Revolutionizing Prostate Cancer Treatment: Gold and selenium Nanoparticles in Precision Photothermal Therapy

Afifa Marium[1], Farah Abid[2], Rimsha Kanwal[3], Hadeeqa Arshad[4], Hafiz Muhammad Javed[5], Sidra Rani[5], Faisal Arif[6], Fakhar Abbas[7], Sania Arif[8] and Mahjabeen Abid[9]

[1]Department of Biochemistry, Quaid-i-Azam University, Faculty of scienceIslamabad-45320, Pakistan
[2]Department of Pharmacy, Faculty of Pharmacy, University of South Asia, Lahore, Pakistan
[3]Center of Advanced Studies and Technology, Department of innovative Technology in Medicine and Dentistry, Gomal University, Dera Ismail Khan, Pakistan
[4]Department of Biochemistry, Faculty of Sciences University of Agriculture, Faisalabad-38000, Pakistan
[5]Department of Biochemistry & Biotechnology, Faculty of Sciences, University of Gujrat, Gujrat, Pakistan
[6]Department of Pharmacy, Faculty of Sciences, The University of Faisalabad, Faisalabad-37500, Pakistan
[7]Department of physics, Faculty of Sciences, University of the Punjab, Lahore-05422, Pakistan
[8]Department of physics, Faculty of Sciences University of Agriculture, Faisalabad-38000, Pakistan
[9]National Institute of food science and technology, University of Agriculture, Faisalabad-38000, Pakistan
*Corresponding author: saniaarif626@yahoo.com

Abstract

Nanotheranostics, a single modality that combines therapeutic monitoring and optically multiplexed disease detection, has the potential to advance nanomedicine toward truly personalized medicine such as Abirateron. Due to its numerous potential and ability to bridge the gaps in the existing treatment modalities' limitations, nanoparticle technology has gained acceptance in the fight against cancer. Prostate cancer tumor ablation can also benefit from the synergistic effects of photodynamic therapy reactive oxygen species (ROS) are used in Photodynamic therapyPDT and photothermal therapy (PTT), which offers insights into the potential for even more from this technology. This review explores the use of gold (Au) and selenium (Se) nanoparticles in photothermal therapy (PTT) and photodynamic therapy (PDT) drug delivery for prostate cancer treatment. It covers key subtopics, including the complex biology and chemistry of pharmacologically active Se- and Au-containing compounds, their mechanisms of action, and their synergistic effects. By investigating their therapeutic potential, this review aims to establish a comprehensive understanding of their role as a targeted and effective approach for prostate cancer therapy. Additionally, this chapter presents a comprehensive review of the current state of research, challenges, and future prospects in the ongoing fight against prostate cancer.

Keywords: Cancer nanotechnology, Photothermal therapy, Gold nanoparticles, Selenium nanoparticles

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Introduction

Recently, 1900, novel nanoparticle (NP) technology has become a major creative force behind the integration of medical diagnosis and therapy into a "unified" single-step platform called "nanotechnology." Although still in its early stages, this approach shows great promise as advanced optical technologies and treatment modalities gain importance in cancer management. However, many of the mechanisms underlying its use in medicine still need to be clarified (Siegel et al., 2019). Globally, prostate cancer is a common condition that significantly contributes to the mortality rates linked to cancer in men. Prostate cells are usually the source of the disease which frequently presents as a localized or metastatic tumor (Karavitakis et al., 2017). Prostate cancer has a significant death and disability rate, which makes the investigation and application of innovative therapeutic strategies imperative. Using gold and selenium in delivery systems is one potentially beneficial for treating prostate cancer. The capacity of selenium to alter redox signaling pathways and promote oxidative stress-induced apoptosis has demonstrated its anticancer effects.

1.1. Why Selenium is Important for Research on Prostate Cancer

1.1.1. Properties of Antioxidants

Selenium, an essential trace mineral, plays a crucial role in antioxidant enzymes like glutathione peroxidase. These enzymes help reduce oxidative stress by neutralizing free radicals, which can damage DNA and contribute to cancer development. A variety of cellular processes,

such as governing the cell cycle and apoptosis (programmed cell death), have been demonstrated to be impacted by selenium. This is especially important since one of the characteristics of cancer is the ability of cancer cells to evade apoptosis. By encouraging apoptosis in cancer cells, selenium can stop the growth and multiplication of these cells (Hirsch et al., 2003). Selenium is necessary for the immune system, which is crucial for identifying and getting rid of abnormal or cancerous cells. According to research findings, selenium could hinder the process of angiogenesis, which creates new blood vessels and supplies nutrients to cancers (Grzelczak et al., 2020). Gold nanoparticles have distinct photoactive properties that enable specific hyperthermia and precise tumor adaptation. One promising application of gold nanoparticles is photothermal therapy (PTT), which uses them to specifically target and kill cancer cells.

1.2. Gold's Importance in the Study of Prostate Cancer

Research suggests that selenium may prevent angiogenesis, the process that creates new blood vessels and gives tumours nourishment. The growth as well as spread of cancer may be hindered by the element selenium through the restriction of angiogenesis (Hu et al., 2024). The unique photoactive properties of gold nanoparticles enable precise tumor adaptation and targeted hyperthermia. One ensuring use is photothermal therapy (PTT), which uses particles of gold to focus on and kill cancer cells specifically. The gold nanoparticles which have been provided to the cancerous cells are irradiated using near-infrared (NIR) light in photothermal therapy (Lal et al., 2008). The gold nanoparticles absorb light and convert it to heat. This localized heating causes thermal damage to the cancer cells, killing them without causing damage to the surrounding healthy tissue.

The following ways are used to treat prostate cancer

1.3.1. Targeting

Gold nanoparticles are functionalized using specific ligands, peptides, or antibodies that can attach to prostate cancer cells (Cheng et al., 2021).

1.3.2. Accumulation

After being injected into the bloodstream, nanoparticles acquire in the tumor site because of the improved and permeability effect of retention (EPR) because they are more likely to do so in tumor tissues than in normal tissues (Bastús et al., 2011).

1.3.3. Tumor Destruction

By inducing necrosis, coagulation, programmed cell death, or apoptosis, the heat generated can effectively destroy cancer cells. Numerous techniques, including sound waves, microwave stimulation, laser-assisted photothermal therapy (PTT) () and photodynamic therapy (PDT) (), are being investigated for their potential to treat cancer by inducing hyperthermia (Valerio et al., 2014). Like traditional cancer treatments, these alternative therapies may not be tumor-specific and may have unintended side effects. Therefore, it is necessary to produce new therapeutic strategies which may improve tumor control by means of mutually beneficial effects, fewer side effects, and greater practical applicability. However, the infectious and lytic nature of Oncolytic Viruses OVs also comes with a number of drawbacks: pathogenicity is of great concern for OVs due to the risk of uncontrollable viral replication, even when attenuated through genetic modifications, safety issues are not completely eliminated, and there is a potential that the OVs might return back to their infectious wild type through the recombination with wild type viral strains. The immune system produces an anti-OV immune response within 1-2 weeks that eliminates the OV infection, which is another drawback of OVs. Finally, it is more difficult to impart new functionalities to OVs than to VLPs or VMNs. As viruses evolved to have an optimized structure as well as genome that carries out their entire lives, surface alteration and genetic fusions may adversely impact viral fitness. Our body uses blood clots as a natural defense against blood loss. These thick blood clots seal wounds, scrapes, and blood vessels that are leaking. Your body may bleed excessively if it takes too long to form them. Your blood clotting time is measured by a partial thromboplastin time (PTT) test. The activated partial thromboplastin time (aPTT) test is another name for this test that doctors use (Leite et al., 2011). Due to their high surface-to-volume ratio, they can also more easily penetrate tumor sites through a phenomenon called enhanced permeation and retention (EPR). The production of reactive oxygen species by selenium nanoparticles (Se NPs) may be an additional way to prevent tumor growth (Omiyale et al., 2023). The combined effect of these elements increases the efficiency of thermal energy evaporation in the designed capsule, so the combined effect of Se NPs and Au NPs leads to dual pharmacological effects.

1.4. Principles of Photothermal Therapy (PTT)

Photothermal therapy is the application of heat that is photoinduced to treat cancer. This therapeutic strategy has been seen as a promising anti-cancer treatment because it can be spatially controlled, avoiding harm to non-targeted areas. Photothermal therapy is a subset of nanomedicine since most materials that cause photothermal heating are nano scaled. For photothermal therapy to be effective, a few basic prerequisites must be met. First and foremost, template nanomaterials intended for therapeutic use must have high photothermal conversion efficiency—that is, the ability to transform light energy into heat energy. Second, to guarantee deep tissue penetration, the photothermal effects ought to be triggered by near-infrared (NIR) light. Finally, for photothermal treatment to be effective, the surface of the nanomaterials should be easily modified. According to earlier studies, these conditions can be met by using nanoparticles with targeting ligands, which enable selective internalization and laser irradiation to create photothermal effects inside the target cell (Figure 1).

1.5. Gold Nanoparticles for PTT

AgNPs used in photothermal applications must meet several design specifications, such as plasmon resonance tunability and high photothermal conversion efficiency) (Hirsch et al., 2003). These parameters indicate that nanoshells, nanostars, nanorods, and nanocages are the most used photothermal transducers (Jing et al., 2014). Using these formulations as examples, the desirable properties of AuNPs for PTT are discussed here. AuNPs used in PTT must first be made using light from the first NIR window because AuNPs embedded in tumors can be safely and deeply penetrated through healthy tissue by these light wavelengths (Bastús et al., 2011).

The ability to adjust the structural dimensions of AuNPs to achieve maximum absorption in one of these two light regions is a significant characteristic. Most AuNPs are made to absorb as much as possible within the first NIR window, which is safe to enter between two and three centimeters of tissue (Prodan et al., 2003). For instance, by varying the ratio of core diameter to shell thickness, NSs—which are made up of thin gold shells surrounding spherical silica cores—can have their peak plasmon resonance tuned. Because they can maximally absorb light at 800 nm, NSs with cores that are 120nm in diameter and shells that are 15nm thick are commonly used for PTT. The longitudinal surface plasmon resonance (SPR) ($\lambda \approx 650–850$nm) and transverse ($\lambda \approx 500–550$nm) are represented by two absorption peaks that are provided by NRs' short and long axes. To attain the highest longitudinal SPR in the NIR region, the rod length can be either elongated or shortened. NRs that are around 10nm ×40nm are the most common for PTT due to their ability to absorb light up to 800nm. New AuNP designs for PTT in the second NIR window has recently surfaced, whereas the majority of AuNPs were created to absorb as much as possible within the first NIR window. The reason for this is that these wavelengths can safely reach deeply embedded tumors by penetrating up to 10cm of tissue. Nanotubes of carbon with a single wall coated with AuNP as a multipurpose platform for PTT and imaging in the second NIR window (Pelaz et al., 2017).

1.6. Applications in Prostate Cancer Treatment

Prostate cancer (PCa) treatment now heavily relies on genetics, genomics, and biomarker applications. Nowadays, risk assessment, treatment course determination, prognosis, and monitoring all frequently use germline Tumor genomics, genetic testing, and additional biomarkers. When it comes to PCa diagnosis and treatment response tracking, molecular imaging is essential (Riley et al., 2017). The following are some noteworthy uses in the treatment of prostate cancer:

1.6.1. Surgery

A radical prostatectomy, which is frequently done in cases of early-stage cancer, entails excising the prostate gland entirely along with some surrounding tissue. Techniques that are not too invasive are Precision, a quicker recovery, and fewer complications are all benefits of robotic-assisted laparoscopic surgery, such as that provided by the da Vinci surgical system (Zhou et al., 1994).

1.6.2. Radiation Treatment

High-energy radiation is used to destroy cancer cells, external beam radiation therapy (EBRT) is focused on the prostate. By directly implanting radioactive seeds into the prostate, brachytherapy offers targeted treatment with the least amount of tissue damage possible.

1.6.3. Androgen Deprivation Therapy (ADT)

ADT is a type of hormone therapy. The goal is to lessen or stop the synthesis of androgens, or male hormones, which can promote the growth of cancer (Ashikbayeva et al., 2019).

1.6.4. Techniques

1.6.4.1. Drugs: The production of testosterone is decreased by LHRH agonists and antagonists.

- 1.6.4.2. Anti-Androgens: Prevent cancer cells from being affected by androgens. An orchiectomy lowers testosterone levels by surgically removing the testicles.
- 1.6.4.3. Chemotherapy Use: Frequently for hormone-resistant or advanced prostate cancer.
- 1.6.4.4. Common Medications: Prednisone is frequently used in conjunction with docetaxel and cabazitaxel to help reduce symptoms and slow the progression of cancer.

1.6.5. Immunotherapy

One kind of cancer vaccine called Sipuleucel-T (Provenge) is intended to boost the patient's capacity of the immune system to combat prostate cells of cancer. Castration-resistant prostate cancer that has spread is its main application. Checkpoint inhibitors are medications that strengthen the defenses of the body against cancer by blocking particular proteins found on cancerous or immune cells (Songca et al., 2023).

Targeted Therapy

PARP Inhibitors: Medications such as olaparib can prevent cancer cells from repairing their DNA, which can result in cell death in patients with specific genetic mutations (e.g., $BRCA_1$/$BRCA_2$) (Grzelczak et al., 2020).

- Radionuclide Therapy: Radium-223 (Xofigo), which targets cancer cells in the bone while preserving nearby healthy tissue, is used to treat advanced cancer with bone metastases.
- Active Monitoring and Vigilant Waiting

Monitoring without prompt treatment is an option for slow-growing, low-risk prostate cancer. To monitor progress, this routine PSA testing, digital rectal exams, and biopsies (Hu et al., 2024).

Focal Therapy

Methods that target and eliminate cancerous tissue while preserving healthy prostate tissue incorporate HIFU, or high-intensity focused ultrasound and cryotherapy.Using laser light and photosensitizing agents, photodynamic therapy (PDT) kills cancer cells. Its effectiveness in treating prostate cancer is still being studied.Gene therapy is the process of altering a patient's genes to boost immunity or introducing therapeutic genes to stop or eradicate cancer cells (Lou et al., 2023).

Lifestyle Modifications

Stress reduction, exercise, and a healthy diet can enhance general health and support treatment. Counseling, support groups, and palliative care all aid in symptom management and enhance quality of life. The following are some thorough case studies and clinical situations pertaining to the treatment of prostate cancer:

- 1.6.6. Case Study 1: Prostate Cancer in its Early Stages

Gleason score 6 (3+3) and T1c prostate cancer are the diagnoses for the patient, a 55-year-old man with PSA 4.5ng/mL.Active surveillance, including yearly biopsy and routine PSA monitoring, is the treatment. Result: After five years, PSA levels remained stable with no indications of improvement.A fifty-year-old man with a history of prostate cancer in his family is the patient. A BRCA2 mutation was found during genetic testing.

Treatment: ADT plus olaparib, a PARP inhibitor Improved PSA control and the possibility of increased overall survival are the results (Thapa et al., 2018Prostate cancer patient with high-risk characteristics: a 60-year-old man with a Gleason index of 9 (5+4) and PSA of 20 ng/mL is treated with EBRT + ADT + docetaxel chemotherapy, which improves local control and reduces the risk of distant metastases (Ramamoorthy et al., 2020).

A 65-year-old man with PSA recurrence after prostatectomy was treated with ADT and SBRT. This approach improved his PSA control and reduced the risk of further recurrence.

1.7. Gold Nanostructure Synthesis for Theranostics

Notwithstanding the widespread use of nanostructures, there are two methods: top-down and bottom-up. The bottom-up strategy of producing gold salt reduction produces nanostructures of gold from atoms of gold techniques has been well-liked for many years. Ultra-thin NRs, which with the AR of roughly 10–20 that show the mid-IR (MIR) region's LSPR have recently been reported. Even though the transparency window and their LSPR overlap, this should NRs' typical polydispersity (in a synthesized batch) is greater than that of the NPs of spherical, which effectively lowers their total absorption and translates into higher photothermal efficiency (Yu et al., 1997). Another factor to take into account is that heating causes the NRs to melt and change shape, producing NRs that have lower LSPR and AR than the initial. This could make the NRs unsuitable for therapeutic use because it would alter the effectiveness of their transduction light-heat over the course of a treatment cycle. This effect has been thoroughly examined and reported by Jana et al. (2001). Because their peaks of LSPR can be in the region of NIR, gold nano shells and gold nanostars are other nanostructures that have gained popularity (Jana et al., 2001). For nano shells of gold, adjusting the shell thickness between nm1 and 30nm and for gold nano stars, adjusting the number of branches, length of tip, and tip sharpness gives control over the λLSPR tunability. Initial synthesis of nano shells onto dielectric silica cores involved the formation of seeds of gold that eventually formed a sphere of silica with nano roughness, ultimately resulting in covering the silica core with a smooth gold shell. The LSPR blueshifts as the shell thickness increases.

1.8. Impact of Shape and Size of Particles

The primary factor influencing the physiochemical characteristics of the size of AgNPs has a significant impact on the theranostic platform's behavior both *in vitro* and *in vivo*. Crucial factors that regulate their cellular absorptions, biodistribution, and the geometric effects of their size and clusters order are endocytosis efficiency, clearance places, and clearance rates (Chhatrec et al., 2018). According to reports, although pristine NPs with a diameter of less than 100nm might be able to enter cells, those smaller than 40nm might approach the cellular nuclei. NPs less than 100nm in diameter might likewise have access to cells. However, the renal filter removes NPs from the body that have a diameter of less than 10nm. As a result, size and surface functionalization/coating are crucial for Gold nanostructures' targeted delivery in tumors (Shields et al., 2010).

These factors can help to achieve the best therapeutic activity while minimizing toxicity and adverse effects on healthy cells and tissues. By employing functionalizing or coating agents that impact NPs' ability to enter or be transported to the cell membrane, as well as the degree of potential entry and clearance pathways. The transfer and growth of gold nanostructures, as well as their associated toxicological impacts on various using both in vitro and in living cells test models, extensively studied in relation to particle shape and surface functionalization (Cheng et al., 2018).

1.9. Conclusions and Future Perspectives

An increasing number of innovative AuNPs are being developed to combine photothermal therapy and optical diagnostics in a single process. Enhancing raman nanotheranostics based on gold nanostructures could be essential for moving towards treatments and detection to more complicated biological processes *in vivo* within clinic. Additionally, SESORS has made significant strides recently in providing damage and optical imaging localization in conjunction using direct optical feedback and PTT to deliver precise *in vivo* pH and temperature monitoring. We have examined the data supporting this expanding consensus and have emphasized the integration of two approaches (treatment and evaluation) into a single, effective, economical, and focused procedure. By addressing the difficulties in developing novel methods for functionalizing AuNPs containing molecules capable of promoting efficient binding, corona formation, clarity, biocompatibility, biodistribution, and toxicity, this review also offers noteworthy advancements. Additionally, it has addressed the translational barrier and unmet clinical need for quick, efficient nonsurgical cancer diagnosis and detection with high sensitivity and specificity using raman spectroscopy. Additionally, it has tackled the translational barrier and lacking medical need of employing gold nanostructures in one, efficient nonsurgical procedure to detect and diagnose cancer with great sensitivity and specificity. Nanostructures of gold have been extensively investigated for potential medical uses, but commercialization of these (NPs) for standard in options for *in vivo* light-triggered therapy has been delayed for a long time.

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