutic index by refining drug biodistribution, ensuring selective accumulation in tumor tissues while minimizing exposure to healthy cells [39]. Hydrogel nanoparticles facilitate precise drug targeting through passive and active mechanisms, allowing increased docetaxel accumulation in malignant tissues while limiting systemic dispersion [40]. This targeted approach reduces the incidence of docetaxel-induced neutropenia, peripheral neuropathy, and hepatic dysfunction, improving tolerability and patient adherence. The controlled release profile of hydrogel nanoparticles prevents sudden plasma concentration spikes, minimizing acute toxicity while ensuring sustained drug action [41].

Surface modifications enhance the pharmacokinetic profile of hydrogel nanoparticles, prolonging circulation time and reducing premature clearance. Polyethylene glycol functionalization prevents immune system recognition, extending nanoparticle persistence in the bloodstream and improving tumor bioavailability [42]. This optimized pharmacokinetics ensures docetaxel delivery remains efficient throughout treatment, reducing the need for dose escalation while maintaining therapeutic efficacy [43].

MECHANISTIC INSIGHTS INTO COMBINATION THERAPY

Apoptosis Induction and Cell Cycle Disruption

The integration of hydrogel nanoparticles with docetaxel in prostate cancer therapy represents a significant advancement in nanomedicine and targeted chemotherapy. The synergy between these two agents improves drug bioavailability, enhances apoptotic induction, disrupts cell cycle progression, overcomes drug resistance mechanisms, and modulates the tumor microenvironment. Understanding these mechanistic interactions is crucial for optimizing therapeutic efficacy and ensuring prolonged tumor suppression [44]. Docetaxel functions as a microtubule stabilizer, disrupting mitotic spindle assembly and leading to prolonged mitotic arrest at the G2/M phase of the cell cycle. This disruption prevents chromosomal segregation, inducing apoptosis through the activation of mitochondrial-dependent pathways [45]. However, systemic administration of docetaxel often leads to variable drug concentrations in tumor tissues, reducing apoptotic efficiency. Hydrogel nanoparticles address this limitation by facilitating controlled and sustained docetaxel release within prostate cancer cells, ensuring prolonged exposure to therapeutic concentrations [33].

Apoptotic induction is primarily mediated by alterations in mitochondrial membrane potential and activation of caspase-dependent pathways. Docetaxel stimulates the release of cytochrome c from mitochondria into the cytosol, activating initiator caspase-9 and executioner caspase-3. This cascade leads to programmed cell death, ensuring the selective elimination of proliferative tumor cells. Hydrogel nanoparticles enhance this mechanism by stabilizing intracellular drug concentrations, preventing early clearance and maintaining apoptotic stimuli over extended periods [46].

Another key aspect of apoptosis regulation is the balance between pro-apoptotic and anti-apoptotic proteins. Tumor cells often evade apoptosis by overexpressing survival proteins such as BCL-2, which inhibit mitochondrial membrane permeability transition. Docetaxel downregulates BCL-2 while increasing the expression of BAX, a pro-apoptotic protein that facilitates cytochrome c release [47]. Nanoparticles further optimize this process by enhancing drug retention and exposure, leading to sustained BAX activation and irreversible apoptotic induction [48].

Another mechanism underlying the therapeutic effects of docetaxel. By inhibiting the progression of cancer cells through mitosis, docetaxel impairs tumor growth and reduces metastatic potential [49]. Hydrogel nanoparticles reinforce this effect by ensuring prolonged drug retention within tumor cells, preventing mitotic adaptation

and facilitating cell cycle arrest. The sustained intracellular presence of docetaxel prevents cancer cells from recovering from mitotic damage, ensuring enhanced therapeutic efficacy [50].

Overcoming Drug Resistance in Prostate Cancer Cells

Drug resistance remains one of the most significant challenges in prostate cancer treatment, leading to therapeutic failure and disease progression [51]. Resistance to docetaxel arises through multiple mechanisms, including overexpression of ATP-binding cassette transporters, modifications in microtubule structure, and activation of compensatory survival pathways [14]. Efflux-mediated resistance is a common issue in docetaxel therapy, as tumor cells actively expel chemotherapeutic agents through ATP-binding cassette transporters such as P-glycoprotein [52]. These transporters recognize and remove docetaxel from intracellular compartments, reducing its effectiveness. Hydrogel nanoparticles circumvent this resistance mechanism by maintaining sustained drug release within tumor cells, preventing excessive efflux while ensuring continued exposure to cytotoxic concentrations. The nanoscale dimensions of hydrogel nanoparticles facilitate passive diffusion across cellular membranes, reducing the likelihood of premature drug removal [44].

Structural modifications in microtubules also contribute to docetaxel resistance. Tumor cells undergoing prolonged exposure to taxane-based therapies frequently exhibit upregulation of β-III tubulin, a tubulin isoform with reduced binding affinity for docetaxel [53]. This adaptation limits the ability of docetaxel to stabilize microtubules, reducing its efficacy in inducing mitotic arrest [54]. Hydrogel nanoparticles counteract this effect by sustaining docetaxel exposure, maintaining sufficient intracellular concentrations to overcome β-III tubulin-mediated resistance [55]. Compensatory survival pathways, including the phosphoinositide 3-kinase and mitogen-activated protein kinase cascades, promote cell survival in response to chemotherapy-induced stress. These pathways are often upregulated in drug-resistant tumors, enabling proliferation despite docetaxel-mediated microtubule disruption [56].

Impact on Tumor Microenvironment Modulation

The tumor microenvironment plays a crucial role in prostate cancer progression, influencing angiogenesis, immune response, and stromal interactions. Hydrogel nanoparticle-assisted docetaxel therapy introduces modifications to the tumor microenvironment, improving drug penetration, reducing immunosuppressive conditions, and inhibiting vascularization [57]. Tumor-associated vasculature supports tumor growth by supplying essential nutrients and facilitating metastatic dissemination. Docetaxel exerts anti-angiogenic effects by inhibiting vascular endothelial growth factor expression, reducing endothelial cell proliferation, and impairing new blood vessel formation [58]. Immune modulation is another critical aspect of nanoparticle-assisted docetaxel therapy. Tumor-associated macrophages contribute to immune evasion by secreting anti-inflammatory cytokines that suppress cytotoxic T-cell activity [59]. Hydrogel nanoparticles influence stromal interactions within the tumor microenvironment. Cancer-associated fibroblasts provide structural support and secrete survival factors that promote tumor cell proliferation and resistance to therapy. Hydrogel nanoparticles disrupt these fibroblast-mediated survival mechanisms by impairing cytokine signaling and reducing fibroblast activation. This effect weakens tumor-stroma interactions, preventing malignant cells from exploiting microenvironmental support networks to evade chemotherapy-induced apoptosis [60].

PRECLINICAL AND CLINICAL STUDIES

Ke Li et al [61], Docetaxel and Doxorubicin codelivery nanoparticles (DDC NPs) were built by using hyaluronic acid (HA) and cationic amphipathic starch (CSaSt) thru a self-assembly technique. The DDC NPs exhibited high-quality loading capacities, performed sustained and enzymatic launch, and were strong in PBS, medium, and serum. After investigations in vitro, the DDC NPs were as effective as the twin drug combination in terms of cytotoxicity, antimigration, and apoptosis. Internalization effects indicated that the DDC NPs ought to effectively supply and absolutely release the payloads into PCA cells, and the manner changed into mediated via the ligand-receptor interplay of HA with the CD44 protein. Low toxicity in vivo was confirmed with the aid of acute toxicity and hemolytic assays. The distribution in vivo showed that DDC NPs ought to enhance the accumulation of medicine in tumors and decrease

nonspecific accumulation in normal organs. more importantly, DDC NPs notably promoted the healing impact of the doc and DOX combination within the PCA cellular xenograft mouse version, indicating that the drugs with NPs did indeed act synergistically.

Jung-Kyo Cho et al [62], reported the improvement of biodegradable/injectable poly(organophosphazene) (PPZ) hydrogels for the delivery of DTX with the usage of natural solvents. An aqueous solution of PPZ containing α-amino-ω-methoxy-poly (ethylene glycol) (AMPEG) 750 instead of AMPEG 550 become prepared, thereby growing the erosion capacity of the hydrogel by way of really apt balance of the hydrophobic/hydrophilic moieties. The protection of the hydrogel turned into demonstrated the usage of a biocompatibility check. The PPZ aqueous solution (8 wt%) containing DTX exhibited a thermosensitive sol–gel–sol transition that turned into unbiased of the attention of DTX (1–three mg/mL). The in vitro release examine indicated that the dominant launch mechanism turned into either erosion or diffusion/erosion-managed launch depending on the DTX content of the hydrogel. The in vivo anticancer impact of the intratumorally injected PPZ gadget in human gastric cancer cell-xenografted mice turned into evaluated, which proven a extensively ($p < zero.01$) superior effect of the DTX-PPZ hydrogel machine as compared to the control (DTX solution, i.v.). In end, the PPZ hydrogel can be a promising candidate for DTX delivery, affecting a decrease within the size of tumors with little toxicity previous to exeresis.

CONCLUSION AND FUTURE PERSPECTIVES

The synergistic combination of hydrogel nanoparticles with docetaxel represents a promising advancement in prostate cancer therapy, addressing several limitations associated with conventional chemotherapy. While docetaxel remains a cornerstone in the treatment of metastatic prostate cancer, its clinical application is frequently hindered by poor solubility, dose-dependent toxicity, rapid clearance, and the development of drug resistance. Hydrogel nanoparticles provide an innovative platform for optimizing docetaxel delivery, enabling controlled drug release, enhanced bioavailability, improved intracellular retention, and selective tumor targeting.

Mechanistic insights into this combination therapy highlight its ability to reinforce apoptotic signaling through mitochondrial disruption and caspase activation, inhibit drug resistance mechanisms by modulating efflux transporter activity, and alter the tumor microenvironment to impair angiogenesis and immune evasion. By integrating hydrogel-based delivery systems with docetaxel, prolonged therapeutic exposure is achieved, maximizing microtubule-targeting cytotoxicity while reducing systemic complications. The sustained release and tumor-selective accumulation of docetaxel improve therapeutic index, offering an effective strategy to overcome the challenges associated with taxane-based chemotherapy.

While the current findings demonstrate significant potential for nanoparticle-assisted docetaxel therapy, several factors require further optimization, including nanoparticle stability, biodegradability, functionalization strategies, and pharmacokinetic profiling. Continued refinement in nanoparticle engineering and drug delivery mechanisms will play a crucial role in translating these therapeutic benefits into clinically viable treatments.

The development of hydrogel nanoparticle-based docetaxel formulations presents several opportunities for advancing prostate cancer treatment. Future research should focus on optimizing nanoparticle properties, including polymer composition, cross-linking density, and surface functionalization, to ensure precise drug release kinetics and enhanced biocompatibility. The integration of tumor-targeting ligands such as folic acid, transferrin, or prostate-specific membrane antigen-binding peptides can improve tumor specificity, minimizing off-target toxicity while maximizing drug accumulation within malignant tissues.

Hybrid nanoparticle systems incorporating multiple therapeutic modalities may further enhance treatment efficacy. The co-delivery of docetaxel with molecular inhibitors targeting resistance pathways, such as phosphoinositide 3-kinase or histone deacetylase inhibitors, could provide a synergistic approach to overcome resistance mechanisms and improve tumor responsiveness. Additionally, combining hydrogel nanoparticles with immunotherapeutic agents could facilitate tumor immune surveillance, improving anti-tumor immune activation.

Advancements in nanoparticle surface

modifications, including polyethylene glycol functionalization and stimuli-responsive coatings, will further refine pharmacokinetic properties, ensuring prolonged circulation time and efficient drug delivery. The development of personalized nanomedicine approaches, incorporating patient-specific drug formulations and biomarker-driven targeting strategies, may enable tailored treatment regimens for optimizing therapeutic responses in individual cases.

Clinical translation of hydrogel nanoparticle-based docetaxel therapy will require extensive preclinical and clinical validation to assess safety, efficacy, and long-term biocompatibility. Standardization of manufacturing processes, regulatory approval pathways, and commercialization strategies will be critical for integrating these technologies into routine oncological care. The continued exploration of nanoparticle-assisted chemotherapy holds significant promise for enhancing treatment precision, improving survival outcomes, and reducing the burden of prostate cancer-related morbidity.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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