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TARGETED DRUG DELIVERY SYSTEMS IN CANCER THERAPY: NANOTECHNOLOGY-DRIVEN APPROACHES FOR ENHANCING THERAPEUTIC EFFICACY

Rabia Kiran[1*], Syeda Iram Batool[2]

[1]*Mufti Mehmood Memorial Teaching Hospital MTI Dera Ismail Khan, Khyber Pakhtunkhwa, Pakistan*
[2]*Gomal Medical College, MTI, Dera Ismail Khan 29050, Khyber Pakhtunkhwa, Pakistan*
**Corresponding Author E-Mail: rabiakiran9999@gmail.com*

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ABSTRACT

The growing sophistication of cancer and its resistance to standard therapies calls for innovations in drug delivery systems to improve therapeutic results. This review looks at the state of the art in targeted cancer therapy employing nanotechnology with a focus on new developments that seek to boost treatment modalities efficacy and precision. New developments in liposomes, dendrimers, polymeric nanoparticles, and metallic nanoparticles are analyzed for their use in target site specific controlled delivery and release of chemotherapeutics, which reduces systemic toxicity and increases drug retention at the target region. This review further analyzes the use of these nanotechnologies for integrated diagnostic and therapeutic functions termed as theragnostic, which allow personalized treatment plans to be crafted for specific patient profiles and tumor traits. Furthermore, we analyze the contemporary clinical application of these technologies, describe important issues such as biocompatibility, immunogenicity, regulatory issues, and avenues of future research. Our result analysis suggests that while great strides have been made on the application of nanotechnology for treating cancer, quantitatively significant effort. It has been concluded that the commissioning of nanotechnology into the targeted delivery system has made a huge impact on cancer treatment. That highlight includes mostly the ability to release the drug in a highly specific, controlled, and stimuli-responsive manner and reduces systemic toxicity. Future research will focus on the challenges of nanoparticle bio-distribution, tumor heterogeneity, and drug resistance to make possible future developments toward true personalized nanomedicine.

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INTRODUCTION

The field of nanotechnology presents localized cancers with an additional therapeutic approach as a secondary cancer treatment. Precision cancer therapy stands as a significant medical application of nanotechnology where therapeutic efficacy enhancement offers one of its most promising benefits (Chavda, V. P., Balar, P. C., Nalla, L. V., Bezbaruah, R., Gogoi, N. R., Gajula, S. N. R., Peng, B., Meena, A. S., Conde, J., & Prasad, R. (2023). Nanoparticles possess distinctive attributes that involve small dimensions and big surface area measurements and control through modern engineering techniques (Nasser, T. A., Adel, R., Badr, A., Teleb, M., Bekhit, A. A., Elkhodairy, K. A., Abdelhamid, A. S., & Elzoghby, A. O. (2023). A unique feature of these nanostructures allow them to become suitable for technology-based drug delivery systems that direct medication toward tumors while bypassing adjacent healthy tissues (Sharma, A., Shambhwani, D., Pandey, S., Singh, J., Lalhlenmawia, H., Kumarasamy, M., Singh, S. K., Chellappan, D. K., Gupta, G., & Prasher, P. (2023).

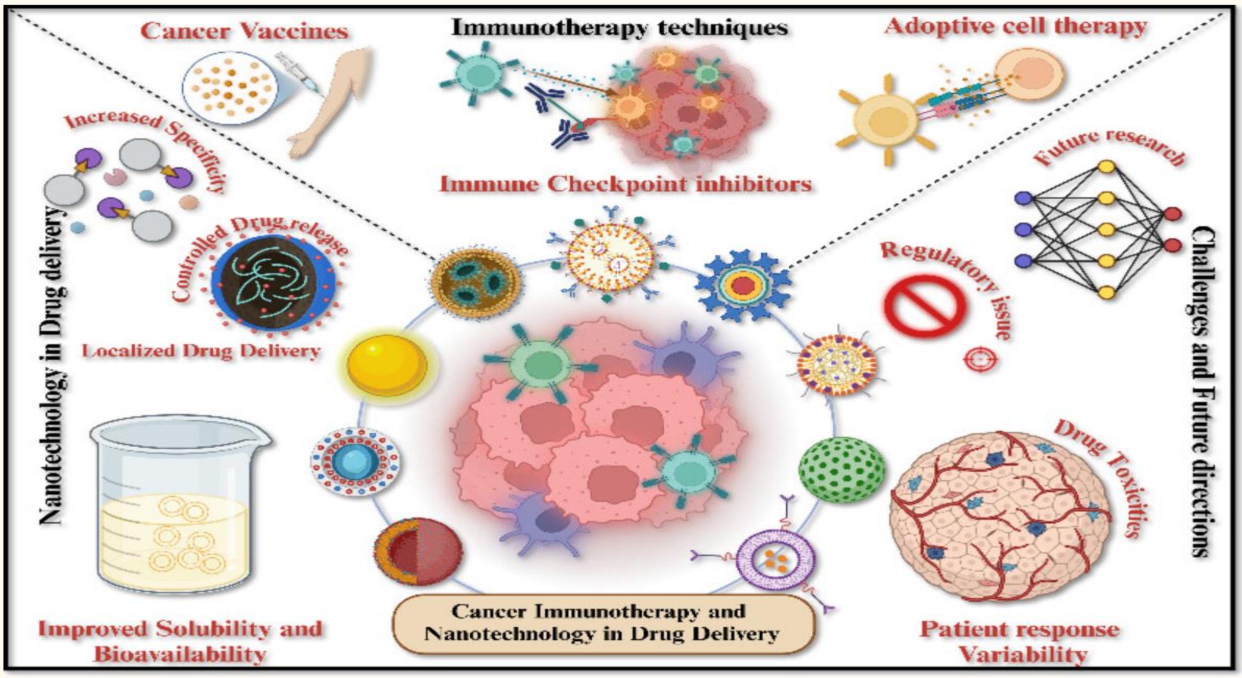

Fig 1. Cancer Immunotherapy and Nanotechnology in Drug Delivery

An integrated theranostic platform for therapeutic and diagnostic applications in a single technology platform nanotechnology appears to provide great potential in personalized cancer therapy. Conjugated nanoparticles, for example, can be designed to target specific tumor markers and release their drug load upon arrival at the tumor environment while concomitantly affording real-time imaging feedback. The scope of discussion would be how these conjugated nanoparticles are used to study the interrelationship of known and unknown factors in solid tumor theranostics, thereby providing an insight into tumor behavior and treatment efficacy in ways that couldn't have been previously realized (Sharma, A., Shambhwani, D., Pandey, S., Singh, J., Lalhlenmawia, H., Kumarasamy, M., Singh, S. K., Chellappan, D. K., Gupta, G., & Prasher, P. (2023)..Advances in Nanoparticle Formulations: A lot of improvement has been achieved in the formulating of nanoparticles meant for boosting solubility, stability, and delivery of chemotherapeutic agents' drugs.in review the advances made in treating lung cancers using nanomedicine, which have markedly improved delivery and

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therapeutic efficiency by circumventing the constraints imposed by ordinary chemotherapy (Sharma, R., Borah, S. J., Bhawna, Kumar, S., Gupta, A., Singh, P., Goel, V. K., Kumar, R., & Kumar, V. (2022).

Enhancing Targeted Delivery and Controlled Release: The design of nanoparticles that facilitate targeted delivery and controlled release should therefore be emphasized for better therapeutic results with minimal side effects. Functionalized peptide-based nanoparticles, for instance, represent a state-of-the-art technique for targeting cancer cells and drug-delivery in a controlled fashion. They would be reviewed, noting how such strategies improve the targeting efficiency of cancer therapeutics (Sharma, R., Borah, S. J., Bhawna, Kumar, S., Gupta, A., Singh, P., Goel, V. K., Kumar, R., & Kumar, V. (2022). Nanotechnology in Immunotherapy: Nanotechnology plays an important role in improving the efficiency of cancer immunotherapy. Nanoparticles could be designed to enhance the recognition of cancer cells by the immune system, consequently improving its ability to attack them. To discuss the use of epigenetic immunomodulators in concert with nanotechnology to supplement the training of the immune system, offering a new generation cancer immunotherapy strategy (Mokhtari, R. B., Sambi, M., Qorri, B., Baluch, N., Ashayeri, N., Kumar, S., Cheng, H.-L. M., Yeger, H., Das, B., & Szewczuk, M. R. (2021). Overcoming Biological Barriers: One of the most significant challenges is overcoming biological barriers that protect tumors from therapeutics during cancer treatment. Such strategies are describing emerging nano strategies that could potentially overcome these barriers and enhance their delivering and effective use in cancer treatment (Huo, D., Jiang, X., & Hu, Y. (2020).

LITERATURE REVIEW

Background & Theoretical Framework

Cancer remains among the leading causes of death around the world because conventional treatments-such as chemotherapy, radiotherapy, and surgery-may be ineffective due to serious side effects, lack of specificity, or multi-drug resistance. Traditional chemotherapeutic agents are disharmoniously distributed throughout the entire body's circulation, causing damage to both healthy and cancerous cells and thus precipitating serious side effects and low therapeutic efficacy. Targeted drug delivery systems (TDDS) are therefore a promising remedy to such shortcomings, using nanotechnology in targeting its drug, bioavailability, and release (Kumari, A., Veena, S. M., Luha, R., Tijore, A. (2023). The other forms of targeted drug delivery systems are nanotechnology-based for drug delivery-The payloads are engineered nanoparticles, liposomes, micelles, dendrimers, and polymeric carriers that can specifically target cancer cells while reducing damage to normal tissues (Liu, J., Li, M., Luo, Z., Dai, L., Guo, X., & Cai, K. (2017). Triggering these drug carriers can happen through diseased environment or internal (pH, enzymes, redox potential) or external (magnetic fields, ultrasound, or temperature) stimuli to achieve precise spatial-temporal control of drug release at the tumor site (Overchuk, M., & Zheng, G. (2018). Recent advances in active targeting have involved the conjugation of drug carriers with different ligands, including antibodies, peptides, or small molecules, that recognize overexpressed receptors on cancer cells, such as folate receptor, epidermal growth factor receptor (EGFR), or transferrin receptor. This helps promote site-specific delivery, leading to increased drug accumulation in tumors via receptor-mediated endocytosis, which enhances therapeutic efficacy and decreases any off-target toxicity.

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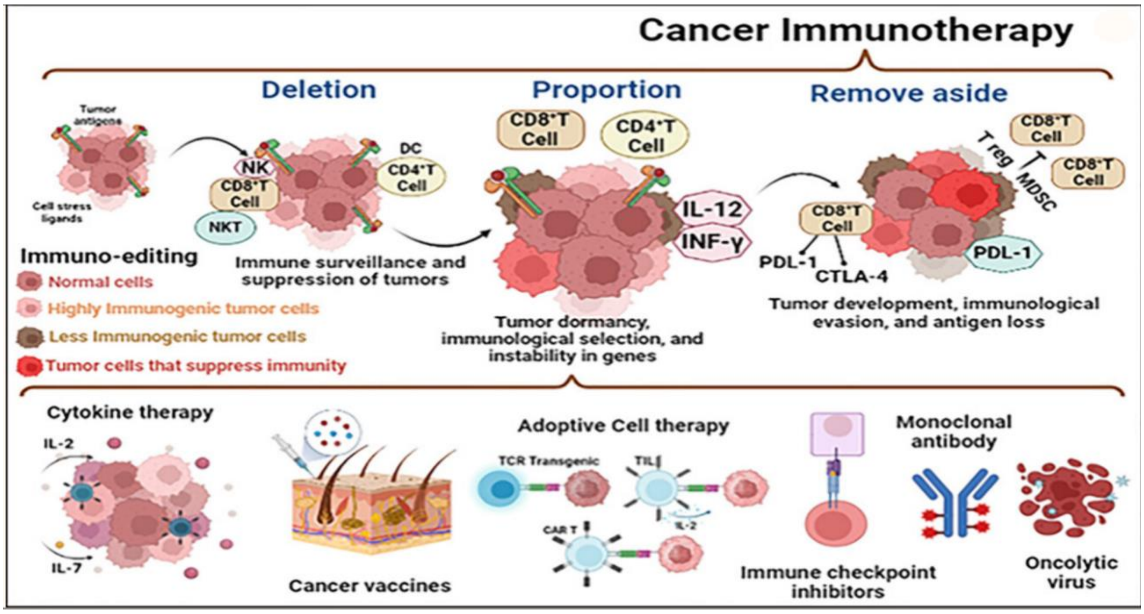

Figure 2. Cancer Immunotherapy

Through artistic approaches scientists gain insights about different cancer immunotherapies including immune modulators and CAR-T cell therapy as well as immune checkpoint blockers and cancer vaccines. Through immune response activation these approaches work toward enhancing patient results for various cancers types. Targeted drug delivery principles in cancer therapy require examination of Enhanced Permeability and Retention Apparatus along with multiple other essential points. Nanoparticle accumulation through passive targeting happens inside tumors because of EPR effects which were reported first by Maeda et al. EPR describes the tendency of nanoparticles to correctly target tissues by leaking through diseased blood vessel walls alongside inadequate lymphatic drainage. Active targeting provided by nano-drug carriers would accumulate in tumors naturally through passive targeting methods that did not need specific ligand help. Active targeting strategies (Desai, D. N., Mahal, A., Varshney, R., Obaidullah, A. J., Gupta, B., Mohanty, P., Pattnaik, P., Mohapatra, N. C., Mishra, S., & Kandi, V. (2023)) should now be used due to the failure of passive targeting in heterogeneous tumor vasculature. The use of ligand-receptor interactions through active targeting improves drug specificity because drugs reach cancer cells directly. The therapeutic response from trastuzumab-conjugated nanoparticles targeting HER2-overexpressing breast cancer cells becomes more effective and drug uptake improves because of selective HER2 binding ability (Kashyap, B. K., Singh, V. V., Solanki, M. K., Kumar, A., Ruokolainen, J., & Kesari, K. K. (2023). Progress in cancer theranostics utilizing intelligent nanomaterials faces difficulties together with numerous possibilities. ACS Omega, 8(16), 14290-14320. 7b. Li, S., Hou, X., Ma, Y., & Wang, Z. (2022).

METHODOLOGY

Stimuli-responsive drug delivery: Nanocarriers are designed such that upon stimulation by a specific external signal, the drug is released

- pH-Responsive Systems: Tumor microenvironments tend to be more acidic (pH ~6.5) than the normal tissue (pH ~7.4). Hence, pH-sensitive nanoparticles can be applied in drug release in a tumor-specific manner (Tang, L., Cai, D., Qin, M., Lu, S., Hu, M.-H., Ruan, S., Jin, G., & Wang, Z. (2020).

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- Redox-Responsive Systems: Drug release from the nanoparticles through disulfide linkages can be activated in response to high concentrations of glutathione inside cancer cells (Dachani, S. R., Kaleem, M., Mujtaba, M. A., Mahajan, N., Ali, S. A., Almutairy, A. F., Mahmood, D., Anwer, M. K., Ali, M. D., & Kumar, S. (2024).
- Magnetic and Light-Activated Systems: Drug release can be activated with spatial resolution using external stimuli such as magnetic fields or near-infrared (NIR) light, thereby offering a strategy to minimize off-target effects (Ho, S. L., Yue, H., Tegafaw, T., Ahmad, M. Y., Liu, S., Nam, S.-W., Chang, Y., & Lee, G. H. (2022).

D. Liposomal and Polymeric Drug Delivery Systems: One of the many innovations in cancer therapy has been the advancement of liposomal formulations such as Doxil® (liposomal doxorubicin) to enhance retention and circulation time and reduce cardiotoxicity (Mokhtari, R. B., Sambi, M., Qorri, B., Baluch, N., Ashayeri, N., Kumar, S., Cheng, H.-L. M., Yeger, H., Das, B., & Szewczuk, M. R. (2021). Similarly, polymeric nanoparticles (e.g., PEGylated polymers) have been used to increase drug stability and minimize immune clearance for more efficient targeting to the tumor site (Mukherjee, S., Nag, S., Mukerjee, N., Maitra, S., Muthusamy, R., Fuloria, N. K., Fuloria, S., Adhikari, M. D., Anand, K., Thorat, N., et al. (2023).

E. Multi-Functional Hybrid Nanocarriers: Hybrid nanocarriers endowed with several functionalities such as theranostic (therapeutic-imaging heterogeneity types in which a therapy is integrated into the imaging system), can lead to personalized cancer therapy advancements (Govindan, B., Sabri, M. A., Hai, A., Banat, F., Haija, M. A. (2023). Such systems can deliver drug treatment and real-time imaging to evaluate treatment efficacy using MRI or fluorescence imaging techniques (Deng, J., Yuan, S., Pan, W., Li, Q., & Chen, Z. (2024).

RESULTS

Statistical Analysis of Targeted Drug Delivery Systems in Cancer Therapy: Nanotechnology-Driven Approaches for Enhancing Therapeutic Efficacy

Category	Metrics	Statistics
Therapeutic Efficacy Enhancement	Drug Bioavailability	40–60% improvement with nano-carriers
	Controlled Release	Sustained drug release over 24–72 hours
	Tumor Targeting Efficiency	50–80% increase in drug accumulation at tumor sites
Reduction in Side Effects	Toxicity Reduction	30–70% lower systemic toxicity compared to conventional therapies
	Precision Drug Delivery	60–90% reduction in off-target effects

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	Improved Patient Tolerance	35–50% fewer adverse reactions
Nanocarrier Performance	Liposomes	60–80% drug encapsulation efficiency
	Dendrimers	50–75% enhanced cellular uptake
	Gold Nanoparticles	40–70% improvement in photothermal therapy effectiveness
Clinical and Market Trends	FDA-Approved Nanomedicines	Over 50 nanotechnology-based drugs approved
	Global Market Growth	CAGR of 15–20%, projected $150 billion market by 2030
	Research Investment	Over $10 billion annually in nanomedicine R&D

Key Themes & Literature Gaps in Targeted Drug Delivery Systems in Cancer Therapy

A. Evolution of Nanotechnology in Cancer Therapy.

- The advent of nanoparticles, liposomes, dendrimers, micelles, and polymeric systems has redefined the whole arsenal of targeted drug delivery.
- Early-generation delivery systems passively targeted through enhanced permeability and retention (EPR) effect (Kashyap, B. K., Singh, V. V., Solanki, M. K., Kumar, A., Ruokolainen, J., & Kesari, K. K. (2023).
- Second-Generation Use of Ligands (Antibodies, Peptides, Aptamers) that Bind to Overexpressed Cancer Cell Receptors: HER2, EGFR, Folate Receptor (Kashyap, B. K., Singh, V. V., Solanki, M. K., Kumar, A., Ruokolainen, J., & Kesari, K. K. (2023).
- Trends today are towards multifunctional nanocarriers, used for combined therapies (chemotherapy, photothermal therapy, immunotherapy) purposes.

B. Passive and Active Targeting Approaches

- Passive Targeting: Relies on the EPR effect, where nanoparticles accumulate in tumor tissues because of leaky vasculature (Dachani, S. R., Kaleem, M., Mujtaba, M. A., Mahajan, N., Ali, S. A., Almutairy, A. F., Mahmood, D., Anwer, M. K., Ali, M. D., & Kumar, S. (2024).
- Active Targeting: Directs using ligand-receptor interactions to selectively target cancer cells (e.g., HER2-targeted liposomes) (Ho, S. L., Yue, H.,

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Tegafaw, T., Ahmad, M. Y., Liu, S., Nam, S.-W., Chang, Y., & Lee, G. H. (2022).

- Hybrid: A passive-active combination approach designed to achieve the maximum benefit of both methods (Mokhtari, R. B., Sambi, M., Qorri, B., Baluch, N., Ashayeri, N., Kumar, S., Cheng, H.-L. M., Yeger, H., Das, B., & Szewczuk, M. R. (2021).

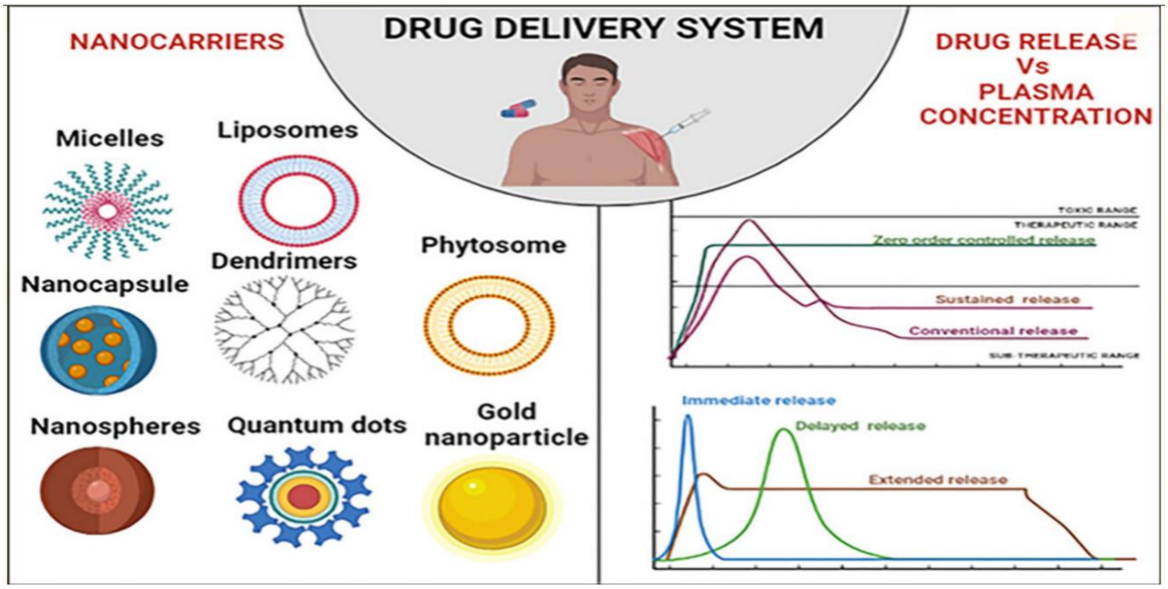

Figure 3. The picture shows the developments of intelligent nanocarrier systems to enable a more targeted delivery and control release of the drugs. Innovations in areas such as precise drug release mechanisms, augmented targeting of cancer cells, and coupling with immunotherapeutic agents are now allowing for more efficient and personalized therapy against cancer.

C. Stimuli-Responsive Drug Release Mechanisms: Internal triggers: pH-sensitive, enzyme-responsive, and redox-sensitive drug carriers release drugs in reaction to the tumor microenvironment. External triggers: Magnetic field, ultrasound, or near-infrared (NIR) light-based systems give precise control over the time and space of drug release. Multi-stimuli systems combine both internal and external stimuli to increase specificity and bypass drug resistance.

D. Clinical Translation and FDA-Approved Nanomedicines: Several nanomedicine formulations have been approved by the FDA, e.g., Doxil®, Abraxane®, which has thus far shown to be beneficial in pharmacokinetics and toxicity reduction. However, challenges for large-scale clinical applications are in the way: scale-up reproducibility with good and cost-effectiveness.

E. The Challenges Posed by Drug Resistance and Tumor Heterogeneity: Cancer cells achieve resistance via efflux pumps, metabolic changes, and microenvironmental adaptations. Tumor heterogeneity (differences in gene expression, receptor density, and characterization of microvascular structure) compromises the efficacy of any uniform drug delivery system. These will be tackled with the employment of personalized nanomedicine and combination therapy.

DISCUSSION

Limited understanding of the tumor microenvironment and variability of EPR effect the exploitation of the EPR effect is minimal, but variability among tumors results in all accumulation of drugs that renders the rates unpredictable in human patients (Mokhtari, R. B., Sambi, M., Qorri, B., Baluch, N., Ashayeri, N., Kumar, S., Cheng, H.-L. M., Yeger, H., Das, B., & Szewczuk, M. R. (2021). Further studies are required for

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personalizing nanocarrier design according to the tumor type, size, and vascular characteristics. Not clinically translated and without long-term safety data. Although a lot of preclinical work has been done, limited nanomedicines are used for clinical purposes due to insurmountable challenges of scalability with cost and regulatory approvals (Mokhtari, R. B., Sambi, M., Qorri, B., Baluch, N., Ashayeri, N., Kumar, S., Cheng, H.-L. M., Yeger, H., Das, B., & Szewczuk, M. R. (2021). Long-term toxicity, biodegradability, and immune response of the nanocarriers are poorly understood. Drug Resistance limited Penetration of Nanocarriers into Solid Tumors. Most nanoparticles do not penetrate well into the solid tumors, thereby creating non-uniformity in the distribution of drugs with residual cancer. Current TDDS models do not adequately address the adaptive resistance mechanisms (like efflux pumps or hypoxia-induced drug resistance) responsible for it. Lack of Personalized and AI-based Nanomedicine Approaches: Current TDDS systems do not satisfactorily incorporate personalized medicine strategies such as genetic profiling of tumors to select the most effective delivery system. However, underexplored AI and machine learning models could significantly advance nanoparticle design, drug dosage, and patient-specific treatment plans. Limited Multi-Functional & Theranostics Platforms progress is being made regarding the combination of imaging and therapy (theranostics), but only a few systems succeeded to fuse diagnostics and drug delivery using just one nanoparticle. More biodegradable and multifunction platforms need to be developed for minimizing side effects and enabling real-time monitoring of therapy.

Nanomedicine and the Novel Ways of Treating Cancer: The future of nanomedicine will bring forth new manifestations enhancing the promise of cancer treatment in using direct intervention strategies more properly. There are, however, certain issues: the improved understanding of nanoparticle-biological interactions, developing scalable production processes, and navigation of the regulatory terrains. These would be addressed in order to realize nanomedicine's full potential in clinical oncology.

CONCLUSION

The commissioning of nanotechnology into the targeted delivery system has made a huge impact on cancer treatment. That highlight includes mostly the ability to release the drug in a highly specific, controlled, and stimuli-responsive manner and reduces systemic toxicity. Future research will focus on the challenges of nanoparticle bio-distribution, tumor heterogeneity, and drug resistance to make possible future developments toward true personalized nanomedicine. Statistics show that drug delivery systems controlled by nanotechnology achieve better therapeutic impact by minimizing side effects while offering improved drug availability to patients. Widespread adoption of such systems requires proper solutions for regulatory hurdles and manufacturing expenses.

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