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Nanoparticle-Based Drug Delivery Systems in Cancer Therapy: Enhancing Targeted Treatment and Reducing Toxicity

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ABSTRACT

Cancer remains one of the leading causes of mortality worldwide, posing significant challenges to conventional therapeutic approaches due to poor targeting, systemic toxicity, and multidrug resistance. Nanoparticle-based drug delivery systems (NDDSs) have emerged as a revolutionary strategy in oncological treatment, offering improved drug bioavailability, enhanced tumor targeting, and reduced off-target effects. These nanoscale carriers such as liposomes, dendrimers, polymeric nanoparticles, metallic nanoparticles, and lipid-based systems are engineered to optimize the pharmacokinetics and pharmacodynamics of chemotherapeutic agents. By exploiting passive and active targeting mechanisms, NDDSs facilitate preferential accumulation in tumor tissues via the enhanced permeability and retention (EPR) effect and ligand-receptor mediated interactions. Moreover, functionalization with ligands like antibodies, peptides, or aptamers further augments their specificity and uptake by cancer cells. This review provides an in-depth analysis of the types of nanoparticles employed in cancer therapy, design considerations for targeted delivery, recent advancements in stimuli-responsive and multifunctional NDDSs, and the translational challenges impeding clinical adoption. Emphasis is also placed on FDA-approved nanoformulations, emerging preclinical data, and prospects for personalized nanomedicine in oncology. Ultimately, NDDSs represent a promising frontier in improving cancer therapeutic outcomes while minimizing toxicity and enhancing patient quality of life.

Keywords: Nanoparticles, Targeted Drug Delivery, Cancer Therapy, Tumor Targeting, Drug Toxicity Reduction

INTRODUCTION

Cancer remains one of the leading causes of death globally, with millions of new cases diagnosed each year. Despite remarkable progress in our understanding of tumor biology and the advent of advanced therapeutic strategies, cancer treatment still faces several formidable challenges[1–3]. Traditional therapeutic modalities such as chemotherapy, radiation therapy, and surgery have been the cornerstone of cancer treatment for decades. Among these, chemotherapy remains one of the most widely used approaches due to its ability to target rapidly dividing cells. However, conventional chemotherapeutic agents are associated with numerous limitations that severely hinder their long-term success in clinical settings[2, 4–6].

One of the most significant drawbacks of traditional chemotherapy is its lack of specificity. Most chemotherapeutic agents cannot distinguish between malignant and healthy proliferating cells, leading to systemic toxicity[7–9]. This indiscriminate targeting often results in severe side effects, including myelosuppression, gastrointestinal toxicity, alopecia, and cardiotoxicity, which greatly compromise patient quality of life and may even limit the dosage or duration of treatment [10]. In addition to off-target toxicity, many chemotherapeutic drugs suffer from poor solubility and bioavailability, necessitating the use of high drug concentrations that further exacerbate toxicity[11, 12].

Another major hurdle in cancer chemotherapy is the development of multidrug resistance (MDR), a phenomenon whereby cancer cells become resistant to a wide range of chemotherapeutic agents[13–15]. MDR can arise through various mechanisms, including increased drug efflux by ATP-binding cassette (ABC) transporters, enhanced DNA repair, alterations in drug targets, and evasion of apoptosis[16–18]. This resistance severely limits the effectiveness of chemotherapy, leading to disease recurrence and metastasis. Overcoming MDR is therefore a critical priority in the design of next-generation cancer therapies.

To address these pressing challenges, researchers have turned to nanotechnology, an interdisciplinary field that manipulates matter at the nanometer scale (typically between 1–100 nm), to engineer innovative solutions for drug delivery[19]. The development of nanoparticle-based drug delivery systems (NDDSs) represents a groundbreaking advancement in oncology[19]. These systems are engineered to improve the therapeutic index of anticancer agents by enhancing drug solubility, prolonging circulation time, facilitating targeted delivery, and enabling controlled release of the drug payload. NDDSs offer several key advantages over conventional drug formulations. Most notably, nanoparticles can be functionalized with targeting ligands, such as antibodies, peptides, or small molecules, that recognize and bind to specific receptors overexpressed on cancer cells. This active targeting strategy enhances the selective accumulation of therapeutic agents at tumor sites, thereby minimizing exposure to normal tissues and reducing systemic toxicity[20]. Additionally, the enhanced permeability and retention (EPR) effect, a phenomenon wherein nanoparticles preferentially accumulate in tumor tissues due to leaky vasculature and poor lymphatic drainage further promotes passive targeting of tumors[20].

Moreover, NDDSs can be designed to respond to specific stimuli within the tumor microenvironment (TME), such as acidic pH, elevated enzyme activity, or redox conditions. These stimuli-responsive systems enable site-specific drug release, which further improves therapeutic efficacy and limits off-target effects[21]. Some NDDSs also facilitate co-delivery of multiple therapeutic agents, including small-molecule drugs, siRNAs, and immunotherapeutics, to achieve synergistic anticancer effects and combat MDR. Various types of nanocarriers have been developed for cancer therapy, including liposomes, polymeric nanoparticles, dendrimers, solid lipid nanoparticles, gold nanoparticles, mesoporous silica nanoparticles, and carbon-based nanomaterials[21]. Each of these platforms offers unique physicochemical properties that can be tailored to specific therapeutic needs. For example, liposomes have demonstrated clinical success with several FDA-approved formulations such as Doxil® (liposomal doxorubicin), which significantly reduces cardiotoxicity compared to free doxorubicin. Similarly, polymeric nanoparticles offer excellent versatility in terms of size, surface modification, and drug loading capacity[22].

Despite the promising potential of NDDSs, several challenges remain before they can be fully integrated into clinical practice. Issues such as large-scale manufacturing, batch-to-batch reproducibility, long-term safety, and regulatory approval must be carefully addressed. Additionally, the heterogeneity of the tumor microenvironment and interpatient variability can influence nanoparticle distribution and therapeutic outcomes, necessitating personalized approaches[23].

Nanoparticle-based drug delivery systems represent a transformative paradigm in cancer therapy. By addressing the limitations of conventional chemotherapy including poor specificity, systemic toxicity, and multidrug resistance. NDDSs pave the way for more effective, safer, and personalized cancer treatments. Continued interdisciplinary research and clinical translation efforts are essential to fully harness the potential of nanotechnology in the fight against cancer.

2. Overview of Nanoparticles in Drug Delivery

Nanoparticle-based drug delivery systems (NDDSs) represent a transformative approach in modern cancer therapy, offering improved specificity, reduced toxicity, and enhanced drug accumulation at tumor sites[24, 25]. Nanoparticles, defined as structures with dimensions ranging from 1 to 1000 nanometers, are engineered to encapsulate and transport chemotherapeutic agents while overcoming biological barriers. These systems improve pharmacokinetics and bioavailability, protect drugs from premature degradation, and allow for controlled or sustained release. Various nanoparticle types each with unique physicochemical properties are utilized to match the specific requirements of different therapeutic agents and cancer types[26, 27]. Moreover, NDDSs can exploit the enhanced permeability and retention (EPR) effect in tumors for passive targeting or be functionalized with ligands for active targeting of cancer cells. The modularity of nanoparticles enables them to be combined with imaging agents for diagnosis and monitoring, leading to theranostic applications. Current advancements also focus on multi-functional platforms capable of co-delivering drugs, genes, or immunomodulatory agents, enhancing therapeutic outcomes. Importantly, regulatory-approved formulations like liposomal doxorubicin (Doxil®) demonstrate the clinical viability of these systems[27, 28]. The following sections discuss the major nanoparticle types used in drug delivery: liposomes, polymeric nanoparticles, dendrimers, metallic nanoparticles, and lipid-based nanoparticles, outlining their mechanisms, advantages, and clinical relevance.

2.1 Liposomes

Liposomes are spherical vesicles composed of one or more phospholipid bilayers that can encapsulate therapeutic agents, making them versatile carriers for both hydrophilic and hydrophobic drugs[29–31]. Hydrophilic drugs are sequestered within the aqueous core, while hydrophobic drugs integrate into the lipid bilayer, offering dual drug-loading capability. Their biocompatibility, biodegradability, and ability to reduce systemic toxicity make liposomes one of the most studied and clinically used nanoparticle systems in cancer therapy. A notable example is Doxil®, a pegylated liposomal formulation of doxorubicin[32]. This formulation prolongs circulation time, minimizes cardiotoxicity, and enhances drug accumulation in tumors via the enhanced permeability and retention (EPR) effect. Surface modifications, such as PEGylation, prevent opsonization and uptake by the reticuloendothelial system, thus improving pharmacokinetics[33]. Furthermore, liposomes can be functionalized with ligands (e.g., antibodies, peptides) for active targeting, enhancing selective uptake by cancer cells. Thermosensitive and pH-sensitive liposomes are also being developed to release drugs in response to tumor-specific stimuli. Despite their advantages, challenges include limited drug loading, stability during storage, and potential leakage of drugs. Nevertheless, ongoing innovations in liposome design are expanding their clinical applications in oncology, making them foundational components of NDDS strategies[33].

2.2 Polymeric Nanoparticles

Polymeric nanoparticles are solid colloidal particles made from natural or synthetic biodegradable polymers such as polylactic-co-glycolic acid (PLGA), polycaprolactone (PCL), and chitosan[34, 35]. These systems are extensively researched for drug delivery due to their tunable size, surface properties, and degradation rates, which allow precise control over drug release kinetics. Polymeric nanoparticles offer enhanced protection of labile drugs from enzymatic degradation and can improve the solubility and bioavailability of poorly water-soluble agents. They are suitable for both passive and active targeting strategies—passive via the EPR effect and active by surface conjugation with ligands like folate, transferrin, or antibodies for receptor-mediated endocytosis. Additionally, polymeric nanoparticles can co-deliver multiple agents (e.g., chemotherapeutics and siRNAs) in a single formulation, supporting combination therapy approaches [36, 37]. Their surfaces can also be engineered with PEG to increase circulation time or functionalized for stimulus-responsive drug release (e.g., pH, redox, or temperature-sensitive systems). PLGA-based nanoparticles have received FDA approval for various applications, highlighting their clinical potential. Despite challenges related to scale-up, reproducibility, and cost, continuous advancements in polymer synthesis and nanoparticle fabrication techniques are driving their translation from bench to bedside.

2.3 Dendrimers

Dendrimers are highly branched, monodisperse macromolecules with a tree-like architecture, characterized by a central core, internal branching units, and numerous terminal functional groups[2]. Their precise molecular size, shape, and surface chemistry make them ideal platforms for drug delivery, especially in cancer therapy. The multiple terminal groups allow for the conjugation of a wide range of therapeutic agents, targeting ligands, and imaging molecules, enabling multifunctionality in a single nanocarrier[38]. Dendrimers can encapsulate drugs within their internal cavities or covalently bind them to surface groups, offering both physical and chemical loading strategies. Poly(amidoamine) (PAMAM) and poly (propylene imine) (PPI) are among the most widely studied dendrimers. Their nanometric size facilitates cellular uptake via endocytosis, while their well-defined surface chemistry allows fine-tuning of pharmacokinetic and biodistribution profiles. Dendrimers can be functionalized to enhance biocompatibility, reduce cytotoxicity, and provide stimulus-responsive drug release. For example, folate-conjugated dendrimers can selectively target folate receptor-overexpressing tumor cells[38]Challenges with dendrimers include potential cytotoxicity from cationic surface groups, immunogenicity, and complex synthesis procedures. However, their versatility and modular design continue to attract significant research interest, particularly for personalized and targeted cancer therapies, diagnostics, and gene delivery.

2.4 Metallic Nanoparticles

Metallic nanoparticles, particularly gold (AuNPs) and iron oxide nanoparticles (IONPs), are garnering attention in cancer nanomedicine due to their unique optical, magnetic, and surface plasmon resonance properties[38]. These features make them highly suitable for both therapeutic and diagnostic applications a field known as theranostics. Gold nanoparticles are valued for their excellent biocompatibility, ease of functionalization, and ability to convert light into heat for photothermal therapy (PTT). When conjugated with targeting ligands and anticancer drugs, AuNPs can selectively accumulate in tumors and trigger drug release or hyperthermia under near-infrared (NIR) irradiation, causing localized tumor cell death. Iron oxide nanoparticles, on the other hand, possess superparamagnetic properties that make them ideal for magnetic resonance imaging (MRI) contrast enhancement and magnetic drug targeting[39]. Moreover, they can be directed to tumor sites using external magnetic fields, increasing drug accumulation and reducing off-target effects. Surface modifications improve their stability, biocompatibility, and functional capacity. Despite these benefits, metallic nanoparticles face challenges like long-term toxicity, accumulation in organs, and difficulty in degradation. Nevertheless, their multifunctional potential continues to drive research into safe and effective formulations that combine imaging, targeting, and therapy in a single platform.

2.5 Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs)

Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs) are lipid-based nanoparticles developed to overcome the limitations of traditional drug delivery systems, particularly for lipophilic compounds[40, 41]. SLNs consist of solid lipids stabilized by surfactants, which encapsulate drugs within a solid matrix, providing protection from degradation and enabling controlled drug release. However, SLNs often face limitations such as low drug loading and potential drug expulsion during storage. To address this, Nanostructured Lipid Carriers (NLCs) were developed, incorporating a blend of solid and liquid lipids to form a less ordered matrix, which enhances drug loading and minimizes leakage[41, 42]. Both systems are biocompatible and biodegradable, making them suitable for systemic, oral, and topical administration[43, 44]. They can also be surface-modified with PEG or targeting ligands for prolonged circulation and site-specific drug delivery. SLNs and NLCs exhibit excellent physical stability, scalable production, and the ability to bypass multidrug resistance mechanisms in cancer cells. Their applications extend to delivering chemotherapeutics, anti-inflammatory agents, and even nucleic acids. Current research focuses on optimizing their composition and surface characteristics to improve therapeutic outcomes. As lipid-based carriers, SLNs and NLCs present promising alternatives for efficient and targeted cancer therapy with minimal systemic toxicity.

3. Targeting Mechanisms in NDDSs

3.1 Passive Targeting: Passive targeting primarily relies on the Enhanced Permeability and Retention (EPR) effect, a unique feature of solid tumors that enables selective accumulation of nanoparticles in tumor tissue[45]. Tumors often exhibit irregular, leaky vasculature due to rapid and defective angiogenesis, resulting in fenestrations or gaps ranging from 100 to 800 nm in endothelial linings. Additionally, the lymphatic drainage system in tumors is typically poor or dysfunctional, limiting the clearance of macromolecules and nanoparticles. These two pathological features together allow nanoparticles particularly those within the size range of 10–200 nm to preferentially extravasate and accumulate in tumor tissues while sparing normal tissues[46]. Passive targeting does not involve any specific interaction between nanoparticles and tumor cells but depends on physiochemical parameters such as particle size, surface charge, shape, and hydrophilicity, which influence circulation time and biodistribution. Long-circulating nanoparticles, such as PEGylated liposomes, can evade the reticuloendothelial system (RES), prolonging their systemic presence and enhancing their likelihood of reaching the tumor site. This approach has been successfully employed in clinically approved nanomedicines like Doxil® for breast and ovarian cancers. However, variability in the EPR effect among different tumors and patients presents a major challenge to consistent therapeutic outcomes[46].

3.2 Active Targeting: Active targeting enhances the specificity of nanoparticle-based drug delivery systems by modifying their surfaces with ligands that selectively bind to overexpressed receptors on cancer cells or tumor-associated endothelium[47]. Unlike passive targeting, which depends on tumor physiology, active targeting uses a "lock-and-key" mechanism, where the ligand on the nanoparticle acts as a “key” to bind a “lock” specific receptors such as HER2, epidermal growth factor receptor (EGFR), folate receptor, or transferrin receptor found in abundance on tumor cells. Common targeting ligands include monoclonal antibodies (e.g., trastuzumab for HER2), peptides (e.g., RGD peptides for integrins), folic acid, aptamers, and small molecules[47]. Once binding occurs, the nanoparticle-receptor complex may be internalized via receptor-mediated endocytosis, improving intracellular drug delivery and therapeutic efficacy. Active targeting not only enhances drug accumulation at the tumor site but also reduces systemic toxicity by minimizing off-target effects. It can be used in conjunction with passive targeting to increase specificity and drug delivery efficiency. Several preclinical and clinical studies have demonstrated the potential of this strategy in improving therapeutic indices, although challenges such as receptor heterogeneity, immune responses to ligands, and manufacturing complexity remain to be addressed for widespread clinical application[48].

4. Stimuli-Responsive Nanocarriers: Stimuli-responsive nanocarriers represent a cutting-edge advancement in nanoparticle-based drug delivery systems (NDDSs), enabling precise control over the release of therapeutic agents based on specific internal or external stimuli[49, 50]. These smart systems are engineered to exploit the unique characteristics of the tumor microenvironment or respond to externally applied triggers, thereby ensuring that drug release occurs selectively at the desired site and time. This spatiotemporal control minimizes systemic toxicity and enhances therapeutic efficacy, making them highly promising in the field of cancer therapy[50].

Internal stimuli-responsive nanocarriers take advantage of the distinct physiological conditions typically present in tumor tissues. One of the most exploited internal cues is pH[51]. Tumor tissues often exhibit a slightly acidic microenvironment due to altered metabolism and hypoxia. pH-sensitive nanoparticles are thus designed to remain stable at physiological pH (~7.4) but to destabilize or degrade in acidic conditions (~6.5 or lower), leading to the controlled release of the encapsulated drug specifically within the tumor region. This targeted release reduces off-target effects and maximizes drug accumulation at the tumor site[52].

Another common internal trigger is the redox potential, which differs significantly between normal and cancerous cells. Cancer cells generally contain higher levels of intracellular reducing agents such as glutathione. Redox-sensitive nanocarriers incorporate disulfide bonds or other redox-cleavable linkages in their structure, which remain intact in the bloodstream but break down in the presence of elevated glutathione levels inside cancer cells. This mechanism enables the precise release of drugs within malignant cells, sparing healthy tissues from unnecessary exposure[53]. Apart from internal cues, external stimuli can also be harnessed to control drug release from nanocarriers. Thermo-responsive systems are designed to alter their structure or solubility in response to elevated temperatures, which can be induced locally using external heat sources or focused ultrasound. This allows localized release of the drug in heated tumor regions. Similarly, magneto-responsive nanocarriers can be guided to tumor sites using external magnetic fields and subsequently triggered to release their cargo via magnetic heating or mechanical disruption. Ultrasound-triggered systems, on the other hand, use acoustic energy to induce changes in the carrier's structure, leading to drug release with spatial precision.[54]

Overall, stimuli-responsive nanocarriers provide a powerful strategy to overcome the limitations of conventional chemotherapy by enabling site-specific and controlled drug delivery. This innovation not only enhances therapeutic outcomes but also significantly reduces adverse side effects associated with systemic drug distribution.

5. Clinical Applications and Approved NDDSs (Nanoparticle Drug Delivery Systems)

The clinical translation of nanoparticle-based drug delivery systems (NDDSs) marks a significant advancement in oncology, with several formulations already approved for therapeutic use. These approved NDDSs exemplify how nanotechnology can enhance drug pharmacokinetics, improve therapeutic indices, and minimize systemic toxicity compared to conventional chemotherapeutics[55].

One of the earliest and most successful NDDSs is Doxil®, a pegylated liposomal formulation of doxorubicin. It is approved for the treatment of ovarian cancer and AIDS-related Kaposi's sarcoma. By encapsulating doxorubicin in liposomes and coating them with polyethylene glycol (PEG), Doxil® prolongs circulation time, enhances accumulation at tumor sites via the Enhanced Permeability and Retention (EPR) effect, and significantly reduces cardiotoxicity a major side effect of free doxorubicin[56].

Abraxane® is another clinically approved NDDS, consisting of paclitaxel bound to human serum albumin nanoparticles. It is used for the treatment of metastatic breast cancer, non-small cell lung cancer, and pancreatic cancer. The albumin-bound formulation improves drug solubility and facilitates receptor-mediated uptake into tumor cells via albumin-specific pathways, thereby enhancing the cytotoxic effect of paclitaxel while avoiding the need for toxic solvents like Cremophor EL[57].

Onivyde® is a liposomal formulation of irinotecan approved for use in metastatic pancreatic cancer, particularly in patients who have failed prior gemcitabine-based therapies. The liposomal delivery prolongs circulation, increases tumor uptake, and improves the drug's half-life and tolerability[58].

These clinically approved NDDSs illustrate the potential of nanomedicine to transform cancer therapy by improving drug bioavailability, targeting efficiency, and therapeutic response. Ongoing clinical trials continue to evaluate newer nanoparticle-based drugs, expanding the repertoire of nanocarrier-enabled therapies in oncology and other disease domains.

6. Advantages of NDDSs in Cancer Therapy

Nanoparticle-based drug delivery systems (NDDSs) offer several distinct advantages over conventional chemotherapy in cancer treatment. One major benefit is the enhanced solubility and bioavailability of poorly water-soluble drugs, allowing for more effective delivery and absorption in the body[59]. PEGylation, the attachment of polyethylene glycol chains, significantly extends the circulation time of nanoparticles by preventing recognition and clearance by the immune system. NDDSs also protect drugs from premature degradation and clearance, ensuring more of the therapeutic agent reaches the target[60]. Tumor-specific accumulation is achieved through passive targeting using the Enhanced Permeability and Retention (EPR) effect and active targeting via ligands that bind to tumor-specific markers. This selectivity reduces systemic toxicity by minimizing exposure to healthy tissues. Furthermore, NDDS platforms can co-deliver multiple therapeutic agents, such as combinations of chemotherapeutic drugs, genes, or immunotherapeutics, enabling synergistic effects and overcoming drug resistance for improved clinical outcomes[60].

7. Challenges and Limitations

Despite their potential, NDDSs face several challenges that hinder their widespread clinical translation. One major obstacle is the heterogeneity of tumor vasculature, which can limit the effectiveness of the Enhanced Permeability and Retention (EPR) effect and result in uneven nanoparticle distribution. Additionally, some nanomaterials may provoke immune responses or exhibit intrinsic toxicity, raising safety concerns. Scaling up production while ensuring reproducibility, stability, and cost-effectiveness remains a significant hurdle for industrial application. Regulatory pathways for NDDSs are also underdeveloped, with a lack of standardized protocols for safety assessment, quality control, and approval, slowing their entry into clinical use. Moreover, dense extracellular matrices in solid tumors can hinder deep nanoparticle penetration, reducing therapeutic efficacy. These challenges underscore the need for continuous innovation, rigorous safety evaluation, and standardized manufacturing protocols to ensure the successful integration of NDDSs into mainstream cancer therapy.

8. Emerging Trends and Future Directions

The future of NDDSs in cancer therapy lies in the development of next-generation platforms that integrate multiple functionalities. Multifunctional nanocarriers, or theranostics, combine therapeutic delivery with diagnostic imaging, allowing real-time monitoring of drug distribution and treatment response. Personalized nanomedicine is also gaining traction, where nanoparticles are tailored to the molecular profile of individual tumors, enhancing specificity and efficacy. Artificial Intelligence (AI) is increasingly being used to optimize nanocarrier design by predicting drug-nanoparticle interactions, biodistribution, and patient response. Biomimetic nanoparticles, such as those coated with cell membranes or derived from natural exosomes, offer improved biocompatibility, immune evasion, and targeted delivery. Additionally, CRISPR-loaded nanoparticles represent a promising frontier for gene editing in cancer therapy, enabling precise correction of oncogenic mutations. These emerging strategies aim to overcome current limitations and usher in a new era of safer, smarter, and more effective nanomedicine-based cancer treatments.

CONCLUSION

Nanoparticle-based drug delivery systems represent a transformative approach in cancer therapeutics. Through enhanced targeting, controlled drug release, and reduced systemic toxicity, NDDSs offer significant improvements over conventional therapies. Continued advancements in nanoparticle engineering, combined with personalized medicine strategies and robust clinical translation pathways, hold the potential to revolutionize cancer care and significantly improve patient outcomes.

REFERENCES

1. Abbas, Z., Rehman, S., Abbas, Z., Rehman, S.: An Overview of Cancer Treatment Modalities. In: Neoplasm. IntechOpen (2018)
2. Abedi-Gaballu, F., Dehghan, G., Ghaffari, M., Yekta, R., Abbaspour-Ravasjani, S., Baradaran, B., Dolatabadi, J.E.N., Hamblin, M.R.: PAMAM dendrimers as efficient drug and gene delivery nanosystems for cancer therapy. Appl Mater Today. 12, 177–190 (2018). https://doi.org/10.1016/j.apmt.2018.05.002
3. Tufail, T., Uti, D.E., Aja, P.M., Offor, C.E., Ibiam, U.A., Ukaidi, C.U.A.: Utilizing Indigenous Flora in East Africa for Breast Cancer Treatment: An Overview. Anticancer Agents Med Chem. 25, 99–113 (2025). https://doi.org/10.2174/0118715206338557240909081833
4. Akhmetkaliyev, A., Alibrahim, N., Shafiee, D., Tulchinsky, E.: EMT/MET plasticity in cancer and Go-or-Grow decisions in quiescence: the two sides of the same coin? Molecular Cancer. 22, 90 (2023). https://doi.org/10.1186/s12943-023-01793-z
5. Al-Thani, A.N., Jan, A.G., Abbas, M., Geetha, M., Sadasivuni, K.K.: Nanoparticles in cancer theragnostic and drug delivery: A comprehensive review. Life Sciences. 352, 122899 (2024). https://doi.org/10.1016/j.lfs.2024.122899
6. Ali Abdalla, Y.O., Subramaniam, B., Nyamathulla, S., Shamsuddin, N., Arshad, N.M., Mun, K.S., Awang, K., Nagoor, N.H.: Natural Products for Cancer Therapy: A Review of Their Mechanism of Actions and Toxicity in the Past Decade. J Trop Med. 2022, 5794350 (2022). https://doi.org/10.1155/2022/5794350
7. Alum, E.U., Uti, D.E., Ugwu, O.P.-C., Alum, B.N., Edeh, F.O., Ainebyoona, C.: Unveiling the microbial orchestra: exploring the role of microbiota in cancer development and treatment. Discov Oncol. 16, 646 (2025). https://doi.org/10.1007/s12672-025-02352-2
8. Alvarez, N., Sevilla, A.: Current Advances in Photodynamic Therapy (PDT) and the Future Potential of PDT-Combinatorial Cancer Therapies. International Journal of Molecular Sciences. 25, 1023 (2024). https://doi.org/10.3390/ijms25021023
9. Aqil, F., Munagala, R., Jeyabalan, J., Vadhanam, M.V.: Bioavailability of phytochemicals and its enhancement by drug delivery systems. Cancer Lett. 334, 133–141 (2013). https://doi.org/10.1016/j.canlet.2013.02.032
10. Alum, E.U.: AI-driven biomarker discovery: enhancing precision in cancer diagnosis and prognosis. Discov Onc. 16, 313 (2025). https://doi.org/10.1007/s12672-025-02064-7
11. Basheer, I., Wang, H., Li, G., Jehan, S., Raza, A., Du, C., Ullah, N., Li, D., Sui, G.: β-caryophyllene sensitizes hepatocellular carcinoma cells to chemotherapeutics and inhibits cell malignancy through targeting MAPK signaling pathway. Front. Pharmacol. 15, (2024). https://doi.org/10.3389/fphar.2024.1492670
12. Kawish, S.M., Sharma, S., Gupta, P., Ahmad, F.J., Iqbal, M., Alshabrmi, F.M., Anwer, Md.K., Fathi-karkan, S., Rahdar, A., Aboudzadeh, M.A.: Nanoparticle-Based Drug Delivery Platform for Simultaneous Administration of Phytochemicals and Chemotherapeutics: Emerging Trends in Cancer Management. Particle & Particle Systems Characterization. 41, 2400049 (2024). https://doi.org/10.1002/ppsc.202400049
13. Chen, N., Brachmann, C., Liu, X., Pierce, D.W., Dey, J., Kerwin, W.S., Li, Y., Zhou, S., Hou, S., Carleton, M., Klinghoffer, R.A., Palmisano, M., Chopra, R.: Albumin-bound nanoparticle (nab) paclitaxel exhibits enhanced paclitaxel tissue distribution and tumor penetration. Cancer Chemother Pharmacol. 76, 699–712 (2015). https://doi.org/10.1007/s00280-015-2833-5
14. Eslami, M., Memarsadeghi, O., Davarpanah, A., Arti, A., Nayernia, K., Behnam, B.: Overcoming Chemotherapy Resistance in Metastatic Cancer: A Comprehensive Review. Biomedicines. 12, 183 (2024). https://doi.org/10.3390/biomedicines12010183
15. He, J., Lee, H.-J., Saha, S., Ruan, D., Guo, H., Chan, C.-H.: Inhibition of USP2 eliminates cancer stem cells and enhances TNBC responsiveness to chemotherapy. Cell Death Dis. 10, 285 (2019). https://doi.org/10.1038/s41419-019-1512-6
16. Li, B., Shao, H., Gao, L., Li, H., Sheng, H., Zhu, L.: Nano-drug co-delivery system of natural active ingredients and chemotherapy drugs for cancer treatment: a review. Drug Deliv. 29, 2130–2161. https://doi.org/10.1080/10717544.2022.2094498
17. Sousa, C., Videira, M.: Dual Approaches in Oncology: The Promise of siRNA and Chemotherapy Combinations in Cancer Therapies. Onco. 5, 2 (2025). https://doi.org/10.3390/onco5010002
18. Alum, E.U., Akwari, A.Ak., Okoroh, P.N., Aniokete, U.C., Abba, J.N., Uti, D.E.: Phytochemicals as modulators of ferroptosis: a novel therapeutic avenue in cancer and neurodegeneration. Mol Biol Rep. 52, 636 (2025). https://doi.org/10.1007/s11033-025-10752-4

19. Haleem, A., Javaid, M., Singh, R.P., Rab, S., Suman, R.: Applications of nanotechnology in medical field: a brief review. Global Health Journal. 7, 70–77 (2023). https://doi.org/10.1016/j.glohj.2023.02.008
20. Bajracharya, R., Song, J.G., Patil, B.R., Lee, S.H., Noh, H.-M., Kim, D.-H., Kim, G.-L., Seo, S.-H., Park, J.-W., Jeong, S.H., Lee, C.H., Han, H.-K.: Functional ligands for improving anticancer drug therapy: current status and applications to drug delivery systems. Drug Deliv. 29, 1959–1970. https://doi.org/10.1080/10717544.2022.2089296
21. He, Q., Chen, J., Yan, J., Cai, S., Xiong, H., Liu, Y., Peng, D., Mo, M., Liu, Z.: Tumor microenvironment responsive drug delivery systems. Asian J Pharm Sci. 15, 416–448 (2020). https://doi.org/10.1016/j.ajps.2019.08.003
22. Bulbake, U., Doppalapudi, S., Kommineni, N., Khan, W.: Liposomal Formulations in Clinical Use: An Updated Review. Pharmaceutics. 9, 12 (2017). https://doi.org/10.3390/pharmaceutics9020012
23. Ahmad, M.Z., Mustafa, G., Abdel-Wahab, B.A., Pathak, K., Das, A., Sahariah, J.J., Kalita, P., Alam, A., Borthakur, P.P.: From bench to bedside: Advancing liposomal doxorubicin for targeted cancer therapy. Results in Surfaces and Interfaces. 19, 100473 (2025). https://doi.org/10.1016/j.rsurfi.2025.100473
24. Alum, E.U., Nwuruku, O.A., Ugwu, O.P.-C., Uti, D.E., Alum, B.N., Edwin, N.: Harnessing nature: plant-derived nanocarriers for targeted drug delivery in cancer therapy. Phytomedicine Plus. 5, 100828 (2025). https://doi.org/10.1016/j.phyplu.2025.100828
25. Uti, D.E., Atangwho, I.J., Alum, E.U., Ntaobeten, E., Obeten, U.N., Bawa, I., Agada, S.A., Ukam, C.I.-O., Egbung, G.E.: Antioxidants in cancer therapy mitigating lipid peroxidation without compromising treatment through nanotechnology. Discover Nano. 20, 70 (2025). https://doi.org/10.1186/s11671-025-04248-0
26. Abbasi, R., Shineh, G., Mobaraki, M., Doughty, S., Tayebi, L.: Structural parameters of nanoparticles affecting their toxicity for biomedical applications: a review. J Nanopart Res. 25, 43 (2023). https://doi.org/10.1007/s11051-023-05690-w
27. Codullo, V., Cova, E., Pandolfi, L., Breda, S., Morosini, M., Frangipane, V., Malatesta, M., Calderan, L., Cagnone, M., Pacini, C., Cavagna, L., Recalde, H., Distler, J.H.W., Giustra, M., Prosperi, D., Colombo, M., Meloni, F., Montecucco, C.: Imatinib-loaded gold nanoparticles inhibit proliferation of fibroblasts and macrophages from systemic sclerosis patients and ameliorate experimental bleomycin-induced lung fibrosis. J Control Release. 310, 198–208 (2019). https://doi.org/10.1016/j.jconrel.2019.08.015
28. Uti, D.E., Alum, E.U., Atangwho, I.J., Ugwu, O.P.-C., Egbung, G.E., Aja, P.M.: Lipid-based nano-carriers for the delivery of anti-obesity natural compounds: advances in targeted delivery and precision therapeutics. Journal of Nanobiotechnology. 23, 336 (2025). https://doi.org/10.1186/s12951-025-03412-z
29. Abbasi, H., Kouchak, M., Mirveis, Z., Hajipour, F., Khodarahmi, M., Rahbar, N., Handali, S.: What We Need to Know about Liposomes as Drug Nanocarriers: An Updated Review. Adv Pharm Bull. 13, 7–23 (2023). https://doi.org/10.34172/apb.2023.009
30. Lombardo, D., Kiselev, M.A.: Methods of Liposomes Preparation: Formation and Control Factors of Versatile Nanocarriers for Biomedical and Nanomedicine Application. Pharmaceutics. 14, 543 (2022). https://doi.org/10.3390/pharmaceutics14030543
31. Rao, L., Zhu, P., Guo, M., Hu, M., Guo, X., Du, Y., Xu, G.: Nebulized inhalation of nintedanib-loaded biomimetic nano-liposomes attenuated bleomycin-induced interstitial lung fibrosis in mice. Nano Today. 56, 102298 (2024). https://doi.org/10.1016/j.nantod.2024.102298
32. Sercombe, L., Veerati, T., Moheimani, F., Wu, S.Y., Sood, A.K., Hua, S.: Advances and Challenges of Liposome Assisted Drug Delivery. Front Pharmacol. 6, 286 (2015). https://doi.org/10.3389/fphar.2015.00286
33. Suk, J.S., Xu, Q., Kim, N., Hanes, J., Ensign, L.M.: PEGylation as a strategy for improving nanoparticle-based drug and gene delivery. Adv Drug Deliv Rev. 99, 28–51 (2016). https://doi.org/10.1016/j.addr.2015.09.012
34. Begines, B., Ortiz, T., Pérez-Aranda, M., Martínez, G., Merinero, M., Argüelles-Arias, F., Alcudia, A.: Polymeric Nanoparticles for Drug Delivery: Recent Developments and Future Prospects. Nanomaterials (Basel). 10, 1403 (2020). https://doi.org/10.3390/nano10071403
35. Nair, A., Chandrashekhar H., R., Day, C.M., Garg, S., Nayak, Y., Shenoy, P.A., Nayak, U.Y.: Polymeric functionalization of mesoporous silica nanoparticles: Biomedical insights. International Journal of Pharmaceutics. 660, 124314 (2024). https://doi.org/10.1016/j.ijpharm.2024.124314
36. Wang, X.-Q., Zhang, Q.: pH-sensitive polymeric nanoparticles to improve oral bioavailability of peptide/protein drugs and poorly water-soluble drugs. European Journal of Pharmaceutics and Biopharmaceutics. 82, 219–229 (2012). https://doi.org/10.1016/j.ejpb.2012.07.014
37. Zhang, W., Mehta, A., Tong, Z., Esser, L., Voelcker, N.H.: Development of Polymeric Nanoparticles for Blood–Brain Barrier Transfer—Strategies and Challenges. Advanced Science. 8, 2003937 (2021). https://doi.org/10.1002/advs.202003937

38. Li, X., Peng, X., Zoulikha, M., Boafo, G.F., Magar, K.T., Ju, Y., He, W.: Multifunctional nanoparticle-mediated combining therapy for human diseases. Sig Transduct Target Ther. 9, 1 (2024). https://doi.org/10.1038/s41392-023-01668-1
39. Vines, J.B., Yoon, J.-H., Ryu, N.-E., Lim, D.-J., Park, H.: Gold Nanoparticles for Photothermal Cancer Therapy. Front Chem. 7, 167 (2019). https://doi.org/10.3389/fchem.2019.00167
40. Aslam, R., Tiwari, V., Upadhyay, P., Tiwari, A.: Revolutionizing Therapeutic Delivery: Diosgenin-Loaded Solid Lipid Nanoparticles Unleash Advanced Carriers. International Journal of Applied Pharmaceutics. 124–133 (2024). https://doi.org/10.22159/ijap.2024v16i1.49306
41. Greco, G., Agafonova, A., Cosentino, A., Cardullo, N., Muccilli, V., Puglia, C., Anfuso, C.D., Sarpietro, M.G., Lupo, G.: Solid Lipid Nanoparticles Encapsulating a Benzoxanthene Derivative in a Model of the Human Blood–Brain Barrier: Modulation of Angiogenic Parameters and Inflammation in Vascular Endothelial Growth Factor-Stimulated Angiogenesis. Molecules. 29, 3103 (2024). https://doi.org/10.3390/molecules29133103
42. Khan, H., Nazir, S., Farooq, R.K., Khan, I.N., Javed, A.: Fabrication and Assessment of Diosgenin Encapsulated Stearic Acid Solid Lipid Nanoparticles for Its Anticancer and Antidepressant Effects Using in vitro and in vivo Models. Front Neurosci. 15, 806713 (2022). https://doi.org/10.3389/fnins.2021.806713
43. Khatamian, N., Motavalizadehkakhky, A., Homayouni Tabrizi, M., Mehrzad, J., Zhiani, R.: Preparation and characterization of the myricetin-loaded solid lipid nanoparticles decorated with folic acid-bound chitosan and evaluation of its antitumor and anti-angiogenic activities in vitro and in vivo in mice bearing tumor models. Cancer Nanotechnology. 14, 9 (2023). https://doi.org/10.1186/s12645-023-00160-3
44. Gupta, A., Jadhav, S.R., Colaco, V., Saha, M., Ghosh, A., Sreedevi, A., Datta, D., Hebbar, S., Moorkoth, S., Ligade, V.S., Dhas, N.: Harnessing unique architecture and emerging strategies of solid lipid nanoparticles to combat colon cancer: A state-of-the-art review. International Journal of Pharmaceutics. 675, 125562 (2025). https://doi.org/10.1016/j.ijpharm.2025.125562
45. Shinde, V.R., Revi, N., Murugappan, S., Singh, S.P., Rengan, A.K.: Enhanced permeability and retention effect: A key facilitator for solid tumor targeting by nanoparticles. Photodiagnosis and Photodynamic Therapy. 39, 102915 (2022). https://doi.org/10.1016/j.pdpdt.2022.102915
46. Shinde, V.R., Revi, N., Murugappan, S., Singh, S.P., Rengan, A.K.: Enhanced permeability and retention effect: A key facilitator for solid tumor targeting by nanoparticles. Photodiagnosis and Photodynamic Therapy. 39, 102915 (2022). https://doi.org/10.1016/j.pdpdt.2022.102915
47. Attia, M.F., Anton, N., Wallyn, J., Omran, Z., Vandamme, T.F.: An overview of active and passive targeting strategies to improve the nanocarriers efficiency to tumour sites. Journal of Pharmacy and Pharmacology. 71, 1185–1198 (2019). https://doi.org/10.1111/jphp.13098
48. Zhang, M., Liu, C., Tu, J., Tang, M., Ashrafizadeh, M., Nabavi, N., Sethi, G., Zhao, P., Liu, S.: Advances in cancer immunotherapy: historical perspectives, current developments, and future directions. Mol Cancer. 24, 136 (2025). https://doi.org/10.1186/s12943-025-02305-x
49. Ashrafizadeh, M., Delfi, M., Zarrabi, A., Bigham, A., Sharifi, E., Rabiee, N., Paiva-Santos, A.C., Kumar, A.P., Tan, S.C., Hushmandi, K., Ren, J., Zare, E.N., Makvandi, P.: Stimuli-responsive liposomal nanoformulations in cancer therapy: Pre-clinical & clinical approaches. Journal of Controlled Release. 351, 50–80 (2022). https://doi.org/10.1016/j.jconrel.2022.08.001
50. Du, J., Lane, L.A., Nie, S.: Stimuli-Responsive Nanoparticles for Targeting the Tumor Microenvironment. J Control Release. 219, 205–214 (2015). https://doi.org/10.1016/j.jconrel.2015.08.050
51. Hou, J., Xue, Z., Chen, Y., Li, J., Yue, X., Zhang, Y., Gao, J., Hao, Y., Shen, J.: Development of Stimuli-Responsive Polymeric Nanomedicines in Hypoxic Tumors and Their Therapeutic Promise in Oral Cancer. Polymers. 17, 1010 (2025). https://doi.org/10.3390/polym17081010
52. Zhou, W., Jia, Y., Liu, Y., Chen, Y., Zhao, P.: Tumor Microenvironment-Based Stimuli-Responsive Nanoparticles for Controlled Release of Drugs in Cancer Therapy. Pharmaceutics. 14, 2346 (2022). https://doi.org/10.3390/pharmaceutics14112346
53. Salehi, S., Naghib, S.M., Garshasbi, H.R., Ghorbanzadeh, S., Zhang, W.: Smart stimuli-responsive injectable gels and hydrogels for drug delivery and tissue engineering applications: A review. Front Bioeng Biotechnol. 11, 1104126 (2023). https://doi.org/10.3389/fbioe.2023.1104126
54. Majumder, J., Minko, T.: Multifunctional and stimuli-responsive nanocarriers for targeted therapeutic delivery. Expert Opin Drug Deliv. 18, 205–227 (2021). https://doi.org/10.1080/17425247.2021.1828339
55. Sezgin-Bayindir, Z., Losada-Barreiro, S., Bravo-Díaz, C., Sova, M., Kristl, J., Saso, L.: Nanotechnology-Based Drug Delivery to Improve the Therapeutic Benefits of NRF2 Modulators in Cancer Therapy. Antioxidants. 10, 685 (2021). https://doi.org/10.3390/antiox10050685
56. Kumarasamy, R.V., Natarajan, P.M., Umapathy, V.R., Roy, J.R., Mironescu, M., Palanisamy, C.P.: Clinical applications and therapeutic potentials of advanced nanoparticles: a comprehensive review on completed human clinical trials. Front. Nanotechnol. 6, (2024). https://doi.org/10.3389/fnano.2024.1479993
57. Narayanan, V., Weekes, C.D.: Nanoparticle albumin-bound (nab)-paclitaxel for the treatment of pancreas ductal adenocarcinoma. GICTT. 5, 11–19 (2015). https://doi.org/10.2147/GICTT.S55158

58. Milano, G., Innocenti, F., Minami, H.: Liposomal irinotecan (Onivyde): Exemplifying the benefits of nanotherapeutic drugs. Cancer Sci. 113, 2224–2231 (2022). https://doi.org/10.1111/cas.15377

59. Yao, Y., Zhou, Y., Liu, L., Xu, Y., Chen, Q., Wang, Y., Wu, S., Deng, Y., Zhang, J., Shao, A.: Nanoparticle-Based Drug Delivery in Cancer Therapy and Its Role in Overcoming Drug Resistance. Front Mol Biosci. 7, 193 (2020). https://doi.org/10.3389/fmolb.2020.00193

60. Makharadze, D., del Valle, L.J., Katsarava, R., Puiggalí, J.: The Art of PEGylation: From Simple Polymer to Sophisticated Drug Delivery System. International Journal of Molecular Sciences. 26, 3102 (2025). https://doi.org/10.3390/ijms26073102

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