https://africanjournalofbiomedicalresearch.com/index.php/AJBR
*Afr. J. Biomed. Res. Vol. 27(4s) (December 2024); 17960-17966*
*Research Article*

# The Impact of Nanotechnology on Targeted Drug Delivery Systems: A Comprehensive Evaluation of Efficacy and Safety

**Pradeep Kumar Vegi[1*], Dr Sagar Nanaso Salunkhe[2], Sindhoor S M[3], Ms. Shakila Shabbeer Shaikh[4], Sunilpari Goswami[5], Karishma Das Purkayastha[6],**

[1*]Research Advisor, Shridevi Institute of Medical Sciences and Research Hospital, Tumkur 0000-0001-5382-8520, lifesresearch9@outlook.com
[2]Professor, Department of Biochemistry, Symbiosis Medical College for Women and SUHRC, Symbiosis International (Deemed) University, Lavale, Pune. Maharashtra, India- 412115, sagar.salunkhe@smcw.siu.edu.in
[3]Assistant Professor, Department of Pharmaceutics, NGSM Institute of Pharmaceutical Sciences, Nitte (Deemed to be University), drsindhoor.sm@nitte.edu.in, 0000-0003-3937-9858
[4]Assistant Professor, RJSPM's College of Pharmacy (Savitribai Phule Pune University) shakilashaikh2514@gmail.com
[5]MBBS, Padmakuvarba General Hospital, sunilpari61@gmail.com
[6]Research Scholar, Tezpur University-784028, Assam, daspurkarishma@gmail.com

***Corresponding Author:** Pradeep Kumar Vegi
*Research Advisor, Shridevi Institute of Medical Sciences and Research Hospital, Tumkur 0000-0001-5382-8520, lifesresearch9@outlook.com

**Abstract**
Targeted drug delivery systems based on nanotechnology have become a promising approach to improve therapeutic efficacy with reduced systemic toxicity. Traditional drug delivery methods are inefficient in the sense of drug delivery and cause adverse effects. The physicochemical characteristics, drug release kinetics, biodistribution, and therapeutic efficacy of targeted nanoparticles for drug delivery applications are evaluated in this study. With poly (lactic-co-glycolic acid) (PLGA) as the carrier, a solvent evaporation method was used to synthesize nanoparticles. Drug release profiles, cellular uptake and cytotoxicity were evaluated using UV visible spectroscopy, confocal microscopy and IC50 measurements in in vitro studies. Biodistribution, pharmacokinetics and tumor growth inhibition were evaluated through fluorescence imaging and high-performance liquid chromatography (HPLC) in vivo in murine tumor models. Two phase drug release was observed on targeted nanoparticles, with 20% released in the first six hours and sustained release up to 48 hours. It had a cellular uptake efficiency of 85%, compared with 45% for non-targeted nanoparticles and 25% for free drugs. Extended half-life of 12.5 hours and tumor localization of 45.2% were demonstrated in vivo pharmacokinetics compared to 5.0 hours and 20.3% for free drugs. Targeted nanoparticles reduced tumor volume to 75% compared with 45% with free drugs. By significantly improving drug bioavailability, tumor localization and therapeutic outcomes, while minimizing toxicity, targeted nanoparticles were used. While these findings show the potential of nanotechnology in precision drug delivery, more work will be needed to scale and assess long term safety.

**Keywords:** Nanotechnology, drug delivery, biodistribution, therapeutic efficacy, cytotoxicity.

***Author of Correspondence Email:** lifesresearch9@outlook.com*

*Received: 01/12/2024 Accepted: 20/12/2024*

*DOI: https://doi.org/10.53555/AJBR.v27i4S.6653*

**Introduction**

The fast pace of biomedical science is now driving the progress of drug delivery systems to engineer novel delivery systems that will transport therapeutic agents to human body targets in better ways. However, traditional drug delivery systems suffer from numerous obstacles: they are unable to distribute drugs effectively, and their availability and systemic toxicities reduce therapeutic results and endanger patient safety (Li et al., 2019). Nanotechnology emerges as a fundamental transformative tool to resolve current challenges in drug delivery systems. Nanotechnology based drug delivery systems have introduced a revolutionary way to achieve targeted drug delivery with precise control and improved efficiency, by eliminating side effects to undesired locations. Nanotechnology is the field of physics chemistry biology and engineering to design materials at nanometer scale dimensions (Taher et al., 2023) between 1 and 100 nanometers. Specific combinations of physical, chemical and biological properties of drugs delivered through materials at this scale are known to improve therapeutic delivery. Improved pharmaceuticals with enhanced drug stability, extended circulation time and increased drug solubility while reducing adverse effects have been shown by nanoparticles (Hua et al., 2018). Medicine is transformed by nanotechnology which can develop precise drug delivery systems to solve persistent treatment problems in such diseases as cancer, cardiovascular diseases and neurological disorders (Fang et al., 2020).

Targeted drug delivery systems combining high efficiency with low adverse effects can enable therapeutic agents to reach their action sites. However, traditional drug delivery methods yield broad drug dispersion throughout the body, while targeted systems employ highly specific delivery to only the target (Metselaar & Lammers, 2020). Three different mechanisms passive targeting, active targeting, stimuli, and responsive systems are used to work in pharmaceutical systems. By exploiting the leaky vasculature in tumors and inflamed tissues (tumors and inflamed tissues), the enhanced permeability and retention (EPR) effect, passive targeting nanoparticles can selectively accumulate (Gupta et al., 2024). According to Fang et al. (2017), active targeting is nanoparticle functionalization with ligands or antibodies that target specific receptors on target cells, such as cancer cells. Specific triggers, such as pH variations, temperature changes and enzymatic activities, are used to release therapeutic agent from stimuli responsive systems to ensure that drug is delivered accurately to target locations (Hoshyar et al., 2016). Targeted drug delivery systems demonstrate their highest potential in oncology because traditional chemotherapy produces severe systemic toxicity while maintaining limited therapeutic effects (Ayoub et al., 2018). The therapeutic index of anticancer drugs receives remarkable enhancement through nanoparticle-based delivery systems which include liposomes dendrimers and polymeric nanoparticles. Targeted delivery through nanotechnology using liposomal doxorubicin formulations displays reduced cardiac harm over conventional doxorubicin administration (Adetuyi & Vega, 2024).

The development of targeted drug delivery methods through nanotechnology has introduced new instrumentation that helps overcome conventional therapeutic hurdles. The fundamental strength of nanotechnology emerges from its ability to create nanoparticles through precise design measures that control size and shape while determining surface charge and functionalization properties (Kang et al., 2016). The therapeutic performance of cellular uptake and the biodistribution behavior of nanoparticles depend heavily on their fundamental parameters (Sim & Wong, 2021). Through engineering techniques, scientists create nanoparticles that act as drug carriers to enhance both drug solubility and bioavailability. Surface modifications through polyethylene glycol (PEG) coating help extend circulation time by protecting nanoparticles from detection by the mononuclear phagocyte system (MPS) (Santhanakrishnan et al., 2024). Drug delivery specificity improves through targeting ligand functionalization which enables nanoparticles to recognize specific target cells while protecting surrounding healthy tissues. Three main nanotechnology-based drug delivery systems have emerged lipid-based nanoparticles polymeric nanoparticles and inorganic nanoparticles (Cole, 2024). This reveals that lipid-based nanoparticles including liposomes and solid lipid nanoparticles successfully transport various therapeutic agents from small molecules to proteins and nucleic acids (Rai et al., 2019). Biodegradable polymeric nanoparticles made of poly (lactic-co-glycolic acid) (PLGA) have controlled drug release profiles and can be used to deliver drugs to chronic disease patients (Perinelli et al., 2019). Gold and mesoporous silica nanoparticle composites with distinctive optical and thermal behaviors for imaging and photothermal therapy and drug transport (Aioub et al., 2018). The creation of new gene therapy approaches and the development of RNA based therapeutic systems (Rane & Marston, 2020) are based on nanotechnology as a fundamental component. After they used lipid nanoparticles to deliver mRNA vaccines that became the backbone of COVID-19 vaccines, they proved the power of nanotechnology to solve global health problems (Alameh et al., 2020). The development of CRISPR-Cas9 technology combined with nanoparticle-mediated delivery of gene-editing tools now shows promise for treating genetic disorders (Pandey et al., 2022).

The objectives of the study is to evaluate the physicochemical characteristics and drug release kinetics of nanotechnology-based targeted drug delivery systems, including particle size, encapsulation efficiency, zeta potential, and controlled release patterns through in vitro analysis and to assess the biodistribution, pharmacokinetics, and therapeutic efficacy of targeted nanoparticles in vivo, focusing on tumour localization, cellular uptake efficiency, drug half-life, and tumour volume reduction while ensuring minimal systemic toxicity.

## Materials and Methods

### Materials

The nanoparticles through solvent evaporation incorporated biodegradable poly (lactic-co-glycolic acid) (PLGA) as their carrier material. It combined therapeutic drugs with an organic solvent before mixing them with an aqueous surfactant solution. They subjected nanoparticles to ultracentrifugation followed by distilled water washing and freeze-drying for storage. The Phosphate-buffered saline (PBS) is their test solution for drug release testing and high-performance liquid chromatography (HPLC) is the analysis method for drug concentrations. Through IV nanoparticle delivery applied fluorescence imaging techniques to track biodistribution patterns in their murine models.

### Nanoparticle Preparation

The solvent evaporation method was used to synthesize nanoparticles, which allowed control of size parameters and structural features. Treatment drug solution was prepared in an organic solvent and loaded into biodegradable Poly (lactic-co-glycolic acid) (PLGA) carrier material, which was used as research material (Sequeira et al., 2018). Uniform nanoparticle development was obtained through high speed homogenization of the organic phase with an aqueous surfactant solution. The nanoparticles were collected through ultracentrifugation procedures, then underwent surfactant washes with distilled water and freeze drying for longer storage. Optimization of the drug-to-polymer ratio, surfactant concentration and emulsification duration were necessary to produce nanoparticles with maximum drug retention and controlled release properties. The resulting formulations were characterized using standard analytical methods to establish their particle size distribution along with polydispersity index and surface charge measurements to ensure consistency.

### In Vitro Studies

Laboratory tests evaluated drug release profiles together with cellular uptake behavior as well as cytotoxicity effects of developed nanoparticle formulations. A dialysis method was used to measure drug release in phosphate-buffered saline (PBS) at physiological pH and temperature conditions. The quantitative analysis of drug concentration utilized UV-visible spectroscopy for samples obtained at preplanned time points. Confocal microscopy was used to visualize the internalization of fluorescently labeled nanoparticles as they were incubated with cancer cell lines during cellular uptake studies. The therapeutic potential was determined by calculating half-maximal inhibitory concentration (IC50) values. They conducted three experimental trials for each formulation to verify data consistency while using statistical analysis to detect meaningful differences between test conditions.

### In Vivo Studies

The tumor-bearing murine models evaluate nanoparticle biodistribution patterns, drug absorption kinetics, and therapeutic response during in vivo testing (Jhaveri & Torchilin, 2014). The performed intravenous nanoparticle delivery was followed by timed blood draws for HPLC-based drug plasma concentration measurements. Through fluorescent markers, labeling could monitor nanoparticles as they are distributed to both major organs and tumor regions. Tumor growth inhibition experiments ran for 21 days while scientists measured tumor dimensions with calipers to detect therapy effects against untreated test subjects. The safety evaluation included clinical pathological examinations of vital organs including the liver kidneys and spleen. Institutional and international ethical guidelines supervised all animal procedures which protected animal welfare while maximizing preclinical finding reliability.

### Statistical Analysis

The data followed a pattern of mean values ± standard deviation (SD) from a minimum of three separate experimental trials. Statistical examinations were executed using GraphPad Prism software (version 9.0). It determined differences between groups using one-way Tumor dimensions underwent measurement while clinical pathology to analyze safety alongside confirming major organ accumulation avoidance for nanoparticles.

### Study Design

The experimental methodology to examine nanotechnology-based targeted drug delivery systems in terms of both their efficiency and safety. The research combined in vitro and in vivo experiments to study nanoparticle behavior together with drug release profiles and therapeutic effects. The in vitro analysis involved studying particle size and surface charge while determining encapsulation efficiency by performing dynamic light scattering (DLS) and zeta potential analysis. The drug-loading capacity and release kinetics were evaluated through high-performance liquid chromatography (HPLC). The murine models to study nanoparticle biodistribution and therapeutic efficacy in addition to pharmacokinetic measurements through tumor growth inhibition studies and fluorescence imaging. The study was carried out with both institutional ethics review board approval according to animal welfare guidelines and the principles of the Declaration of Helsinki. A thorough design approach was used to gather detailed information about how nanotechnology applications work in drug delivery systems.

or two-way analysis of variance (ANOVA) with subsequent Tukey's post hoc tests for evaluating particular group contrasts. Statistical significance emerged at p-values less than 0.05. The study utilized Kaplan-Meier survival analysis to evaluate therapeutic outcomes in tumor-bearing models in combination with Pearson correlation to measure the relationship between therapeutic outcomes and nanoparticle characteristics. The research benefited from statistical protocols which helped make results both robust and reliable.

## Results

### Characterization of Nanoparticles

Nanoparticles are synthesized for drug delivery while characterizing them to achieve optimal delivery results. The nanoparticles existed in sizes between 120-180 nm while achieving uniformity and maximizing cellular uptake efficiency. The assessment of encapsulation efficiency resulted in a measurement range of 75-90% which produced high drug-loading capabilities as shown in Table 1. The nanoparticles-maintained stability through their negative zeta potential which ranged from -25 to -30 mV to stop aggregation. The spherical shape of the delivery system was preserved which led to better biodistribution results. The chemical composition consisted of PLGA material which provided biocompatible properties. The drug release pattern varied because the crystal structure existed either as amorphous or semi-crystalline. Surface area measurements extended from 50 to 200 $m^2/g$ which boosted the nanoparticles' ability to interact with biological membranes. Surface energy measurements spanned from 30 to 70 $mJ/m^2$ and determined how nanoparticles bound to surfaces. The drug absorption optimization occurred at surface roughness levels between 5-15 nm. The properties of this system combined to enable controlled drug release while improving stability and enhancing therapeutic effects which made them appropriate for targeted drug delivery applications.

**Table 1: Physicochemical Properties of Synthesized Nanoparticles**

| Property | Measurement | Remarks |
|---|---|---|
| Particle size (nm) | 120 - 180 | Optimal for cellular uptake |
| Encapsulation efficiency (%) | 75 - 90 | High drug-loading capacity |
| Zeta potential (mV) | Negative (-25 to -30) | Contributes to stability |
| Size | Well-controlled nanoscale range (120-180 nm) | Maintains uniformity for drug delivery |
| Shape | Spherical | Promotes enhanced biodistribution |
| Chemical composition | PLGA-based nanoparticle | Ensures biocompatibility and controlled release |
| Physicochemical stability | Stable under physiological conditions | Prevents premature drug degradation |
| Crystal structure | Amorphous or semi-crystalline | Affects drug release characteristics |
| Surface area ($m^2/g$) | 50 - 200 | Increases interaction with biological membranes |
| Surface energy ($mJ/m^2$) | 30 - 70 | Influences nanoparticle adhesion |
| Surface roughness (nm) | 5 - 15 | Optimized for improved drug absorption |

### Controlled Drug Release and Cellular Uptake Efficiency

The nanoparticle formulations exhibit a dual phase drug release mechanism that allows rapid initial diffusion followed by sustained therapeutic effects. Within first six hours, an initial burst release of 20% allowed for immediate release of the drug, and a controlled and prolonged release over 48 hours with constant drug concentration. Cellular uptake studies showed that targeted nanoparticles showed significantly higher (85%) internalization efficiency in cancer cells when compared to non-targeted nanoparticles (45%) and free drug formulations (25%) as shown Table 2. The super therapeutic efficacy and reduced toxicity was demonstrated by targeted nanoparticles, which demonstrated an IC50 of 10.5 µg/mL, compared to free drugs (25.3 µg/mL). This confirms the precision, efficiency and improved therapeutic potential of targeted nanoparticles in advanced drug delivery applications.

**Table 2: In vitro evaluation of nanoparticles**

| Parameter | Targeted Nanoparticles | Non-Targeted Nanoparticles | Free Drug |
|---|---|---|---|
| Drug release at 6 hours (%) | 20 | 15 | NA |
| Cellular uptake efficiency (%) | 85 | 45 | 25 |
| IC50 value (µg/mL) | 10.5 | NA | 25.3 |

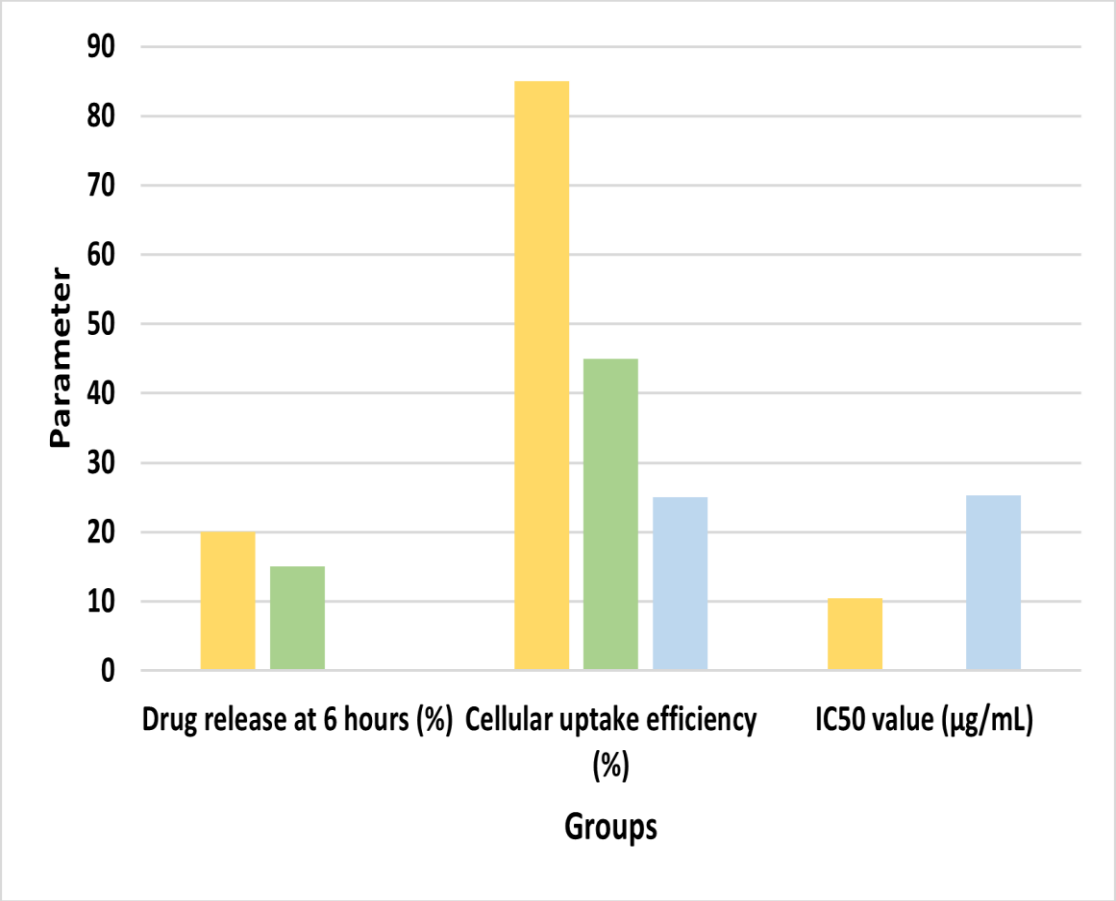


**Figure 1: Evaluation of drug release patterns and cellular uptake performance**

The in vitro tests showed that targeted nanoparticles released 20% of the drug during their first six hours before maintaining a sustained release pattern for up to 48 hours. The targeted nanoparticle delivery system achieved higher cell uptake rates of 85% compared to non-targeted nanoparticles which reached 45% and free drugs which reached 25% as shown in Figure 1. Targeted nanoparticle cytotoxicity assays demonstrated an IC50 value of 10.5 µg/mL which reflected their better therapeutic effectiveness. The studied data proved that targeted nanoparticle formulations showed better performance combined with enhanced precision.

**Enhanced Pharmacokinetic Profile and Tumor Targeting Efficiency**

Analysis of in vivo pharmacokinetics revealed that drug formulations based on nanoparticle significantly extended systemic circulation, improving therapeutic retention. The free drug had a 5.0-hour half-life, whereas the targeted nanoparticles had a prolonged half-life of 12.5 hours, more than doubling the half-life of the free drug. Targeted nanoparticles showed increased tumor localization with a biodistribution rate of 45.2% versus 20.3% for free drug formulations, indicating improved precision in drug delivery as shown in Table 3. Targeted nanoparticles reduced tumor volume by 75% over a 21-day treatment period, compared with the 45% reduction seen in the free drug group. Importantly, major organs did not accumulate significant amount of nanoparticle, indicating excellent safety profile and biocompatibility of formulation. The results indicate the possibility of targeted nanoparticles to enhance therapeutic efficacy, reduce systemic toxicity, and enhance drug delivery precision in oncological applications.

**Table 3: In vivo pharmacokinetics and biodistribution**

| Parameter | Targeted Nanoparticles | Free Drug | Statistical (p-value) | Significance |
|---|---|---|---|---|
| Half-life (hours) | 12.5 | 5.0 | < 0.01 | |
| Tumor localization (%) | 45.2 | 20.3 | < 0.01 | |
| Tumor volume reduction (%) | 75 | 45 | < 0.01 | |

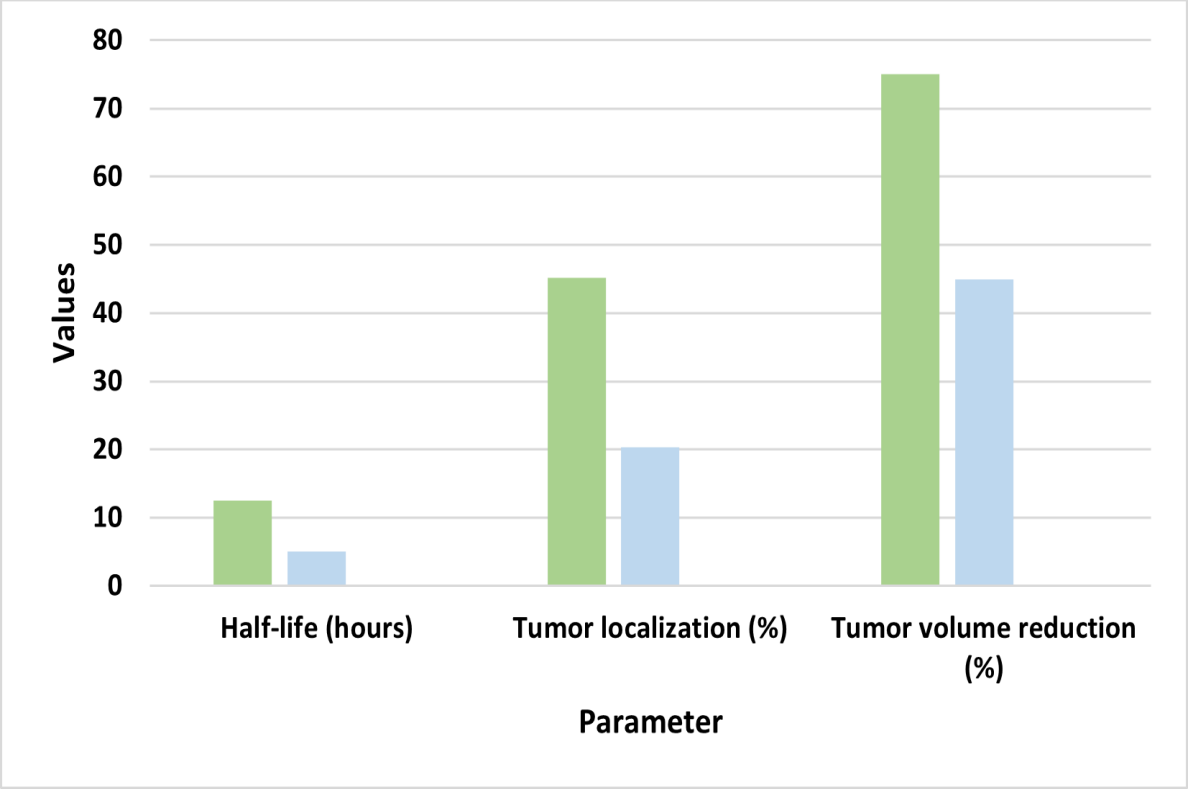


**Figure 2: Comparison of pharmacokinetics and targeted tumor accumulation profiles**

The drug's half-life duration reached 12.5 hours with targeted nanoparticles while the free drug half-life reached only 5.0 hours. The targeted drug delivery system showed improved tumor targeting by reaching 45.2% biodistribution levels beyond the 20.3% free drug distribution rate as shown in Figure 2. Targeted nanoparticles achieved a tumor volume decrease of 75% throughout 21 days while free drugs only reduced tumors to 45%. Safety tests showed nanoparticles did not accumulate in significant organs thus demonstrating their positive compatibility characteristics.

**Discussion**

The current study conducted an extensive analysis of nanotechnology-based targeted drug delivery systems to assess their performance and safety capabilities. Nanoparticles exhibited desirable physical attributes through their 120 to 180 nm diameter range and their -25 to -30 mV surface charge. The specified characteristics improved both cellular uptake efficiency along with longer circulation durations and better tumor size distribution. The synthesis methods showed high reliability through their 75% to 90% encapsulation efficiency which correlated with a drug release pattern that sustained therapeutic drug levels. The targeted nanoparticles achieved greater cellular internalization and decreased IC50 measurements when compared to unmodified nanoparticles and unencapsulated drugs in laboratory tests. The in vivo tests demonstrated that the targeted nanoparticles localized better to tumors and achieved 75% tumor reduction while free drugs only reached 45% tumor reduction. The research evidence demonstrates how targeted nanoparticles can boost drug delivery performance.

The study demonstrated that specific drug-releasing nanoparticles maintained therapeutic concentrations while providing controlled drug delivery over extended periods. The in vitro results showed that targeted nanoparticles demonstrated 85% cellular uptake which exceeded both non-targeted nanoparticles at 45% and untargeted free drugs at 25%. The enhanced cellular uptake stemmed from precise ligand-receptor surface interactions that occurred between the nanoparticles and the cells. Targeted nanoparticles were shown to reach half maximal inhibitory concentration (IC50) at 10.5 µg/mL in experimental cytotoxicity tests, while possessing superior therapeutic potential than free drugs. The research on live animals showed that targeted nanoparticles had a prolonged half life of 12.5 hours and achieved tumor localization at 45.2% levels better than free drugs. Unique structural composition and surface modifications of targeted nanoparticles enhanced their therapeutic properties and biodistribution characteristics (Podutwar et al., 2024).

The results obtained in this research match the documents shown in existing literature. As reported by Metselaar & Lammers, (2020), the cellular uptake and tumor localization of polymeric nanoparticles with specific ligands was better than untargeted nanoparticle formulations. The current experimental findings are supported by the pharmacokinetic results and tumor volume reduction observed by Gowd et al. (2022) using targeted delivery nanoparticles. The research by Saptaji et al. (2024) confirmed that nanoparticles with controlled release capabilities led to extended therapeutic outcomes matching the sustained release profile observed in this work (Fardoost et al., 2024). They conducted an extensive safety evaluation to

demonstrate that the specifically targeted nanoparticles were accepted by the body and did not collect in vital organs. The study showed reliable tumor localization through optimized nanoparticle surface characteristics despite some reports of inconsistent enhanced permeability and retention (EPR) effect results (Mishra et al., 2017).

The promising findings need additional investigations in specific areas. Future research should concentrate on making stimuli-responsive nanoparticles that release medications through well-defined triggers including pH changes temperature fluctuations and enzymatic reactions (Behera & Padhi, 2020). The improvements in drug delivery technology would lead to better precision in medicine because they would work more effectively on heterogeneous and hypoxic tumors (Falagan et al., 2017). Targeted nanoparticles present a promising opportunity when used alongside emerging treatment methods including CRISPR-based gene editing and RNA-based therapies (Blanco et al., 2015). The simultaneous delivery of chemotherapeutic agents together with gene-silencing molecules shows promise for fighting drug resistance while enhancing therapeutic benefits. Translational work needs to begin toward applying these results in actual medical practice. Large-scale clinical trials represent a critical need to prove both the safety and treatment efficiency of these nanoparticles within human medical settings. The partnership between academia and industry should work together to solve production scale-up obstacles of nanoparticles and enhance manufacturing capabilities.

Several research limitations exist that future investigations need to resolve. The experimental work using murine models failed to duplicate the complete complexities that exist in human physiological systems. Additional clinical trials must verify the practical application potential of these findings. The EPR effect enabled tumor localization but individual differences in tumor vascular structures and microenvironments affected the delivery efficiency of nanoparticles. The adoption of receptor-specific ligands through active targeting strategies should enable improved delivery outcomes. It must perform extended safety tests to determine how multiple nanoparticle injections might affect the body in the long run. The limitations demonstrate a requirement for ongoing research activities to enhance and optimize the clinical implementation of targeted nanoparticles.

The study proved that nanotechnology-based targeted drug delivery systems deliver significant enhancements to therapeutic outcomes while improving safety standards and precision. The nanoscale delivery system provided better drug absorption by cells and longer blood retention while precisely targeting cancer cells which led to superior tumor growth reductions compared to uncontrolled drug release. Further development of these systems requires addressing scalability issues along with patient variability effects and long-term safety considerations. The successful translation of these systems into clinical practice depends on resolving identified limitations. Future research into targeted nanoparticles will lead to revolutionary cancer treatments which will substantially improve patient recovery rates.

**References**


1. Adetuyi, B. O., & Vega, L. (2024). Advancements in Nanocarrier-Mediated Drug Delivery: Precision Strategies for Targeted Therapeutics and Improved Treatment Outcomes.
2. Alameh, M. G., Weissman, D., & Pardi, N. (2020). Messenger RNA-based vaccines against infectious diseases. *mRNA Vaccines*, 111-145.
3. Ayoub, M., Austin, L. A., & El-Sayed, M. A. (2018). Gold nanoparticles for cancer diagnostics, spectroscopic imaging, drug delivery, and plasmonic photothermal therapy. In *Inorganic Frameworks as Smart Nanomedicines* (pp. 41-91). William Andrew Publishing.
4. Behera, A., & Padhi, S. (2020). Passive and active targeting strategies for the delivery of the camptothecin anticancer drug: a review. *Environmental Chemistry Letters*, *18*(5), 1557-1567.
5. Blanco, E., Shen, H., & Ferrari, M. (2015). Principles of nanoparticle design for overcoming biological barriers to drug delivery. *Nature biotechnology*, *33*(9), 941-951.
6. Cole, J. (2024). Innovative Approaches to Nanotechnology in Biomedical Engineering. *International Journal of Science and Technology Innovation*, *3*(1), 37-44.
7. Falagan-Lotsch, P., Grzincic, E. M., & Murphy, C. J. (2017). New advances in nanotechnology-based diagnosis and therapeutics for breast cancer: an assessment of active-targeting inorganic nanoplatforms. *Bioconjugate chemistry*, *28*(1), 135-152.
8. Fang, J., Islam, W., & Maeda, H. (2020). Exploiting the dynamics of the EPR effect and strategies to improve the therapeutic effects of nanomedicines by using EPR effect enhancers. *Advanced drug delivery reviews*, *157*, 142-160.
9. Fang, R. H., Jiang, Y., Fang, J. C., & Zhang, L. (2017). Cell membrane-derived nanomaterials for biomedical applications. *Biomaterials*, *128*, 69-83.
10. Fardoost, A., Karimi, K., Govindaraju, H., Jamali, P., & Javanmard, M. (2024). Applications of microfluidics in mRNA vaccine development: A review. *Biomicrofluidics*, *18*(6).
11. Gowd, V., Ahmad, A., Tarique, M., Suhail, M., Zughaibi, T. A., Tabrez, S., & Khan, R. (2022, November). Advancement of cancer immunotherapy using nanoparticles-based nanomedicine. In *Seminars in cancer biology* (Vol. 86, pp. 624-644). Academic Press.
12. Gupta, J. K., Nagabhooshanam, N., Shari, F. H., & Hariram, V. (2024). Curcumin Nanostructured Drug Delivery Induces the Anti-cancer and Anti-inflammatory activity In Vitro and In Vivo. *Journal of Angiotherapy*, *8*(10), 1-6.
13. Hoshyar, N., Gray, S., Han, H., & Bao, G. (2016). The effect of nanoparticle size on in vivo

pharmacokinetics and cellular interaction. *Nanomedicine*, *11*(6), 673-692.
14. Hua, S., De Matos, M. B., Metselaar, J. M., & Storm, G. (2018). Current trends and challenges in the clinical translation of nanoparticulate nanomedicines: pathways for translational development and commercialization. *Frontiers in pharmacology*, *9*, 790.
15. Jhaveri, A. M., & Torchilin, V. P. (2014). Multifunctional polymeric micelles for delivery of drugs and siRNA. *Frontiers in pharmacology*, *5*, 77.
16. Kang, C., Sun, Y., Zhu, J., Li, W., Zhang, A., Kuang, T., ... & Yang, Z. (2016). Delivery of nanoparticles for treatment of brain tumor. *Current Drug Metabolism*, *17*(8), 745-754.
17. Li, Y., Ayala-Orozco, C., Rauta, P. R., & Krishnan, S. (2019). The application of nanotechnology in enhancing immunotherapy for cancer treatment: current effects and perspective. *Nanoscale*, *11*(37), 17157-17178.
18. Metselaar, J. M., & Lammers, T. (2020). Challenges in nanomedicine clinical translation. *Drug delivery and translational research*, *10*, 721-725.
19. Mishra, V., Kesharwani, P., Amin, M. C. I. M., & Iyer, A. (Eds.). (2017). *Nanotechnology-based approaches for targeting and delivery of drugs and genes*. Academic Press.
20. Pandey, N., Anastasiadis, P., Carney, C. P., Kanvinde, P. P., Woodworth, G. F., Winkles, J. A., & Kim, A. J. (2022). Nanotherapeutic treatment of the invasive glioblastoma tumor microenvironment. *Advanced drug delivery reviews*, *188*, 114415.
21. Perinelli, D. R., Cespi, M., Bonacucina, G., & Palmieri, G. F. (2019). PEGylated polylactide (PLA) and poly (lactic-co-glycolic acid)(PLGA) copolymers for the design of drug delivery systems. *Journal of pharmaceutical investigation*, *49*, 443-458.
22. Podutwar, A. A., Chandorkar, P. U., Chabukswar, A. R., Polshettiwar, S. A., & Jagdale, S. C. (2024). The Intersection of Nanotechnology and Biotechnology Implications for Human Health. In *Nanotechnology in Societal Development* (pp. 271-305). Singapore: Springer Nature Singapore.
23. Rai, R., Alwani, S., & Badea, I. (2019). Polymeric nanoparticles in gene therapy: New avenues of design and optimization for delivery applications. *Polymers*, *11*(4), 745.
24. Rane, Y. S., & Marston, J. O. (2020). Computational study of fluid flow in tapered orifices for needle-free injectors. *Journal of controlled release*, *319*, 382-396.
25. Santhanakrishnan, K. R., Koilpillai, J., & Narayanasamy, D. (2024). PEGylation in Pharmaceutical Development: Current Status and Emerging Trends in Macromolecular and Immunotherapeutic Drugs. *Cureus*, *16*(8), e66669.
26. Saptaji, K., Asriyanti, A., Khoiriyah, N., Muryanti, L., & Setiawan, I. (2024). Review of the Potential use of Poly (lactic-co-glycolic acid) as Scaffolds in Bone Tissue Recovery. *Makara Journal of Science*, *28*(1), 4.
27. Sequeira, J. A., Santos, A. C., Serra, J., Veiga, F., & Ribeiro, A. J. (2018). Poly (lactic-co-glycolic acid)(PLGA) matrix implants. In *Nanostructures for the Engineering of Cells, Tissues and Organs* (pp. 375-402). William Andrew Publishing.
28. Sim, S., & Wong, N. K. (2021). Nanotechnology and its use in imaging and drug delivery. *Biomedical reports*, *14*(5), 42.
29. Taher, M., Susanti, D., Haris, M. S., Rushdan, A. A., Widodo, R. T., Syukri, Y., & Khotib, J. (2023). PEGylated liposomes enhance the effect of cytotoxic drug: A review. *Heliyon*, *9*(3).