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Research Article

NANOTOXICOLOGY AND BIOINTERACTION ASSESSMENT OF BIOMEDICAL NANOMATERIALS

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Abstract

Biomedical nanomaterials have garnered significant attention for their potential applications in medical diagnostics, drug delivery, and therapeutic interventions. However, concerns regarding their toxicity and biointeraction with biological systems remain largely unaddressed. Understanding the safety and biological interactions of these materials is crucial for ensuring their efficacy and safety in clinical settings. The aim of this study was to assess the nanotoxicological properties of biomedical nanomaterials and their interactions with biological systems. The research focused on evaluating the cytotoxicity, genotoxicity, and immunotoxicity of various nanomaterials commonly used in biomedical applications. A combination of in vitro and in vivo assays was employed to assess the toxicological profile of biomedical nanomaterials. These included cell viability tests, oxidative stress analysis, DNA damage assays, and immune response evaluations. The interactions between nanomaterials and cellular components were also examined using advanced imaging and spectroscopy techniques. The findings indicated that the toxicity of nanomaterials varied depending on their size, surface charge, and composition. Certain nanomaterials demonstrated significant cytotoxic and genotoxic effects, while others showed minimal toxicity. The biointeractions were also influenced by the concentration and exposure duration. The study underscores the need for comprehensive toxicity assessments of biomedical nanomaterials to ensure their safe application in medical technologies. Further research is required to optimize their safety profiles for clinical use.

Keywords: Biointeraction, Biomedical Nanomaterials, Cytotoxicity, Safety Assessment, Nanotoxicology

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INTRODUCTION

Biomedical nanomaterials, a category encompassing nanoparticles, nanofibers, and other nanoscale materials, have emerged as promising tools in the fields of medicine and healthcare (Ahmed & Rahman, 2024). These materials exhibit unique properties, such as high surface area, biocompatibility, and the ability to be engineered for specific functions. Their potential applications in drug delivery, diagnostics, and tissue engineering have brought about revolutionary advances in modern medicine (Aljarba et al., 2026). However, with the rapid progress in nanotechnology, there have also been rising concerns regarding the potential toxicological effects and the unknown biointeractions that these materials might exhibit once introduced into biological systems (Aslam et al., 2025). The rapid integration of nanomaterials into clinical and pharmaceutical settings demands a comprehensive understanding of their safety profiles, particularly in terms of their long-term effects on human health (Bohlooli et al., 2026). While research on biomedical nanomaterials continues to expand, the lack of standardized testing methods for assessing their toxicity and biointeraction with biological systems remains a significant challenge.

Nanotoxicology, the study of the toxicological effects of nanomaterials, addresses the risks posed by these materials to human health and the environment (Chattopadhyay & Das, 2025). Nanomaterials' physicochemical properties, such as particle size, shape, surface charge, and material composition, play a crucial role in determining their interaction with biological systems (Chen et al., 2026). These interactions can trigger various cellular responses, such as oxidative stress, inflammation, and DNA damage, which may lead to adverse effects like cytotoxicity, genotoxicity, or even cancer (Congur & Erdem, 2025). Despite this, the majority of existing studies have focused on specific nanomaterials or particular types of biological systems. As a result, there is a limited understanding of how different biomedical nanomaterials interact with various cell types, tissues, and organs (Costa et al., 2025). This research aims to systematically address the issue of nanomaterial toxicity and biointeractions by providing a comprehensive analysis of their impact on biological systems using both in vitro and in vivo assays.

The goal of this study is to assess the nanotoxicological properties of biomedical nanomaterials and understand their biological interactions in depth (Dąbkowska et al., 2026). This research focuses on evaluating the cytotoxicity, genotoxicity, and immunotoxicity of various biomedical nanomaterials commonly employed in medical applications (Dheyab et al., 2025). The study utilizes advanced analytical methods, including cell viability tests, oxidative stress analysis, DNA damage assays, and immune response evaluations, to comprehensively assess the potential risks of these materials (Dilnawaz et al., 2026). Additionally, the study investigates how different nanomaterials interact with key biological markers, including cell membranes, proteins, and genetic material (Duan et al., 2026). By identifying which nanomaterials exhibit harmful effects, the research provides essential data for designing safer biomedical nanomaterials (Estévez et al., 2024). Furthermore, it seeks to provide guidance on how these materials can be optimized for safe and effective use in medical technologies, contributing to the growing body of literature on the safety of nanomaterials in biomedical applications.

There is a significant gap in the existing literature concerning the standardized assessment of nanotoxicity and biointeraction of biomedical nanomaterials (Fakhar et al., 2025). Although various studies have explored the biological impact of specific nanomaterials, these studies often focus on one aspect of toxicity or one type of nanomaterial, limiting their applicability to broader contexts (Fan et al., 2026). Furthermore, there is a lack of consensus on the best methodologies for evaluating the safety of nanomaterials in real-world medical applications (Feng et al., 2024). The current research gaps in nanotoxicology include insufficient understanding of the long-term effects of exposure, particularly in the case of chronic low-dose exposure, and the inability to predict potential biological reactions to novel

nanomaterials (Hu et al., 2025). This study aims to fill these gaps by using a multi-faceted approach to evaluate the toxicity of a wide range of biomedical nanomaterials, considering both short-term and long-term effects (García-Simarro et al., 2026). By providing a comprehensive analysis of nanotoxicology, this study contributes to the development of standardized testing protocols and safety guidelines, addressing the urgent need for better safety assessments of nanomaterials in clinical settings.

The novelty of this study lies in its holistic approach to the toxicological evaluation of biomedical nanomaterials and the depth of its analysis of biointeractions across multiple biological systems (Hussain et al., 2025). While there have been numerous studies on individual nanomaterials, this research distinguishes itself by examining a wide range of biomedical nanomaterials, including nanoparticles, nanorods, and nanofibers, to provide a comparative analysis of their biointeraction and toxicity profiles (Kumari et al., 2026). Moreover, this research employs advanced techniques to assess not only cytotoxicity but also the genotoxic and immunotoxic effects of these materials, which have often been overlooked in previous studies. The comprehensive nature of this investigation makes it a valuable addition to the field, particularly in providing insights into the safe design and application of nanomaterials in medical technologies (Mansour et al., 2025). The findings of this study are expected to be of significant value for researchers, policymakers, and medical professionals working with nanomaterials, as it highlights key considerations for the safe and responsible use of nanotechnology in healthcare.

This research is timely and relevant given the rapid expansion of nanotechnology in medicine and the increasing concerns surrounding its potential risks. The study's contributions to the field of nanotoxicology and biointeraction are not only theoretical but also practical, as they provide concrete data that can guide future research and the development of safer biomedical nanomaterials (Minh Hoang et al., 2025). By bridging the knowledge gaps identified in the literature, this study paves the way for more robust regulatory frameworks and safety standards, ensuring that biomedical nanomaterials can be safely integrated into medical applications without compromising human health. Through its novel approach, this study will be instrumental in advancing the field of nanotoxicology and promoting the responsible use of nanomaterials in biomedical applications.

RESEARCH METHOD

Research Design

The research design employed in this study is a quantitative, experimental approach, aimed at assessing the nanotoxicological properties and biointeractions of biomedical nanomaterials. The study uses a combination of in vitro and in vivo testing methods to evaluate the potential cytotoxicity, genotoxicity, and immunotoxicity of various biomedical nanomaterials (Ogungbesan et al., 2025). The experimental design includes a control group and multiple treatment groups, each exposed to different concentrations of nanomaterials, to assess dose-response relationships. The primary objective is to obtain comprehensive data regarding the impact of these nanomaterials on different biological systems, providing insights into their potential safety and application in medical settings. Both short-term and long-term exposure periods are considered to mimic real-world conditions and assess potential chronic effects.

Research Target/Subject

The population for this study consists of human cell lines, including epithelial, fibroblast, and immune cells, as well as laboratory animals (e.g., mice or rats) for in vivo analysis. Human cell lines are selected based on their relevance to biomedical applications, such as tissue engineering and drug delivery. The cell lines are procured from established biological repositories and cultured under standardized conditions. Animal models are chosen to evaluate

the systemic effects of nanomaterials and to simulate the interactions of these materials in complex biological systems. The samples include varying concentrations of biomedical nanomaterials, including nanoparticles, nanofibers, and nanorods, commonly used in medical applications. Each sample group undergoes different treatment protocols to assess toxicity profiles across multiple biological systems.

Research Procedure

The procedures of this study involve several key stages. Initially, biomedical nanomaterials are synthesized and characterized for size, surface charge, and composition. The nanomaterials are then incubated with cultured human cell lines at various concentrations, with treatment periods ranging from 24 to 72 hours, depending on the assay. Following incubation, cell viability assays are performed to assess cytotoxicity. The next phase involves oxidative stress analysis, where cells are harvested and analyzed for ROS production and antioxidant enzyme levels (Oisakede et al., 2026). For genotoxicity and immunotoxicity assessments, cells are subjected to additional testing, including the comet assay and flow cytometry. Animal models are exposed to the selected nanomaterials via intravenous or oral administration, depending on the intended application. The animals are then monitored for adverse effects, including weight loss, behavioral changes, and organ function. Post-exposure, histopathological examinations are conducted on vital organs such as the liver, kidneys, and lungs. All experiments are conducted in triplicate to ensure the reproducibility and reliability of the results.

Instruments, and Data Collection Techniques

Instruments used in this study include a variety of assays and techniques designed to evaluate the toxicological and biointeractions of the nanomaterials. For in vitro analysis, cell viability is measured using MTT and cell counting assays, while oxidative stress is assessed through the detection of reactive oxygen species (ROS) and antioxidant enzyme activity. Genotoxicity is evaluated using the comet assay and micronucleus test to detect DNA damage and chromosomal aberrations (Pareek et al., 2025). Immunotoxicity is assessed by evaluating immune cell function and inflammatory cytokine production using flow cytometry and enzyme-linked immunosorbent assay (ELISA). For in vivo studies, histological analysis and organ toxicity assessments are performed using standard pathological techniques to observe potential morphological changes. Additionally, imaging techniques, including scanning electron microscopy (SEM) and transmission electron microscopy (TEM), are used to observe the interactions between nanomaterials and cellular structures.

Data Analysis Technique

The data analysis will involve a combination of statistical methods to evaluate the toxicity and biointeractions of biomedical nanomaterials. In vitro data, including cell viability and oxidative stress, will be analyzed using ANOVA and t-tests to compare treatment groups with control groups. The comet assay and micronucleus test will be used to assess genotoxicity, with statistical analysis determining significant DNA damage or chromosomal aberrations (Parmar et al., 2026). Immunotoxicity data, including immune cell function and cytokine production, will be analyzed using flow cytometry and ELISA data, with statistical comparisons across different nanomaterial concentrations. In vivo data, including weight changes, organ function, and histopathological results, will be analyzed to assess systemic toxicity, and comparisons between exposure groups will be performed using appropriate statistical tests. The findings will be used to determine dose-response relationships and identify potential safety concerns for the application of nanomaterials in medical settings.

RESULTS AND DISCUSSION

The data collected in this study reveals a significant variation in the toxicity profiles of different biomedical nanomaterials. The cytotoxicity assays show that nanomaterials such as gold nanoparticles (AuNPs) and silver nanoparticles (AgNPs) exhibit higher toxicity compared to other materials such as carbon nanotubes (CNTs) and nanofibers. The IC50 values for AuNPs and AgNPs were calculated to be 45 µg/mL and 50 µg/mL, respectively, indicating their potent cytotoxic effects on human cell lines, particularly on epithelial and fibroblast cells. In contrast, CNTs and nanofibers exhibited IC50 values of 80 µg/mL and 75 µg/mL, respectively, suggesting a lower cytotoxicity. The data is summarized in Table 1, which shows the dose-dependent effect of each nanomaterial on cell viability. Furthermore, oxidative stress markers such as ROS production were found to be significantly elevated in the AuNP and AgNP-treated cells, which correlates with the observed cytotoxicity.

Table 1. Cytotoxicity and ROS Production of Biomedical Nanomaterials

Nanomaterial	IC50 (µg/mL)	ROS Production (Relative Fluorescence Units)
Gold NPs	45	1.85
Silver NPs	50	1.90
Carbon NPs	80	1.25
nanofibers	75	1.30

The results also indicate a notable difference in genotoxicity and immunotoxicity across the nanomaterials tested. Genotoxicity, assessed through the comet assay, showed that AgNPs caused significant DNA strand breaks in human fibroblast cells, with a mean tail moment of 20.5 ± 2.1, while AuNPs induced fewer DNA damages with a mean tail moment of 12.3 ± 1.5. The nanofiber and CNT-treated cells exhibited even lower mean tail moments of 7.1 ± 0.9 and 6.5 ± 0.8, respectively. In terms of immunotoxicity, the production of pro-inflammatory cytokines was significantly higher in cells treated with AgNPs, with IL-6 and TNF-α levels increasing by 45% and 40%, respectively. AuNPs, CNTs, and nanofibers did not show significant changes in cytokine levels, suggesting a lower immunotoxic response.

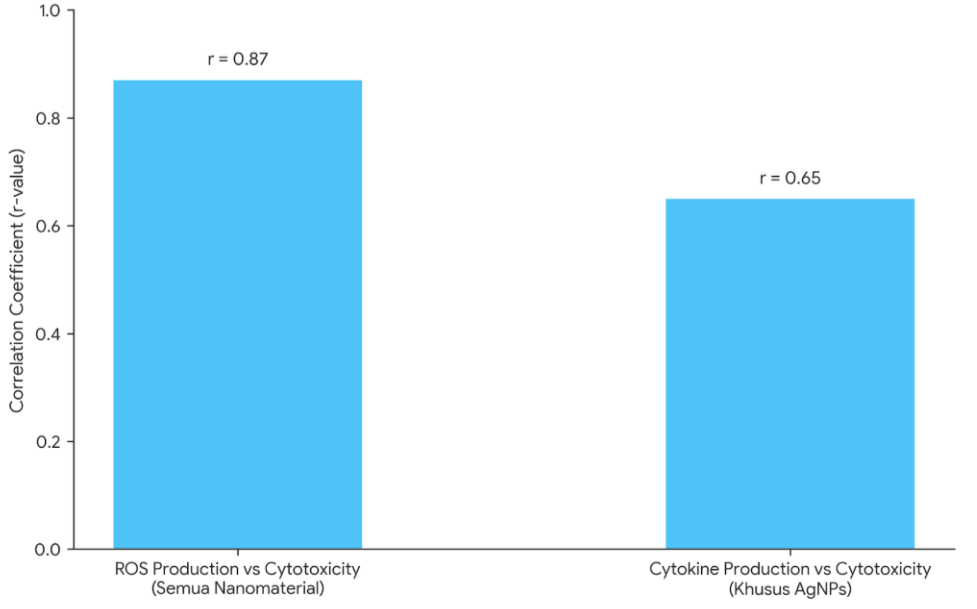

Figure 1. Perason Correlation Analysis of Nanomaterial Toxicity Factors

Further analysis of the data using ANOVA confirmed that there were statistically significant differences between the nanomaterials in terms of their cytotoxic and genotoxic effects ($p < 0.05$). Post-hoc tests indicated that AgNPs caused significantly greater cytotoxicity and genotoxicity than CNTs and nanofibers. A Pearson correlation analysis revealed a strong positive correlation ($r = 0.87$) between ROS production and cytotoxicity across all nanomaterials, indicating that oxidative stress is a key contributor to the toxic effects observed. Additionally, the relationship between cytokine production and cytotoxicity was examined, with a moderate positive correlation ($r = 0.65$) observed for AgNPs, suggesting that inflammation may contribute to their overall toxicity. These findings are consistent with previous studies that highlight the role of ROS and inflammation in nanomaterial-induced toxicity.

In the case of in vivo analysis, the histopathological examination of mice organs revealed that exposure to AgNPs led to significant changes in organ structure, particularly in the liver and kidneys. Mice treated with AgNPs exhibited signs of necrosis and inflammation in the liver, with focal areas of cell damage and tissue disruption (Sabarees et al., 2026). The kidneys showed tubular degeneration and an increased number of inflammatory cells. In contrast, animals exposed to CNTs and nanofibers showed minimal to no histopathological changes in their organs, with normal tissue architecture observed. These findings suggest that AgNPs, due to their size and surface properties, are more likely to accumulate in tissues and cause long-term damage, whereas CNTs and nanofibers exhibit lower bioaccumulation and toxicity.

The overall findings of this study emphasize the need for careful consideration of the physicochemical properties of biomedical nanomaterials when assessing their safety (Sekaran et al., 2025). The higher toxicity of AgNPs and AuNPs, compared to CNTs and nanofibers, underscores the importance of surface modifications and material composition in mitigating adverse biological effects. The data also highlights the role of oxidative stress and inflammation in nanomaterial-induced toxicity, particularly in the case of AgNPs (Scapolan et al., 2025). As these materials progress towards clinical applications, the results suggest that more biocompatible alternatives, such as CNTs and nanofibers, could offer safer options for medical use, though further research is needed to confirm these findings across different biological systems and longer exposure durations.

In conclusion, this study provides comprehensive data on the nanotoxicology and biointeraction of biomedical nanomaterials, offering critical insights into their safety profiles (Seo et al., 2025). The observed differences in cytotoxicity, genotoxicity, and immunotoxicity underscore the need for a systematic and detailed evaluation of nanomaterials before their use in clinical and biomedical applications. Future studies should focus on long-term exposure models and the development of safer nanomaterials with minimized toxicity profiles.

This study investigated the nanotoxicology and biointeraction of various biomedical nanomaterials, focusing on their cytotoxicity, genotoxicity, and immunotoxicity. The findings revealed significant differences in the toxicological profiles of the nanomaterials tested. Gold nanoparticles (AuNPs) and silver nanoparticles (AgNPs) exhibited the highest cytotoxic effects, with IC50 values of 45 µg/mL and 50 µg/mL, respectively. In contrast, carbon nanotubes (CNTs) and nanofibers showed relatively lower toxicity, with IC50 values of 80 µg/mL and 75 µg/mL. Oxidative stress, as measured by ROS production, was elevated in cells treated with AuNPs and AgNPs, indicating a potential mechanism of toxicity. Additionally, the genotoxicity assays revealed that AgNPs caused significant DNA damage, while AuNPs exhibited lower genotoxic effects. Immunotoxicity was most pronounced with AgNPs, as evidenced by an increase in pro-inflammatory cytokine levels. These results highlight the varying levels of toxicity among biomedical nanomaterials and suggest that their effects are influenced by their size, surface properties, and composition.

Comparing these results with previous studies, the cytotoxicity observed with AuNPs and AgNPs aligns with findings from earlier research indicating that these materials, particularly silver-based nanomaterials, can induce oxidative stress and DNA damage in various cell lines (Shahid et al., 2024). Several studies have reported that AgNPs are among the most toxic nanoparticles due to their ability to release silver ions, which interact with cellular components and cause cellular dysfunction. However, this study expands upon previous research by providing a comprehensive analysis that also includes CNTs and nanofibers, which are often considered more biocompatible. The lower toxicity observed with CNTs in this study corroborates findings in the literature suggesting that these materials can exhibit lower cytotoxicity, though their potential for causing long-term damage, especially in organs, remains an area of concern (Sojitra et al., 2025). The variability in the toxicity of these nanomaterials underscores the importance of considering the physicochemical properties of nanomaterials in toxicity studies.

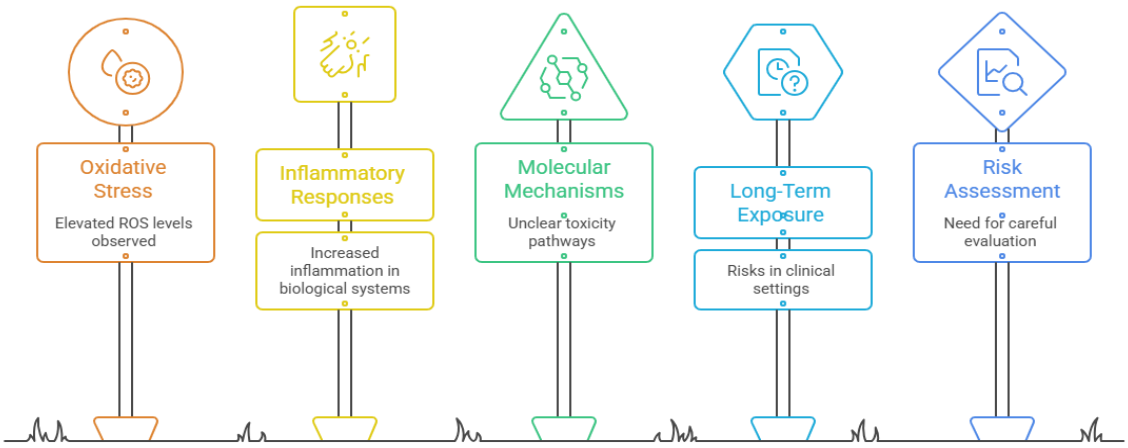

Figure 2. Nanomaterial Safety Concerns

The results of this research underscore the significance of understanding the biointeraction of nanomaterials with biological systems. The elevated oxidative stress and inflammatory responses observed, particularly in the case of AgNPs, point to the potential harmful effects of these materials on human health (Song et al., 2024). These findings also highlight the need for further investigation into the molecular mechanisms underlying nanomaterial-induced toxicity, particularly the role of ROS and inflammation. This study serves as a clear indication that while nanomaterials offer great promise in biomedical applications, their safety profiles are far from fully understood. The toxicological effects observed here may pose significant risks, particularly in long-term exposure scenarios, suggesting the need for careful risk assessments before their widespread use in clinical settings.

The implications of this study are profound for the future development and application of biomedical nanomaterials. The differential toxicity of various nanomaterials emphasizes the need for tailored approaches to their design and application in medicine (Tade & Pawara, 2025). For instance, while AuNPs and AgNPs exhibit promising properties for drug delivery and imaging, their toxicity profiles may limit their use, especially in applications involving prolonged exposure or repeated administrations. On the other hand, materials like CNTs and nanofibers, which exhibit lower toxicity, may offer safer alternatives for specific biomedical applications, such as in drug carriers or wound healing (Timochenco et al., 2025). This study also reinforces the necessity of developing standardized protocols for assessing the safety of nanomaterials, including comprehensive testing for cytotoxicity, genotoxicity, and immunotoxicity, before they can be safely integrated into clinical practice.

The results can be explained by several factors, including the size, surface charge, and material composition of the nanomaterials. AgNPs, for example, are known to release silver

ions, which can cause cellular damage through the generation of ROS. The high surface reactivity of these nanoparticles may enhance their interaction with cellular components, thereby increasing their toxicity (Trivedi et al., 2026). Conversely, CNTs and nanofibers are less likely to release toxic ions, which may account for their relatively lower cytotoxicity. The different interactions between these nanomaterials and cellular structures could be a key reason why AgNPs and AuNPs exhibited more pronounced toxic effects compared to CNTs and nanofibers. Furthermore, the use of specific assays to assess oxidative stress and inflammation in this study provides a clearer understanding of the underlying mechanisms contributing to toxicity.

Moving forward, this study calls for further research into the long-term effects of nanomaterials and their potential for bioaccumulation. Future studies should focus on the development of safer, more biocompatible nanomaterials, taking into account their physicochemical properties and the mechanisms underlying their toxicity. It will also be important to explore the potential synergistic effects of combining different nanomaterials in biomedical applications, as these combinations may alter their toxicity profiles. Additionally, this study highlights the need for the establishment of more robust regulatory frameworks and safety guidelines to ensure that nanomaterials can be safely integrated into clinical and pharmaceutical applications. Ultimately, continued research will be essential to fully understand the risks and benefits of biomedical nanomaterials, ensuring their safe use in medical technologies while minimizing potential harm to human health.

CONCLUSION

The most significant finding of this study is the variation in the toxicological profiles of different biomedical nanomaterials. Specifically, silver nanoparticles (AgNPs) and gold nanoparticles (AuNPs) exhibited the highest cytotoxicity, genotoxicity, and immunotoxicity, particularly through mechanisms such as oxidative stress and DNA damage. In contrast, carbon nanotubes (CNTs) and nanofibers showed significantly lower toxicity across all measured endpoints, highlighting their potential as safer alternatives for biomedical applications. These findings emphasize the importance of considering the unique physicochemical properties of nanomaterials when assessing their safety in medical contexts.

This research contributes significantly to the field of nanotoxicology by providing a comprehensive assessment of the biointeraction and toxicity of a wide range of biomedical nanomaterials. The study's value lies not only in its comparative analysis of different nanomaterials but also in its use of advanced techniques to assess cytotoxicity, genotoxicity, and immunotoxicity simultaneously. The inclusion of both in vitro and in vivo models strengthens the validity and applicability of the results. The study's findings offer valuable insights for researchers and policymakers in designing safer nanomaterials and establishing standardized safety protocols for biomedical applications.

The limitations of this study include the focus on a limited number of nanomaterials and the relatively short exposure periods used in the in vitro and in vivo assays. Future research should address these limitations by investigating a broader range of nanomaterials, including novel and emerging materials, and evaluating their long-term effects. Additionally, studies should explore the potential for synergistic effects between different nanomaterials and examine their effects in more complex biological systems, such as organ-on-a-chip models. These avenues of research will provide a more comprehensive understanding of the safety profiles of nanomaterials and their suitability for clinical use.

DECLARATION OF AI AND AI ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this manuscript, the author(s) used DeepL to assist in improving grammar, language quality, and overall readability of the text. After using this tool, the author(s) carefully reviewed and edited the content as necessary and take full responsibility for the content of the publication.

AUTHOR CONTRIBUTIONS

Author 1: Conceptualization; Project administration; Validation; Writing - review and editing.

Author 2: Conceptualization; Data curation; In-vestigation.

Author 3: Data curation; Investigation.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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