

Nanoparticle-Protein Corona Interactions in Biological Milieu: Differential Toxicity Profiles in Prostate Cancer and Normal Cell Lines

M. Karbalae^{1,3}, Z. Sadeghi¹, M. V. Ahmadianpour¹, B. Jahangiri¹, R. Valipour⁴, S. A. Aleyasin², J. Raheb^{1*}

¹ National Institute of Genetic Engineering and Biotechnology, Molecular Medicine, Tehran, Islamic Republic of Iran

² National Institute of Genetic Engineering and Biotechnology, Medical Genetic, Tehran, Islamic Republic of Iran

³ Faculty of Basic Sciences, Islamic Azad University, Science and Research Branch, Tehran, Iran Islamic Republic of Iran

⁴ Department of Urology, Faculty of Medicine Tehran Medical Sciences Islamic Azad University, Tehran, Islamic Republic of Iran

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Abstract

Prostate cancer stands as the second most prevalent cancer among men globally and represents a significant cause of mortality in Iran. Notably, nanotechnology has emerged as a valuable tool in the realm of medical research, offering advancements in both cancer diagnosis and treatment. Prior research has shown that nanoparticles, when entering biological environments like plasma or serum, are surrounded by a layer of proteins referred to as the protein corona. The protein coronas' composition differs across various disorders, affecting the kind and amount of proteins that attach to the nanoparticle surface. This study aimed to assess the toxicity of protein coronas loaded onto various nanoparticles, including gold, graphene, and superparamagnetic iron oxide nanoparticles (SPIONs), in prostate cancer and normal cell lines. Plasma samples from cancer patients and healthy individuals were procured, and nanoparticles (gold, SPIONs, graphene oxide) were synthesized, with their charge and size verified using zeta method. Subsequently, the MTT assay was used to study the toxicity of combinations of nanoparticles (gold, SPIONs, graphene oxide) and their associated protein coronas on the LNCaP prostate cancer cell line and healthy HFF fibroblast cells. Gold nanoparticles exhibited higher toxicity towards cancer cells compared to the other two nanoparticles. Conversely, SPIONs and graphene oxide did not manifest significant toxicity on healthy cells. The increased toxicity of graphene oxide-associated protein coronas highlights the complex relationship between nanoparticle composition and protein corona properties, offering important insights for targeted cancer therapy techniques the quantisation of aromatic amines simultaneously in fairly complex matrix

* Corresponding Author: Tel: +989397962203; Email: Jam@nigeb.ac.ir

of dyes effluents and biological samples (human serum) by simple GC-FID with adequate sensitivity.

Keywords: Prostate Cancer; Gold Nanoparticles; SPION; Graphene Oxide; Corona Protein.

Introduction

Prostate cancer, a frequently diagnosed malignancy among men, initially confines itself to the prostate and exhibits slow growth, seldom causing the substantial harm. Diagnostic modalities such as magnetic resonance imaging (MRI), biopsy, prostate-specific antigen (PSA) testing, and medical examinations serve as critical tools for detecting prostate cancer (1, 2). Treatment options encompass surgery, chemotherapy, radiation therapy, hormone therapy, and immunotherapy (3).

The safe and targeted delivery of therapeutic proteins using the nanoparticles is a topic of significant interest in the field of medical research (4). Nanotechnology has provided innovative platforms for the efficient transport of bioactive agents, offering new possibilities for the delivery of therapeutic proteins to the body (5). They can be synthesized from various organic or inorganic materials, such as lipids, proteins, synthetic/natural polymers, and metals, and can be tailored to achieve specific delivery properties (6). The type of nanoparticle used in the targeted delivery of therapeutics has its own positive and negative effects, and the properties of nanoparticles, such as particle size, charge, and surface, have a significant effect on drug delivery (7). The safe and targeted delivery of therapeutic proteins with nanoparticles is particularly important for the treatment of various diseases, including cancer (8). Nanoparticles have distinctive physicochemical and biological features, and their conjunction with medicinal drugs may augment the agent's concentration inside cells and tissues (4). The surface charge of therapeutic nanoparticles plays an important role in their clearance and targeted delivery, and the surface modification of nanoparticles can alter their recognition ability for targeted delivery (4, 9). In addition to their unique properties, nanoparticles offer the potential for multifunctional delivery systems, allowing for designing the pathways for suitable targeting (10). The association of therapeutic agents with nanoparticles and the design of their pathways for suitable targeting is a promising approach in delivering a wide range of molecules to certain locations in the

body (11).

Nanoparticles, owing to their high surface-to-volume ratio and energy, undergo complete surface coverage upon interaction with the biological molecules. This phenomenon, facilitated by the interaction of nanoparticles with the surrounding environment, results in the formation of a protein corona predominantly composed of proteins (12). The charge, surface properties, and dimensions of nanoparticles affect the behavior of the protein corona, which may be classified into hard and soft corona types. Vroman effect is a phenomenon in which high-concentration proteins gradually displace low-concentration, high-affinity plasma proteins on the nanoparticle surface, therefore solidifying the protein corona (13, 14).

Studies suggested that alterations in plasma structures induced by various diseases impact the production of protein corona on nanoparticle surfaces, leading to variations in protein corona composition among patients (15, 16). The absorption of proteins onto nanoparticles is affected by the factors, such as surface hydrophilicity or hydrophobicity and protein structural stability, thereby affecting the toxicity and distribution of nanoparticles in biological systems (17, 18).

Gold nanoparticles, available in various forms such as nanospheres, nanorods, nanoshells, and nanocages, offer unique physical and chemical characteristics that make them highly desirable for cancer treatment. These include their size, shape, ease of handling, and drug delivery capabilities (19). Gold nanoparticles have already been shown to be effective in the delivery of medication, imaging, cancer treatment, and laboratory testing. They have the potential to eradicate bacteria and cancer cells (20). Alterations to the gold surface impact its cytotoxicity, absorption, and interactions with cellular components, with the oxidative stress identified as a mechanism of gold-induced cytotoxicity (21). Graphene nanoparticles, renowned for their large surface area, superior conductivity, light sensitivity, and low cellular toxicity, are used in cancer treatment (22). The cytotoxicity of graphene oxide is contingent upon various factors, including exposure dose, culture

duration, incubation temperature, cell type, as well as physicochemical characteristics such as size, shape, and surface function (23, 24).

One clinically authorized metal oxide nanoparticle, SPION (superparamagnetic iron oxide nanoparticle), exhibits promise across diverse medical applications, including tissue engineering, targeted cancer/tumor destruction, drug/gene delivery, and imaging. Its nanoscale size and surface area ratio, along with biodegradability and biocompatibility, contribute to its low cytotoxicity, sustained effectiveness, and great selectivity, giving SPION nanoparticles important instruments in cancer therapy (25, 26).

In summary, the safe and targeted delivery of therapeutic proteins using nanoparticles presents exciting opportunities for advancing treatment strategies across various diseases. Nanoparticles possess unique physicochemical and biological properties that, when combined with therapeutic agents, can significantly enhance their concentration in target cells and tissues. The development of targeted drug delivery nano-systems has facilitated the creation of precise and effective delivery strategies, addressing the inherent challenges in administering therapeutic proteins. This research specifically investigates the toxicity effects of nanoparticles on both cancerous and healthy cells, as well as the impact of protein corona-nanoparticle complexes on these cell types. By comparing the efficiency of these nanoparticles in transferring corona proteins and their differential effects on healthy versus cancerous cells, our study aims to elucidate the potential of nanoparticle-based systems for improving targeted therapy in prostate cancer treatment.

Materials and Methods

Plasma Sample Collection

Plasma samples were collected from healthy individuals and patients diagnosed with prostate cancer under ethical approval (Ethics code: A.1397,8,23. IR.NIGEB.EC) from the National Institute of Genetic Engineering and Biotechnology of Iran.

Nanoparticle Characterization

Graphene, SPION, and gold nanoparticles were procured from US Research Nanomaterials, Inc. Particle size and surface charge analyses were conducted using zeta sizing method.

Nanoparticle-Protein Corona Complex Preparation

Nanoparticles were diluted to concentrations of 50, 100, and 150 $\mu\text{g}/\mu\text{l}$. To form the protein corona complex, each nanoparticle type (graphene oxide, gold, SPION) was exposed to plasma for 1 hour at 37°C.

Centrifugation was then conducted at 15°C and 14,000g for 20 minutes to eliminate weakly bound proteins and acquire a stable protein corona complex. The resultant sediment was rinsed three times with phosphate buffer solution (PBS) under identical circumstances, producing the protein corona hard complexes (graphene oxide, gold, SPION).

SDS-PAGE Analysis

The protein corona's stability was evaluated by dissolving obtained complex from different patients in loading buffer, heating to 100 degrees for 10 minutes, and running equal amounts in gel electrophoresis. Gel analysis was conducted at 120 mV and approximately 80 milliamps for nearly 90 minutes. Staining with silver nitrate confirmed protein corona formation at various concentrations of plasma and nanoparticles.

Cell Culture

Prostate cancer cells (LNCaP) and healthy skin cells (HFF) were obtained from Tarbiat Modares University. LNCaP cells were cultured in RPMI medium, while HFF cells were cultured in DMEM medium, both supplemented with 10% fetal bovine serum and antibiotics. Nanoparticle deposition and solutions were introduced after 24 hours of culture.

MTT Analysis

The toxicity of nanoparticles and protein corona complex (graphene oxide, gold, SPION) was assessed using MTT assay on both healthy and cancer cells. After 24 hours of exposure to nanoparticles and the protein corona complex, MTT solution (0.5 mg/ml) was added, followed by incubation for 3 hours. Absorbance was measured at 570 nm after removing MTT and adding dimethyl sulfoxide (DMSO). The control group included healthy or cancerous cells cultured simultaneously with the treatment group but received no nanoparticle or nanoparticle-protein corona treatments.

Results

Characterization of Nanoparticles

Zeta Potential analysis was performed to scrutinize the size and surface charge of SPION nanoparticles. The obtained results showed a negative zeta potential (0-60 mV), indicating a net negative charge on the nanoparticle surface. Moreover, Dynamic Light Scattering (DLS) confirmed that the size of SPION nanoparticles fell within the typical nanoparticle range, ranging from 70 to 100 nanometers (Figure 1A, B). This characterization is crucial as it provides insights into the stability and behavior of SPION nanoparticles in

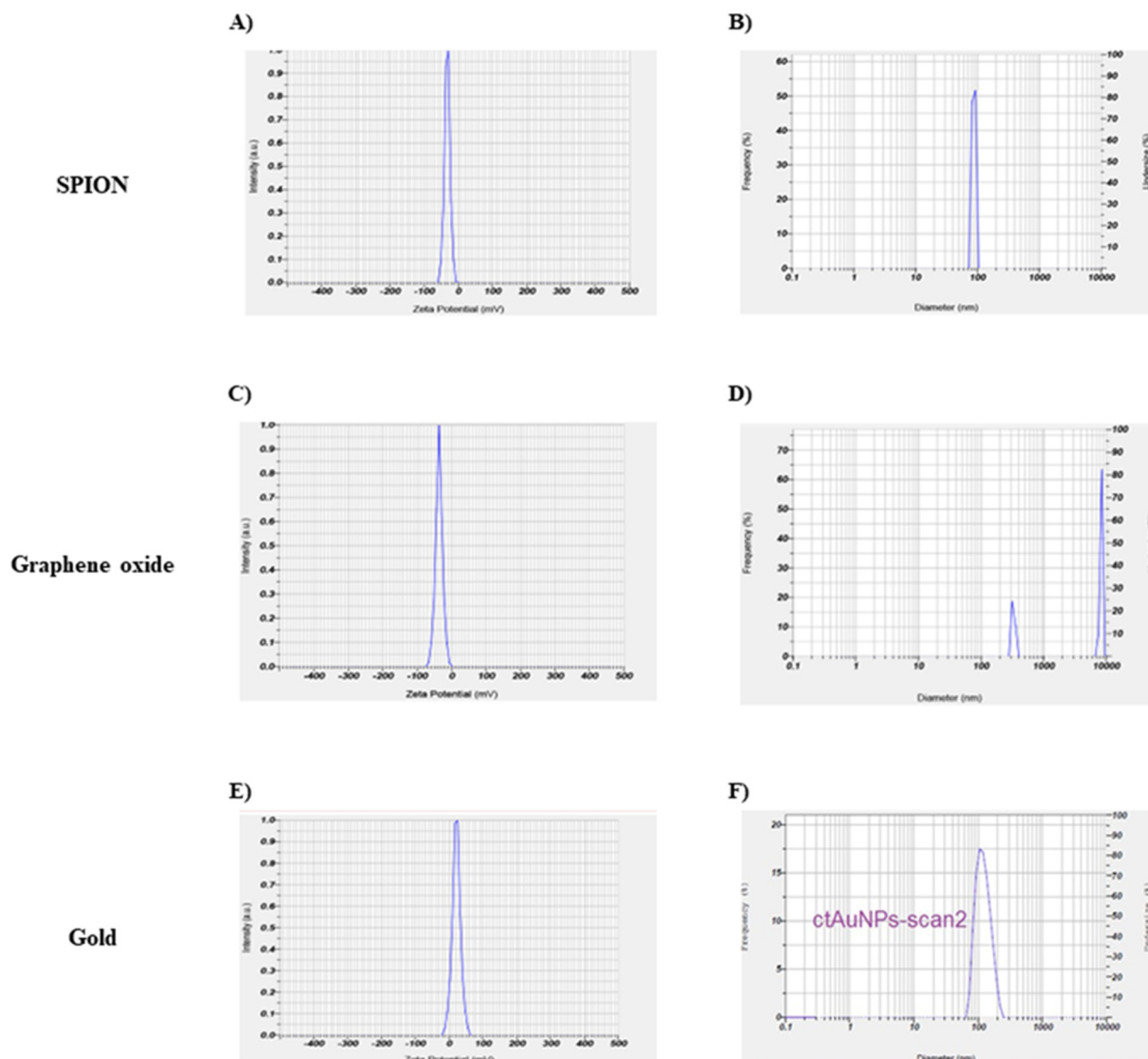


Figure 1. Dynamic Light Scattering Analysis of Nanoparticles. A) Surface Electric Charge Analysis of SPION Nanoparticles: The graph illustrates the surface electric charge of SPION nanoparticles, providing insights into their electrostatic characteristics. B) Size Distribution of SPION Nanoparticles: The curve depicts the size distribution profile of SPION nanoparticles, showing their dimensions as determined by Dynamic Light Scattering (DLS). C) Surface Electric Charge Analysis of graphene Oxide Nanoparticles: The graph illustrates the surface electric charge of graphene oxide nanoparticles, offering insights into their electrostatic characteristics. D) Size Distribution of Graphene Oxide Nanoparticles: The curve presents the size distribution profile of graphene oxide nanoparticles, as determined by DLS analysis. E) Surface Electric Charge Analysis of Gold Nanoparticles: The graph illustrates the surface electric charge of gold nanoparticles, providing insights into their electrostatic characteristics. F) Size Distribution of Gold Nanoparticles: The graph shows the size distribution profile of gold nanoparticles, as determined by DLS analysis.

biological environments.

Graphene oxide nanoparticles were subjected to similar analyses. DLS confirmed that the size of graphene oxide nanoparticles was constant throughout the nanoparticle scale, ranging from 300 to 400 nanometers, and Zeta Potential tests showed a negative

surface charge (0-70 mV) (Figure 1C, D). Understanding the physicochemical properties of these nanoparticles is fundamental for predicting their interactions with biological entities.

Gold nanoparticles were characterized using Zeta Potential and DLS. The results showed a negative zeta

potential (20-60 mV), and DLS confirmed a size range within the nanoparticle scale, varying from 250 to 60 nanometers (Figure 1E, F). These findings contribute to a comprehensive understanding of the unique properties of gold nanoparticles, which are crucial for their applications in cancer treatment.

Protein Corona Formation

Electrophoresis via SDS-PAGE was employed to examine the proteins loaded onto the nanoparticles, showing efficient protein corona formation (Figure 2). Distinct bands in the 70-100 kDa range indicated the presence of a well-formed protein corona on all three

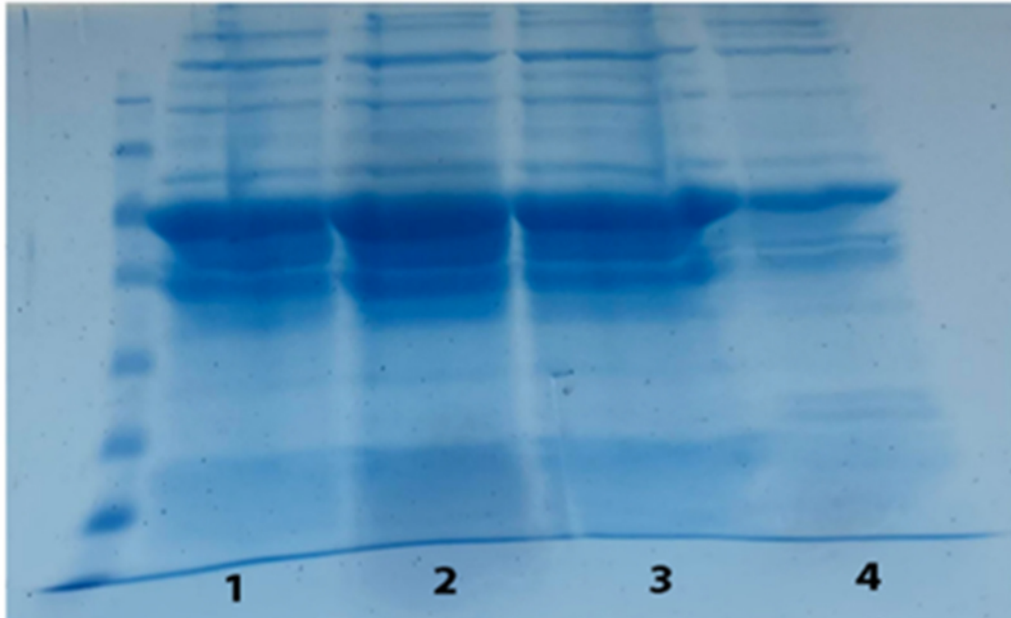


Figure 2. SDS-PAGE Analysis of Protein Corona Adsorbed on Nanoparticles. Lane 1: Graphene oxide nanoparticles with a concentration of 200, featuring a Protein Corona constituting 50% of loaded material. Lane 2: Gold nanoparticles with a concentration of 200, exhibiting a Protein Corona accounting for 50% of the loaded material. Lane 3: SPION (Superparamagnetic Iron Oxide Nanoparticles) with a concentration of 200, showcasing a Protein Corona representing 50% of the loaded material. Lane 4: Graphene oxide nanoparticles with a concentration of 200, displaying a Protein Corona constituting 5% of the loaded material. As depicted in Figure 4, the presence of a 70-100 kDa band confirms the existence of a Protein Corona on the nanoparticles.

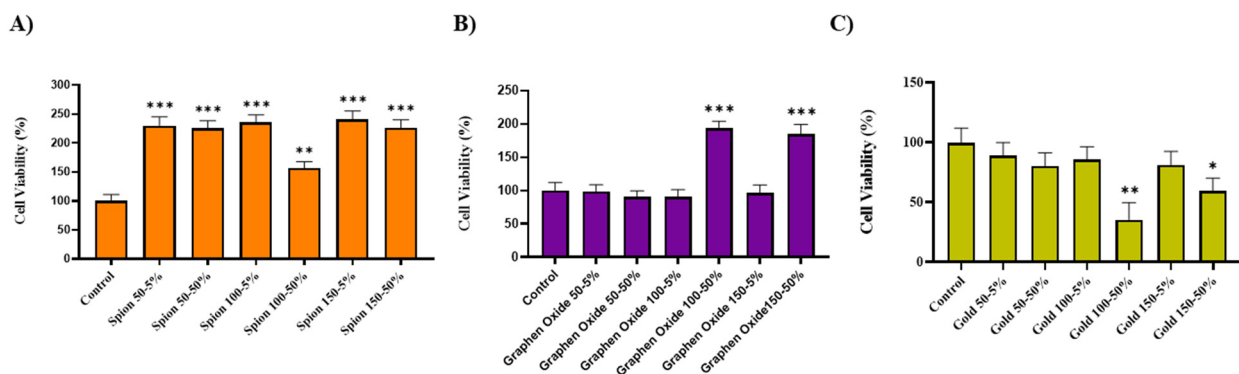


Figure 3. Investigating nanoparticle-induced toxicity on LNCAP cancer cells. This figure depicts the investigation into the potential toxicity of varying concentrations of SPION, graphene oxide, and gold nanoparticles on LNCAP cancer cells, providing crucial data on cell survival and viability via MTT testing after a 24-hour incubation period. A) MTT test evaluating cancer cell survival rates following 24-hour incubation with SPION nanoparticles. Analysis of the survival rate of LNCAP cancer cells after 24 hours of incubation with SPION nanoparticles at concentrations of 50, 100, and 150 $\mu\text{g}/\mu\text{l}$. B) MTT Test assessing cancer cell viability post 24-hour incubation with graphene oxide nanoparticles. Examination of the viability of cancer cells following a 24-hour incubation with graphene oxide nanoparticles at concentrations of 50, 100, and 150 $\mu\text{g}/\mu\text{l}$. C) MTT test used to investigate the viability of cancer cells following a 24-hour incubation with gold nanoparticles. Assessment of cancer cell viability following a 24-hour incubation with gold nanoparticles, utilizing concentrations of 50, 100, and 150 $\mu\text{g}/\mu\text{l}$.

types of nanoparticles. This successful loading of protein corona is pivotal as it influences the subsequent biological interactions of the nanoparticles.

Nanoparticle Toxicity on Cancer Cells

MTT assay was conducted to evaluate the toxicity of SPION, graphene oxide, and gold nanoparticles on LNCaP cancer cells across various concentrations (Figure 3). The results were intriguing in that they suggested that SPION and graphene oxide had no significant toxicity on cancer cells. However, gold nanoparticles exhibited a concentration-dependent toxicity, resulting in a significant drop in cell viability. This observation underscored the importance of discerning the differential effect of various nanoparticles on cancer cell lines.

Protein Corona Complex Toxicity on Cancer Cells

Expanding the study, the MTT test was extended to assess the toxicity of the protein corona complex (SPION, graphene oxide, gold) on cancer cells, incorporating both nanoparticle concentrations and different plasma percentages (Figure 4). The findings revealed that the protein corona complex of SPION exhibited no significant toxicity. In contrast, the toxicity of the graphene oxide complex increased and varied with concentration, although the gold complex was less hazardous than the individual nanoparticles. This nuanced response emphasizes the intricate interplay between nanoparticles, protein coronas, and plasma conditions in a biological milieu.

Nanoparticle Toxicity on Healthy Cells

Shifting the focus to healthy cells, the MTT test evaluated the effect of SPION, graphene oxide, and gold nanoparticles on HFF cells across varying concentrations (Figure 5). Consistent with the findings in cancer cells, SPION showed no toxicity, while graphene oxide exhibited minimal toxicity on healthy cells. In contrast, gold nanoparticles demonstrated concentration-dependent toxicity. This outcome highlights the selective effect of nanoparticles on cancer cells versus healthy cells.

Protein Corona Complex Toxicity on Healthy Cells

The examination of protein corona complex toxicity on healthy HFF cells was conducted using MTT test, considering different concentrations and plasma percentages (Figure 6). Intriguingly, the protein corona complex of SPION and graphene oxide demonstrated negligible toxicity. However, the gold complex exhibited increased toxicity, indicating a heightened impact in the presence of plasma. This nuanced response underscores the importance of considering the interplay between protein coronas and nanoparticles in the context of healthy cell viability.

These comprehensive results shed light on the delicate link between nanoparticle properties, protein coronas, and cellular responses, setting the groundwork for targeted and individualized cancer treatments.

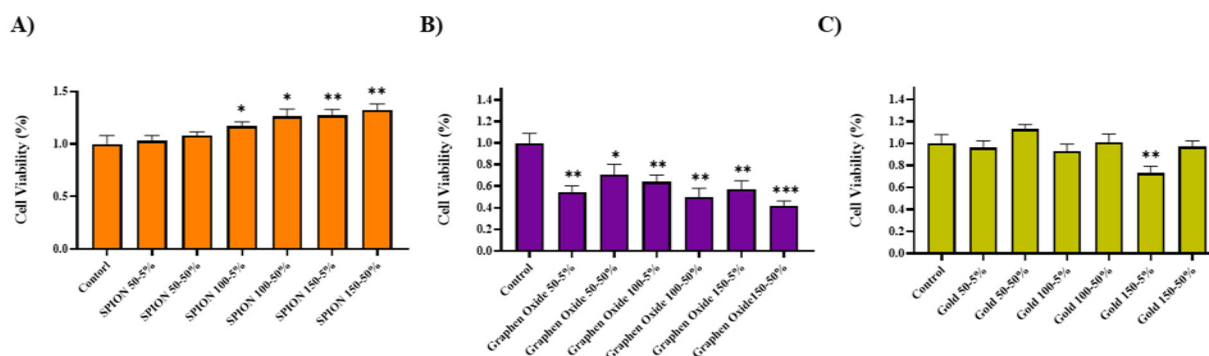


Figure 4. Evaluation of Nanoparticle-Induced Toxicity on LNCaP Cancer Cells. This figure illustrates the effect of various concentrations of protein corona complex nanoparticles on the toxicity levels observed in LNCaP cancer cells, providing valuable insights into the potential effects of SPION, graphene oxide, and gold nanoparticles on cell survival and viability. A) MTT test assessing cancer cell survival rates post 24-hour incubation with SPION nanoparticles. Examining of the survival rate of LNCaP cancer cells after 24 hours of incubation with SPION nanoparticles featuring 5% and 50% protein corona complexes. Concentrations employed: 50, 100, and 150 µg/µl. B) MTT test evaluating cancer cell viability post 24-hour incubation with graphene oxide nanoparticles. Assessment of the viability of LNCaP cancer cells following a 24-hour incubation with graphene oxide nanoparticles, including 5% and 50% protein corona complexes. Concentrations utilized: 50, 100, and 150 µg/µl. C) MTT test investigating cancer cell viability post 24-hour incubation with gold nanoparticles. Evaluation of the viability of LNCaP cancer cells after a 24-hour incubation with gold nanoparticles, featuring 5% and 50% protein corona complexes. Concentrations tested: 50, 100, and 150 µg/µl.

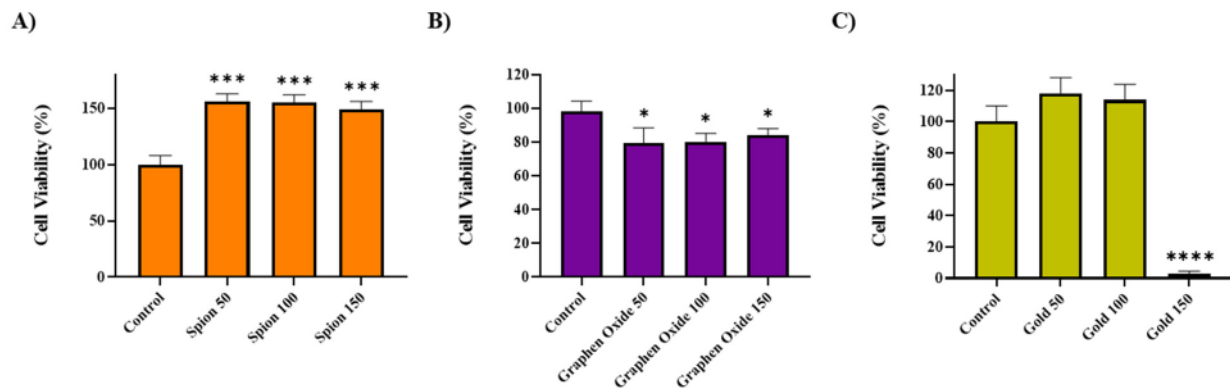


Figure 5. Assessment of Nanoparticle Toxicity on HFF Cells. This figure depicts the possible toxicity of SPION, graphene oxide, and gold nanoparticles at different doses on healthy HFF cells. MTT assays were used to determine cell viability following a 24-hour incubation period, giving significant information on the effects of these nanoparticles on healthy cell populations. A) MTT Test Evaluating the Viability of Healthy HFF Cells Post 24-Hour Incubation with SPION Nanoparticles. Studying the viability of healthy HFF cells following a 24-hour incubation with SPION nanoparticles at concentrations of 50, 100, and 150 µg/µl. B) MTT Test Examining the Viability of Healthy HFF Cells Post 24-Hour Incubation with graphene Oxide Nanoparticles. Evaluating of the viability of healthy HFF cells after a 24-hour incubation with graphene oxide nanoparticles, utilizing concentrations of 50, 100, and 150 µg/µl. C) MTT Test Investigating the Viability of Healthy HFF Cells Post 24-Hour Incubation with Gold Nanoparticles. Analysis of healthy HFF cell viability following a 24-hour incubation with gold nanoparticles, employing concentrations of 50, 100, and 150 µg/µl.

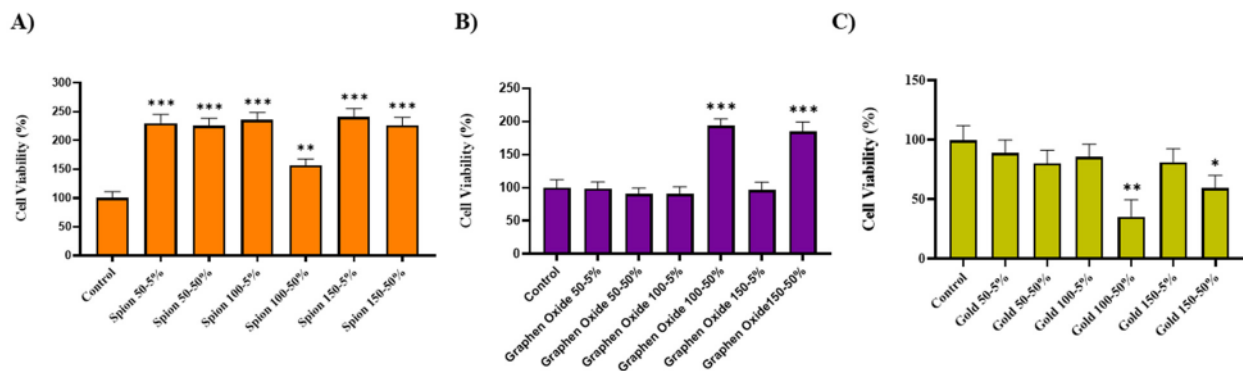


Figure 6. Assessment of Nanoparticle-Induced Toxicity on HFF Cells. This figure presents a comprehensive exploration of nanoparticle-induced toxicity on healthy HFF cells, employing MTT tests to assess survival rates, and viability after a 24-hour incubation period. The study investigates the impact of SPION, graphene oxide, and gold nanoparticles, each featuring 5% and 50% protein corona complexes, across various concentrations. A) MTT Test for Evaluating Survival Rates of Healthy HFF Cells After 24-Hour Incubation with SPION Nanoparticles. Examination of the survival rate of healthy HFF cells following a 24-hour incubation with SPION nanoparticles, featuring 5% and 50% protein corona complexes, at concentrations of 50, 100, and 150 µg/µl. B) MTT Test Assessing Viability of Healthy HFF Cells Post 24-Hour Incubation with graphene Oxide Nanoparticles. Evaluating of the viability of healthy HFF cells after a 24-hour incubation with graphene oxide nanoparticles, incorporating 5% and 50% protein corona complexes, with concentrations of 50, 100, and 150 µg/µl. C) MTT Test Investigating Viability of Healthy HFF Cells After 24-Hour Incubation with Gold Nanoparticles. Analysis of healthy HFF cell viability after a 24-hour incubation with gold nanoparticles, presenting 5% and 50% protein corona complexes, at concentrations of 50, 100, and 150 µg/µl.

Discussion

Our investigation into the complex interactions between nanoparticles and protein coronas, as well as their implications for prostate cancer and healthy cells, has produced nuanced findings that have substantial implications for personalized medicine. The systematic

characterization of SPION, graphene oxide, and gold nanoparticles, guided by the principles of personalized medicine, provided a robust foundation for understanding their behavior in biological systems.

The negative zeta potentials observed for SPION, graphene oxide, and gold nanoparticles, coupled with their consistent sizes within the nanoparticle range,

align with the understanding that these characteristics are pivotal ensure stability and effective cellular interactions. Our findings resonate with previous studies emphasizing the importance of well-defined sizes and negative zeta potentials in facilitating enhanced cellular uptake and therapeutic efficacy.

Comparisons with prior research highlight the consistency in nanoparticle behavior across different studies. However, it's crucial to acknowledge that variations in synthesis methods, nanoparticle coatings, and experimental conditions can contribute to differences in outcomes. This underscores the need for standardization and careful consideration of experimental variables when interpreting and comparing results across studies.

Our study into protein corona formation on nanoparticles revealed efficient loading across all three types, as evidenced by SDS-PAGE analyses. The distinct bands in the 70-100 kDa range signify successful protein corona formation. This aligns with the dynamic nature of protein coronas, where proteins in biological milieu bind to nanoparticle surfaces, influencing their subsequent interactions with cells. Comparisons with previous studies highlight the advancing understanding of protein corona dynamics. Research has shown that the composition of protein coronas may fluctuate based on nanoparticle characteristics and the surrounding environment, affecting cellular interactions. Our findings align with this perspective, emphasizing the need to consider the intricate relationship between nanoparticles and protein coronas for a nuanced understanding of their biological impact.

MTT assay results indicated selective toxicity of gold nanoparticles on LNCaP prostate cancer cells, while SPION and graphene oxide exhibited minimal effect. These observations align with the growing interest in tailoring nanoparticle-based therapies for targeted and effective cancer treatments, minimizing adverse effects on healthy cells.

Comparisons with previous studies highlight the diversity in nanoparticle responses across various cancer cell lines. While our findings align with research demonstrating the potential of gold nanoparticles in inducing cytotoxic effects on cancer cells (27), nuanced response observed with SPION and graphene oxide underscores the importance of tailoring nanoparticle selection based on specific cancer types.

In recent advancements in nanomedicine, a novel hypothesis surfaced, proposing that individuals possess distinctive protein coronas exclusive to their unique physiological makeup. This notion suggests that alterations in the structure and concentration of plasma

proteins during various diseases may impact their propensity to bind to nanoparticle surfaces, thereby influencing the interaction with nanoparticles (14). In our investigation of protein corona complexes, we found little toxicity for SPION, concentration-dependent toxicity for graphene oxide, and a complicated reaction for gold complexes. The PSA aptamer aggregated on a QCM gold electrode, and frequency alterations were observed upon the introduction of the PSA antigen. Furthermore, this method has the potential to be employed for detecting other cancer-associated biomarkers (28). These findings underscored the influence of protein coronas on the biological fate of nanoparticles, with potential implications for therapeutic strategies. The comparisons with prior studies highlight the variability in protein corona complex toxicity. Some studies suggest protective roles for protein coronas in mitigating nanoparticle toxicity, while others indicate modulatory effects on nanoparticle interactions. Our findings contribute to this nuanced understanding, emphasizing the need for comprehensive investigations into protein corona dynamics for informed therapeutic interventions.

In assessing nanoparticle toxicity on healthy HFF cells, we observed a selective effect, with gold nanoparticles displaying concentration-dependent toxicity. This selective cytotoxicity aligns with the principles of personalized medicine, emphasizing tailored treatments with minimal side effects on healthy cells. Comparisons to previous research highlight the relevance of addressing nanoparticles' dual influence on cancer and healthy cells. While previous research has investigated the potential toxicity of various nanoparticles, our results add to the increasing knowledge of selective cytotoxicity by offering insights into the varied responses of healthy and cancer cells to different nanoparticle forms.

Examining the protein corona complex toxicity on healthy HFF cells revealed intriguing results. SPION and graphene oxide complexes showed negligible toxicity, while gold complexes exhibited increased toxicity, particularly in the presence of plasma. This heightened impact emphasizes the dynamic nature of protein coronas, influencing nanoparticle behavior in the context of healthy cell viability.

Comparisons with prior research highlight the complex and multifaceted nature of protein corona interactions. While some studies imply that protein coronas play protective roles in nanoparticle toxicity, our results are consistent with previous research showing that protein coronas may control nanoparticle interactions, altering their biological consequences. This nuanced perspective underscored the need for a

comprehensive understanding of protein corona dynamics to unravel the intricacies of nanoparticle behavior in biological systems.

Graphene, due to its superior biocompatibility, lower cost, and absence of toxic metal pollutants, is less toxic compared to gold. However, studies on graphene oxide's cytotoxicity present contradictory findings, suggesting toxicity may depend on size, synthesis method, route of administration, and exposure time. Uncoated SPION is more toxic than coated particles. Pre-incubation of SPION with nanoparticles before exposure reduces cellular absorption and toxicity, preventing unfavorable cell-nanoparticle or serum protein-nanoparticle interactions. Results indicate that SPION nanoparticles exhibit lower toxicity, even with protein corona, making them weaker than other nanoparticles. Gold nanoparticles show increased toxicity to healthy cells with rising concentrations, and protein corona loading reduces toxicity in cancer cells. Graphene oxide, less toxic than gold, shows increased toxicity to cancer cells with protein corona loading. Considering these findings, graphene oxide emerges as a potentially superior option compared to other nanoparticles.

In addition to the availability of various effective pharmaceutical medications, the factors, such as inadequate peptide synthesis techniques, technological constraints, high manufacturing costs, insufficient understanding of their mechanisms, and a lack of sophisticated computational resources may have contributed significantly to the challenges faced (29). Our study's implications for individualized medicine are significant. The observed selective toxicity and unique behaviors of nanoparticles and protein corona complexes highlight the significance of personalizing therapy to particular patient features. This aligned with the core tenets of personalized medicine, where treatment strategies are customized to optimize efficacy while minimizing adverse effects.

Conclusion

This study explored the interactions between nanoparticles and protein coronas, focusing on their differential toxicity in the prostate cancer and normal cell lines. It highlights that gold nanoparticles exhibit greater toxicity towards prostate cancer cells compared to superparamagnetic iron oxide nanoparticles (SPIONs) and graphene oxide, which show minimal toxicity to healthy cells. These results underscore the importance of protein corona composition in determining nanoparticle effectiveness and safety in medicinal applications. Future study should look at the individual proteins involved in corona formation and their influence on nanoparticle behavior, as well as how

changing plasma conditions alter these interactions. Such insights could lead to personalized medicine approaches that enhance targeted cancer therapies while minimizing harm to healthy tissues.

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