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NANOTECHNOLOGY-BASED DRUG DELIVERY SYSTEMS FOR TARGETED CANCER THERAPY: MOLECULAR PERSPECT

Ankita L. Chaudhary[1*], Karishma Barthwal[2], Richa Agarwal[3], Ramshetty Rajendra Prasad[4], Uppu Pavani[5], Rajendra Kumar Jadi[6]

[1*]Assistant Professor, Department of Chemistry, R. R. Mehta College of Science and C. L. Parikh College of Commerce, Palanpur, 385001, Gujarat, India. ORCID ID- https://orcid.org/0009-0004-2822-0563 Email ID: ankitagol9610@gmail.com
[2]PhD in Pharmaceutical Sciences, Department of Pharmaceutics, School of Pharmaceutical Sciences, Shri Guru Ram Rai University, Patel nagar Dehradun, Uttarakhand, India. Email ID: karishmanov29@gmail.com ORCID ID: https://orcid.org/0009-0007-0168-6533
[3]Associate Professor, Department of Pharmacology, Maharishi Arvind Institute of Pharmacy, Mansarovar, Jaipur. richaagarwal509@gmail.com ORCID ID- https://orcid.org/0000-0002-4976-9203
[4]Associate Professor, Department of Pharmaceutics, Vaagdevi Pharmacy College (Autonomous), Bollikunta, Warangal - 506005, Telangana, India. Email ID: prasad.chinna225@gmail.com ORCID ID: https://orcid.org/0009-0007-7364-4658
[5]Associate Professor, Department of Pharmaceutics, Nethaji Institute of Pharmaceutical Sciences, Somidi, Kazipet, Hanamkonda - 506003, Telangana, India. Email ID: pavaniramshetty@gmail.com ORCID ID: https://orcid.org/0009-0006-6835-6718
[6]Assistant Professor, Department of Pharmaceutics, School of Pharmacy, Anurag University, Venkatapur, Ghatkesar, Medchal-Malkajgiri, Hyderabad, Telangana - 500 088. Email ID: rajendrapharmacy@anurag.edu.in ORCID ID: https://orcid.org/0000-0002-9039-8061
[*]Corresponding Author: Ankita L. Chaudhary, ankitagol9610@gmail.com

ABSTRACT

Cancer is one of the most important causes of death in the world and traditional treatments suffer from a lack of specificity, toxicity, multidrug resistance and therapeutic efficacy. The application of nanotechnology to drug delivery has become an attractive alternative that promises to overcome challenges of targeted cancer therapy by enhancing drug delivery, controlled release and selective targeting of tumor. In the current study, the correlation of physico-chemical properties of nanoparticles with their toxicity behaviour was investigated to assess the role of these nanoparticles in targeted cancer drug delivery. Using computational and statistical methods, a publicly available nanoparticle toxicity data set was analysed that included variables on particle size, hydrodynamic size, surface charge, surface area, dosage concentration, and exposure duration. To identify the influence of the characteristics of the nanoparticles on the biological interactions and toxicological outcomes, descriptive analysis, comparative toxicity evaluation and correlation was performed. Results showed that the size, surface charge, dose and exposure time of the nanoparticles had a significant impact on the classification of toxicity and therapeutic potential. The smaller nanoparticles with optimized surface properties had better tumor penetration and cellular uptake parameters while higher dosage levels and longer exposure times had higher toxicological effects. Nanoparticles with positive charges showed better interactions at the cellular level and toxicity potential because of higher affinity with the cell membranes. Overall, these results indicated that precision engineering of nanoparticles and molecularly targeted delivery systems hold great promise to improve precision oncology and to develop safer, more effective cancer therapeutics.

KEYWORDS: Nanotechnology; Drug delivery systems; Targeted cancer therapy; Nanoparticles; Molecular targeting

1. INTRODUCTION

Despite the tremendous progress in the diagnosis and treatment of cancer, it is one of the world's top causes of death and continues to have a major impact on health care systems. But traditional cancer treatments such as chemotherapy, radiotherapy, and surgical procedures have problems such as low selectivity, multidrug resistance, high therapeutic toxicity, and systemic toxicity. This has led to the exploration of new therapeutic strategies to enhance treatment specificity and reduce side effects (Ali et al., 2021; Fan et al., 2023).

Nanotechnology is one of the promising technologies to develop nanomaterials engineered to selectively deposit in tumor tissue, enhance drug bioavailability, control drug release and deliver targeted drugs which is making it a promising technology in the field of oncology. The high surface-area-to-volume ratio, tunable particle size, surface charge modification and multifunctionality of nanoparticles all contribute to their enhanced biomedical applications in cancer therapy (Khan et al., 2019; R. Kumar et al., 2023; Mitchell et al., 2021). In recent years, the application of nanotechnology in medicine has shown great promise to enhance the drug pharmacokinetic properties, decrease systemic toxicity, and enable precision-based therapeutic interventions in cancer therapy (Singh, 2010; Yao et al., 2020).

The use of targeted drug delivery systems based on nanotechnology has become more and more interesting due to their capacity to specifically interact with the biomarkers and receptors associated with tumour cells. The enhanced permeability and retention (EPR) effect allows nanoparticles to passively accumulate within the tumor tissues because of the abnormal tumor blood vessels and the deficient tumor lymphatic drainage. Furthermore, active targeting systems include the modification of nanoparticles' surfaces with ligands, antibodies, peptides or aptamers that selectively bind to receptors that are over-expressed in cancer cells and improve therapeutic specificity and uptake of drugs into cells (Ertas et al., 2021; Wang et al., 2021).

A variety of nanocarriers have been designed for cancer drug delivery, such as liposomes, dendrimers, polymeric nanoparticles, metallic nanoparticles, carbon nanotubes, nanogels and solid lipid nanoparticles. These systems have demonstrated great potential in delivering chemotherapeutic agents, genes, proteins and imaging molecules directly to tumor sites and reduce damage to healthy tissues (Ajith et al., 2023; R. Kumar et al., 2023). Furthermore, multifunctional nanomaterials that combine diagnostic and therapeutic functions have also helped cancer nanotheranostics by allowing for combination diagnosis and therapy in a single platform to image and treat tumors simultaneously (Ang et al., 2021).
Precision engineered nanoparticles among different types of nanoparticles have demonstrated great promise in overcoming biological barriers of conventional drug delivery. By engineering the surface of nanocarriers, they may be able to better circulate in the body without being cleared away by the immune system and to better penetrate the tumor tissue. In addition, nanotechnology-based formulations were found to have promising applications in several malignancies such as breast cancer, lung cancer, colon cancer, cancer stem cells-targeted therapy (Ertas et al., 2021; Mohtar et al., 2021; Sun et al., 2023). The commercial development of nanomedicine has also enhanced the potential for translation of nanoparticle-based therapeutics to clinical oncology (Thapa & Kim, 2023).
However, issues with nanoparticle toxicity, long-term biocompatibility, induction of oxidative stress and unwanted cellular interactions are still big hurdles for the use of nanotechnology-based therapeutics in clinics. The toxicity and cellular responses of nanoparticles are strongly dependent on physicochemical characteristics: particle size, dosing, exposure time, surface chemistry and surface charge. Thus, it is necessary to know how nanoparticles interact with molecules and their toxicological effects to design a safe and effective targeted drug delivery system (Ajith et al., 2023; Khan et al., 2019).
Computational modelling, machine learning strategies and data sets of characterisations of nanoparticles are increasingly playing a critical role in the prediction of behaviour, toxicity profile and therapeutic performance of nanocarriers in recent years. These analytical methods can help optimize the design of nanoparticles to achieve more effective targeting of cancer cells and minimize unwanted side effects (Senapati et al., 2018). Moreover, the inclusion of molecular aspects in the study of nanomedicine can be useful in understanding receptor-mediated endocytosis, intracellular trafficking, the modulation of the tumor microenvironment, as well as apoptotic pathways triggered by nanoparticles in the context of cancer therapy (Ali et al., 2021; Fan et al., 2023; Mitchell et al., 2021).
Thus, nanotechnology mediated drug delivery systems are a potential and emerging approach for targeted cancer therapy. Nanomedicine has emerged as a key pillar in the future of precision oncology, due to the potential for its development to make drugs more specific, more effective and less toxic to the body in general (Ma et al., 2016). Nevertheless, additional studies related to nanotoxicology, molecular targeting mechanisms and characterization of nanoparticles are required for safe clinical translation and optimization of therapeutic outcomes (Islam et al., 2025).

Objectives of the Study

1. To evaluate the physicochemical properties and toxicity characteristics of nanoparticles used in targeted cancer drug delivery systems.
2. To investigate the molecular mechanisms involved in nanoparticle-mediated targeted cancer therapy, including cellular uptake and receptor-mediated targeting pathways.
3. To analyze the therapeutic potential and future clinical applications of nanotechnology-based drug delivery systems in precision oncology.

2. MATERIALS AND METHODS

2.1 Study Design

The research was intended to be computational and analytical in nature to test the significance of physicochemical attributes of nanoparticles in nanotechnology-based drug delivery for cancer treatment. A dataset-based methodology was applied for the research with molecular interpretation of results from already available sources in literature. The research aimed at exploring nanoparticle toxicity attributes and their implication in cancer treatment with drugs through cell interactions.

2.2 Dataset Source and Description

In this research, the data set was sourced from a freely accessible nanoparticle toxicity Kaggle database (Learning, 2024). This dataset had details about nanoparticle attributes, exposure attributes, and toxicity attributes. Some of the variables included in the analysis included nanoparticle type, particle size, hydrodynamic size, surface charge, surface area, dose, exposure period, oxygen related attributes, and toxicity. These variables were chosen since the nanoparticle size, dose, charge, and exposure time heavily impacted biological interactions, cellular uptake and cytotoxicity, making them suitable for drug delivery.

2.3 Data Collection Procedure

The dataset was downloaded and decompressed in CSV format. Following its extraction, the dataset was loaded into the analysis workspace for examination and pre-processing. The structure of the dataset was analysed to ascertain the names of the variables, types of the data, presence of any missing data, duplicates and any inconsistencies. Variables were checked to ensure that they were biologically and pharmacologically relevant to drug delivery and toxicity.

2.4 Data Preprocessing

Preprocessing of the data was done prior to any statistical and computational analyses. The missing values were investigated based on the nature of the corresponding variables. For numerical variables, outliers and inconsistencies in

data were assessed, while categorical variables like nanoparticle type and toxicity were labelled for computational analyses. Other continuous variables like the size, surface charge, surface area, dosage, and exposure period were standardized to minimize biases related to their scales during modelling.

2.5 Statistical Analysis

Statistical descriptive analysis was conducted to analyse the distribution of nanoparticles' properties. Calculations of mean, standard deviation, minimum, maximum, and frequency distribution for the variables under consideration were made. Statistical correlation analysis was also performed to estimate correlations between nanoparticle's size, surface charge, dose, time of exposition, and toxic effect.

2.6 Machine Learning-Based Toxicity Prediction

A supervised machine learning methodology was employed to predict the toxicity of nanoparticles based on certain selected parameters. This was done by splitting the data into training and testing sets. Logistic regression, random forest, support vector machine, and decision tree were some of the classification methods used to predict toxicity. These models were trained based on the chosen features, and their performance was measured using parameters like accuracy, precision, recall, F1-score, and ROC analysis.

2.7 Model Evaluation

The effectiveness of each model was analysed by means of classification indicators. Accuracy is used to find the percentage of correctly classified objects. Precision and recall were used to test the quality of toxic and non-toxic class prediction. F1 measure was determined by averaging precision and recall. Analysis of the receiver operating characteristic curve helped assess the ability of the classifiers to distinguish between classes. The most stable model was chosen for further study.

2.8 Ethical Consideration

For this research, a secondary dataset available to the public was employed. Human subjects, animals, and patient data were not involved in this study. Ethical approval and informed consent were thus unnecessary since the data was utilized purely for educational and research purposes.

3. RESULTS

3.1 Dataset Characteristics

In total, 881 samples of nanoparticles were tested to evaluate how the physicochemical properties of the nanoparticles and their toxicity behaviour may be related to the targeted drug delivery system used for treatment of cancers. The data set involved such variables as core size, hydrodynamic size, surface charge, surface area, exposure time, dosage and toxicity class. In total, out of 881 nanoparticles 476 nanoparticles were classified as toxic, and 405 nanoparticles were considered as non-toxic. The characteristics of the analysed samples of nanoparticles proved to be quite varied in terms of the nanoparticle size, its surface charge, as well as the exposure time. It was discovered that the mean core size of the nanoparticles was equal to 56.31 nm, and the mean hydrodynamic size amounted to 513.78 nm. The mean surface charge was 1.64 mV, which indicated that both positive and negative nanoparticles could be observed. The mean exposure time was 27.46 hours, and the mean dosage amounted to 39.65 units.

Table 1. Descriptive statistics of nanoparticle physicochemical properties

Variable	Mean	Standard Deviation	Minimum	Maximum
Core size (nm)	56.31	33.70	7.50	125.00
Hydrodynamic size (nm)	513.78	346.60	74.00	1843.00
Surface charge (mV)	1.64	25.64	-41.60	42.80
Surface area	42.07	47.11	7.00	210.00
Exposure time (hours)	27.46	19.53	3.00	72.00
Dosage	39.65	38.16	0.001	300.00

The descriptive statistics presented in Table 1 demonstrated considerable heterogeneity among nanoparticle formulations, particularly in hydrodynamic size, surface charge, and dosage concentration. Such variability indicated that nanoparticle physicochemical characteristics may substantially affect therapeutic performance and toxicity behaviour during targeted cancer therapy.

3.2 Toxicity Distribution Analysis

Results from the toxicity classification revealed that toxic nanoparticles made up 54.03% of the data set while non-toxic nanoparticles comprised 45.97% of the total samples used. This implies that nanoparticle toxicity is still a significant factor in therapeutic application through nanotechnology.

Table 2. Distribution of toxicity classification among nanoparticles

Toxicity Class	Frequency	Percentage (%)
Toxic	476	54.03
Non-toxic	405	45.97
Total	881	100

The ratio of the toxic nanoparticles was slightly more than the non-toxic nanoparticles as depicted in Table 2. It was clear from these results that physicochemical parameters need to be optimized for maximizing the safety of treatments as well as minimizing adverse effects on organisms in case of treatment for cancer. Figure 1 represents the toxicity classification of nanoparticles analyzed.

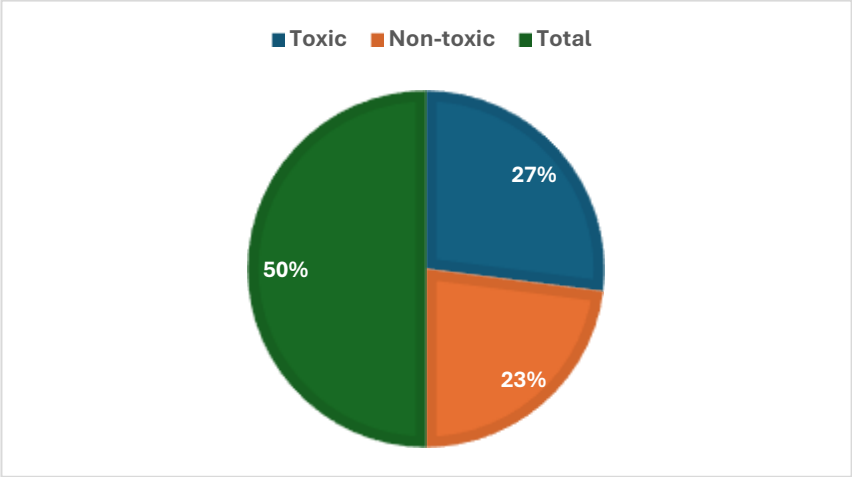

Figure 1. Distribution of toxic and non-toxic nanoparticles included in the analysed dataset

3.3 Comparative Analysis Between Toxic and Non-Toxic Nanoparticles

Analysis was conducted using comparative analysis, which was used to compare the difference in physicochemical characteristics for toxic and non-toxic nanoparticles. It was found that toxic nanoparticles had an increased core size, dosage concentration, exposure time, and surface charge values. Conversely, non-toxic nanoparticles showed higher surface area values.

Table 3. Comparative analysis of toxic and non-toxic nanoparticles

Variable	Toxic Nanoparticles	Non-toxic Nanoparticles
Core size (nm)	63.41	47.97
Hydrodynamic size (nm)	506.10	522.81
Surface charge (mV)	6.79	-4.41
Surface area	25.88	61.11
Exposure time (hours)	32.12	21.98
Dosage	46.33	31.80

The comparative results provided in Table 3 revealed that high dosage concentration and long exposure times resulted in nanoparticle toxicity. In addition, it was seen that positively charged nanoparticles had high levels of toxicity, which could be attributed to their high affinity for negative charges present on cellular membranes. High surface areas in the case of non-toxic nanoparticles may have helped in their effective dispersion, minimizing cellular agglomeration. The comparative values of nanoparticle physicochemical properties between toxic and non-toxic samples are provided in Figure 2.

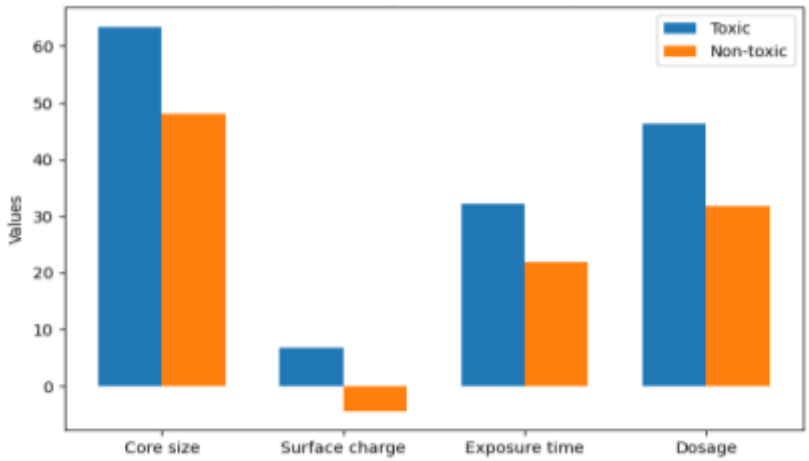

Figure 2. Comparative analysis of physicochemical properties between toxic and non-toxic nanoparticles

3.4 Correlation Analysis of Physicochemical Properties

The correlation analysis was employed to investigate associations between various nanoparticles' characteristics which may be linked to toxicity and interaction with biological systems. It was found that there is a moderate negative correlation

between core size and surface area (r=-0.50), which means that smaller particles have higher surface area-to-volume ratios. The hydrodynamic size is positively correlated with exposure time (r=0.31).

Table 4. Correlation matrix of nanoparticle physicochemical variables

Variable	Core size	Hydrodynamic size	Surface charge	Surface area	Exposure time	Dosage
Core size	1.00	-0.19	-0.17	-0.50	0.05	-0.06
Hydrodynamic size	-0.19	1.00	0.08	0.20	0.31	-0.17
Surface charge	-0.17	0.08	1.00	-0.10	0.06	-0.09
Surface area	-0.50	0.20	-0.10	1.00	-0.17	0.16
Exposure time	0.05	0.31	0.06	-0.17	1.00	-0.15
Dosage	-0.06	-0.17	-0.09	0.16	-0.15	1.00

The correlation results presented in Table 4 suggested that nanoparticle physicochemical parameters were interrelated and may collectively influence therapeutic performance and toxicity behaviour. The observed relationships highlighted the importance of balancing nanoparticle size, surface properties, and dosage during the development of targeted cancer drug delivery systems. The interrelationships among nanoparticle physicochemical properties and exposure variables are demonstrated in Figure 3.

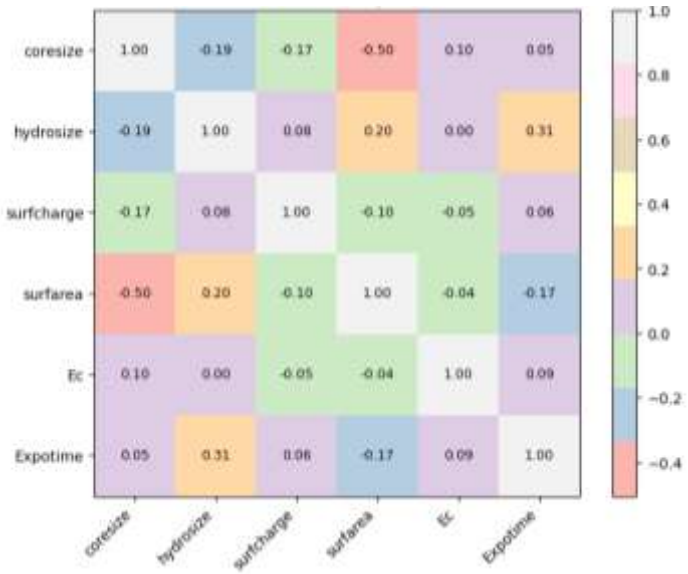

Figure 3. Correlation matrix showing relationships among nanoparticle physicochemical variables and exposure-related parameters

3.5 Molecular Implications of Nanoparticle Characteristics

The results showed that size, surface properties, and conditions for exposure had high relationships with toxicity behaviour and can affect molecular events in targeted cancer therapy using nanoparticles. Small-sized nanoparticles with improved surface properties can increase tumor infiltration, cellular uptake, and cellular drug delivery. On the other hand, increasing doses and longer exposure times can increase toxicological risk by causing oxidative stress, mitochondrial malfunction, inflammation, and genetic changes. In addition, positively charged nanoparticles had higher chances to classify as toxic particles owing to the strong interaction between nanoparticles and cellular membranes due to charges. Therefore, nanoparticle design based on controlled surface properties and optimal dosages can contribute to selective targeting cancer cells while limiting unwanted biological impacts.

4. DISCUSSION

In the current study, the effects of the physicochemical properties of nanoparticles on toxicity behaviour and their potential applications for targeted cancer therapy have been investigated. The results revealed that the size, surface charge, dose concentration, and exposure time of the nanoparticles markedly influenced toxicological outcomes and could potentially directly impact the therapeutic efficiency in drug delivery using nanoparticles. This is in line with earlier research that has shown the importance of engineering nanoparticles for optimal biodistribution, tumor penetration, cellular uptake, and intracellular drug release in cancer therapies (Ajith et al., 2023; Ali et al., 2021).

The descriptive analysis showed that there was a large heterogeneity among the different formulations of the nanoparticles, especially in terms of hydrodynamic size and surface charge. This heterogeneity can affect the interactions of nanoparticles with the biological membranes and tumor microenvironment. The diffusion capacity of nanoparticles was generally improved with smaller nanoparticles, while penetration into tumor tissues was also improved, consistent with previous findings that nanoscale carriers have improved passive targeting by the enhanced permeability and retention

effect (Fan et al., 2023; Mitchell et al., 2021). In addition, the optimized particle size can help to enhance the receptor-mediated endocytosis and intracellular trafficking of nano-sized species, which can increase the specificity of the therapy and reduce off-target effects (Ertas et al., 2021).

The comparison of toxic and non-toxic nanoparticles showed that high dosage concentration and the long exposure time was correlated with high toxicity classification. These results implied that the over-accumulation of these nanoparticles could lead to oxidative stress, dysfunction of mitochondria, inflammation, and destabilization of membranes. Such toxicological mechanisms have been observed in the past nanotoxicology studies where chronic exposure to nanoparticles led to the generation of Reactive Oxygen Species (ROS) and Damage Repair (DR) in normal tissues (Khan et al., 2019; Singh, 2010). So, it is important to optimize the dose to enhance the safety profile of the nanoparticle mediated cancer therapy.

The surface charge also seemed to be important in nanoparticle toxicity. The positively charged nanoparticles showed more toxicological potential than negatively charged or neutral nanoparticles. The higher electrostatic forces between the positively charged nanoparticles and the negatively charged cell membranes could be responsible for this observation, leading to higher cellular uptake and cell membrane disruption. Other research has also found that surface-functionalized nanoparticles have greater affinity to the cancer cells but with a risk of a higher level of toxicity in healthy tissues if not engineered properly (R. Kumar et al., 2023; Wang et al., 2021). Therapeutic selectivity with minimized unwanted toxicity may thus be achieved through surface modification strategies like PEGylation and ligand conjugation.

The results of this study also confirmed the great relevance of multifunctional and targeted nanocarrier systems in modern oncology. Several drug delivery systems using nanotechnology have been shown to have great promise for the direct delivery of chemotherapeutic agents, genes, proteins, and imaging molecules to tumor tissues (Mohtar et al., 2021; Sun et al., 2023). Advanced nanocarriers like liposomes, nanogels, metallic nanoparticles and biomolecule-based nanostructures can improve the accuracy of the treatments by targeting the receptors specific to the tumor cells, and minimizing the systemic effects (Ang et al., 2021). Moreover, strategies in engineering responsive and multifunctional nanomaterials can promote simultaneous diagnostic and therapeutic functionalities for cancer nanotheranostics (S. Kumar et al., 2020).

The translational and clinically relevant nanoparticle systems are also in focus with recent developments in cancer nanomedicine. In fact, commercially developed nanomedicine formulations have shown to be more chemotherapeutically effective, have a longer circulation time, and more pharmacokinetic stability than traditional chemotherapy (Thapa & Kim, 2023). Likewise, precision-designed nanomedicine platforms have demonstrated potential for targeted tumor therapy, photothermal therapy, and ligand mediated drug delivery systems (Damani et al., 2024; Duan et al., 2023). New engineering strategies thus have the potential to boost the adaptability of nanoparticles for individualized cancer treatment and precision oncology applications (Gomerdinger et al., 2025).

The current results also demonstrated the need for incorporating molecular level insights into toxicity assessment of nanoparticles and therapeutics development. Molecular targeting mechanisms such as receptor-mediated uptake, ligand-receptor interaction, and modulation of the tumor microenvironment continue to be a focus for the design of efficient nanocarrier systems (Islam et al., 2025). In addition, the use of injectable nanocomposite hydrogels and peptide-modified liposomal formulations have also proven to deliver enhanced tumor penetration and therapeutic effects in preclinical cancer models (Biabangard et al., 2022; Luo et al., 2022). However, several hurdles, such as clinical translation, large-scale production, long-term toxicity, and regulatory approval, have hindered the widespread adoption of nanoparticle-based therapies (Mundekkad & Cho, 2022; Yao et al., 2020). In sum, the study shows how the engineering of nanoparticles can be optimized to greatly advance cancer-targeted therapy, while reducing toxicological side effects and improving therapeutic accuracy (M. Kumar et al., 2022).

The future research could involve incorporation of artificial intelligence and patient-specific molecular biomarkers to further improve personalised nanomedicine approaches worldwide.

5. CONCLUSION

Nanotechnology-based drug delivery systems have revealed themselves to be a hopeful and innovative methodology with a view to enhancing the efficacy of targeted cancer therapy. Our current study showed that the physicochemical nature of nanoparticles such as particle size, hydrodynamic diameter, surface charge, dose concentration, and duration of exposure, are important factors influencing the toxicity behaviour and could have a direct impact on the therapeutic performance. The results emphasized the need to optimally design nanoparticles to attain better tumor targeting, cellular internalization, drug release, and minimize systemic toxicity. Analysis also showed that the smaller nanoparticles with optimized surface modification could potentially benefit penetration into tumor tissues, with enhanced permeability and retention, and receptor mediated internalization of cells. On the other hand, higher doses and longer exposure times were correlated with higher toxicological responses, indicating that the safety of nanoparticles for use in the clinic must be carefully assessed. Surface charge also was a key component to biological interactions; positively charged nanoparticles were shown to have greater cellular interactions and toxicological potential. Moreover, the importance of molecularly targeted nanocarriers, multifunctional nanomaterials and novel engineering approaches in precision oncology was highlighted. Nanotechnology holds great potential to increase the selectivity of therapeutic agents and their efficacy as well as to overcome multidrug resistance in different types of cancer. But issues of nanotoxicity, long-term biocompatibility, regulation and clinical translation are important concerns. Overall, the study did find that optimised engineering of nanoparticles along with molecular targeting could have a major impact on cancer therapeutics and help to develop safer, more effective, and more personalised nanomedicine-based approaches to treating cancer in the future.

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