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Research

Targeted Drug Delivery Systems for Breast Cancer Therapy: Advances in Nanomedicine

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Abstract

Breast cancer remains one of the leading causes of cancer-related morbidity and mortality among women worldwide, despite significant advances in early detection and systemic therapy. Conventional chemotherapy is often limited by poor tumor selectivity, dose-limiting toxicity, multidrug resistance, and inadequate intracellular drug accumulation. Targeted drug delivery systems enabled by nanomedicine have emerged as a transformative strategy to overcome these barriers by improving pharmacokinetics, enhancing tumor localization, and enabling molecularly guided therapy. This review critically examines the design principles, mechanistic foundations, and translational progress of nanotechnology-based targeted drug delivery systems for breast cancer therapy. Passive targeting through the enhanced permeability and retention effect and active targeting using ligand–receptor interactions are discussed in relation to tumor microenvironment heterogeneity, vascular permeability, and cellular internalization pathways. Major nanocarrier platforms, including liposomes, polymeric nanoparticles, dendrimers, inorganic nanostructures, and biomimetic systems, are analyzed with respect to drug loading capacity, release kinetics, biocompatibility, and clinical scalability. Particular attention is given to receptor-specific targeting strategies directed

against HER2, estrogen receptors, folate receptors, and CD44, as well as emerging stimuli-responsive and theranostic systems. Recent preclinical and clinical evidence highlights meaningful improvements in therapeutic index, reduced systemic toxicity, and enhanced treatment personalization. Remaining challenges related to immunogenicity, manufacturing reproducibility, regulatory pathways, and long-term safety are critically evaluated. Overall, nanomedicine-based targeted delivery offers a compelling pathway toward precision breast cancer therapy and supports the continued integration of advanced materials science with molecular oncology for improved patient outcomes.

Keywords: Nanomedicine; Targeted drug delivery; Breast cancer; Nanoparticles; Precision oncology.

Introduction

Breast cancer accounts for a substantial proportion of global cancer incidence and remains a major public health burden despite advances in diagnostics, molecular profiling, and therapeutic regimens [1]. Conventional systemic chemotherapy relies on non-selective cytotoxic mechanisms that damage rapidly dividing normal tissues, leading to significant adverse effects and compromised patient adherence [2]. Furthermore, heterogeneous tumor biology, multidrug resistance mechanisms, and poor drug penetration into solid tumors limit therapeutic efficacy [3]. These challenges have driven the exploration of targeted drug delivery strategies aimed at improving tumor specificity while minimizing systemic toxicity.

Nanomedicine provides an adaptable platform for engineering drug carriers with tunable size, surface chemistry, and functional ligands capable of modulating biodistribution and cellular uptake [4]. Nanoparticles typically range from 10 to 200 nm, enabling prolonged circulation, preferential tumor accumulation through leaky vasculature, and protection of labile drugs from premature degradation [5]. Passive targeting exploits the enhanced permeability and retention effect characteristic of tumor vasculature, whereas active targeting incorporates ligands such as antibodies, peptides, or small molecules that bind overexpressed receptors on cancer cells [6]. These dual mechanisms enhance intracellular delivery and promote selective drug accumulation at the tumor site.

Breast cancer is particularly amenable to targeted nanotherapeutics because of its well-characterized molecular subtypes, including HER2-positive, hormone receptor–positive, and triple-negative phenotypes [7]. Targeted nanocarriers can deliver chemotherapeutics, nucleic acids, proteins, and imaging agents, thereby supporting both therapeutic and diagnostic functions [8]. Liposomal formulations such as pegylated doxorubicin have already demonstrated clinical benefits by reducing cardiotoxicity while maintaining antitumor efficacy [9]. However, translation of more complex nanoplatforms remains limited by manufacturing scalability, regulatory complexity, and long-term safety considerations [10].

This article reviews the mechanistic foundations, major nanocarrier platforms, receptor-targeted strategies, stimuli-responsive systems, clinical progress, and translational challenges in nanomedicine-driven targeted drug delivery for breast cancer therapy.

Mechanistic Basis of Targeted Nanocarrier Delivery

The effectiveness of nanomedicine-based drug delivery relies on complex biological interactions that govern circulation stability, tumor accumulation, cellular internalization, and intracellular trafficking [11]. Passive targeting exploits abnormal tumor vasculature characterized by fenestrations and impaired lymphatic drainage, enabling nanoparticles to accumulate within the tumor interstitium [12]. However, variability in vascular permeability across tumor subtypes and patient populations introduces heterogeneity in therapeutic response.Active targeting enhances specificity through ligand-mediated recognition of cell surface receptors

overexpressed in breast cancer, such as HER2, folate receptor, transferrin receptor, and CD44 [13]. Ligand–receptor binding promotes receptor-mediated endocytosis, increasing intracellular drug concentration and overcoming efflux transporter–mediated resistance [14]. Surface functionalization also modulates protein corona formation, influencing circulation half-life and immune recognition.Intracellular trafficking determines therapeutic outcomes, as nanoparticles must escape endosomal compartments to release payloads effectively in the cytoplasm or nucleus [15]. pH-sensitive polymers and membrane-disruptive peptides facilitate endosomal escape, enhancing gene and drug delivery efficiency [16]. Additionally, tumor microenvironment features such as acidic pH, hypoxia, and elevated enzymatic activity can be leveraged for stimuli-responsive release mechanisms [17].Understanding nano–bio interactions at the molecular and cellular levels remains essential for rational carrier design and predictive translation into clinical settings.

A diverse array of nanocarriers has been developed to accommodate varying drug properties and therapeutic objectives [18]. Liposomes are among the most clinically validated systems, offering biocompatibility, high drug encapsulation efficiency, and flexible surface modification [9]. Polymeric nanoparticles provide controlled release profiles and structural stability, enabling sustained drug exposure [19]. Dendrimers exhibit highly branched architectures with precise molecular weights and multivalent surface functionality, supporting targeted ligand conjugation [20].

Inorganic nanoparticles such as gold, silica, and iron oxide possess unique optical and magnetic properties that enable imaging-guided therapy and hyperthermia applications [21]. Hybrid nanostructures integrate organic and inorganic components to optimize drug loading and imaging capabilities. Biomimetic carriers, including cell membrane–coated nanoparticles and exosomes, enhance immune evasion and homotypic tumor targeting [22].

Nanocarrier Platforms for Breast Cancer Therapy

Table 1. Representative nanocarrier platforms for breast cancer drug delivery

Nanocarrier Type	Key Advantages	Limitations	Typical Payloads
Liposomes	Biocompatible, clinically approved	Limited stability	Doxorubicin, paclitaxel
Polymeric NPs	Controlled release, scalable	Polymer toxicity risk	Small molecules, genes
Dendrimers	Precise architecture, multivalency	Cost, complexity	siRNA, anticancer drugs
Inorganic NPs	Imaging capability	Long-term safety	Photothermal agents
Biomimetic systems	Immune evasion	Manufacturing challenges	Proteins, nucleic acids

Selection of carrier systems requires balancing safety, drug compatibility, and translational feasibility.

Ligand-Based Targeting Strategies

Active targeting exploits molecular markers unique to breast cancer cells to enhance selective uptake and therapeutic precision [13]. HER2-targeted nanoparticles functionalized with trastuzumab or affibody ligands demonstrate enhanced accumulation in HER2-positive tumors and improved cytotoxicity [23]. Folate receptor targeting supports uptake in aggressive breast tumors exhibiting elevated folate metabolism [24]. CD44-targeted hyaluronic acid–based nanoparticles facilitate internalization in cancer stem cell populations, potentially reducing recurrence [25].

Ligand density, orientation, and binding affinity significantly influence targeting efficiency and off-target interactions [14]. Excessive ligand density may trigger rapid clearance, while insufficient coverage limits receptor engagement. Multivalent targeting approaches that combine multiple ligands may address tumor heterogeneity and improve binding robustness.

Figure 1. **Schematic illustration of ligand-mediated active targeting of nanoparticles to breast cancer cells via receptor-specific endocytosis.**

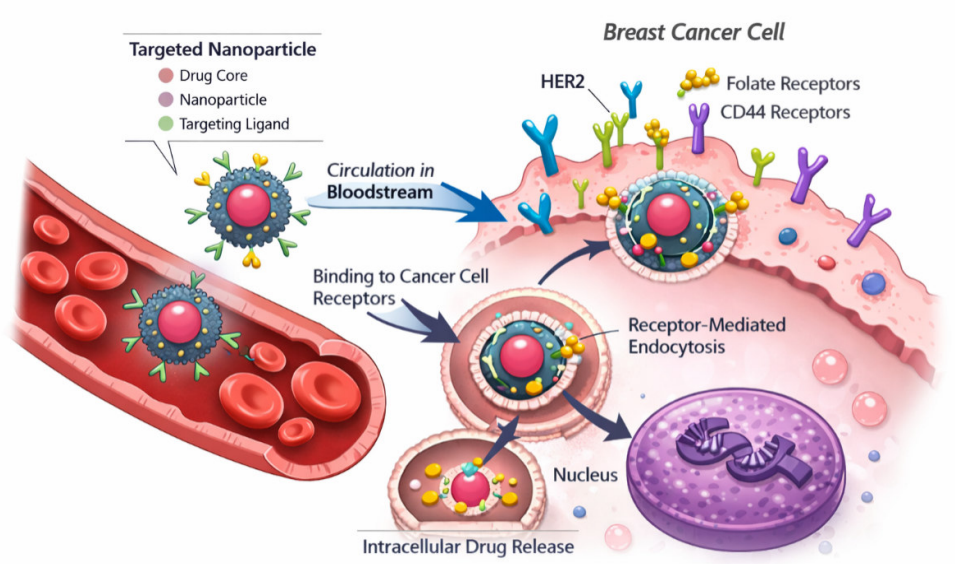


Figure 1. Schematic illustration of ligand-mediated *active targeting of nanoparticles to breast cancer cells via receptor-specific endocytosis.*

Stimuli-Responsive and Smart Nanomedicines

Smart nanocarriers are engineered to release drugs in response to intrinsic or external stimuli, improving site-specific activation and minimizing premature leakage [17]. pH-responsive polymers degrade in acidic tumor microenvironments, while enzyme-responsive systems exploit elevated matrix metalloproteinase activity. Thermoresponsive nanoparticles enable localized release under hyperthermia conditions [21]. Redox-sensitive carriers respond to elevated intracellular glutathione concentrations, enhancing cytosolic drug delivery [16].

Externally triggered systems using ultrasound, light, or magnetic fields allow spatiotemporal control over drug release and imaging integration [18]. These approaches enhance therapeutic precision and support personalized dosing strategies.

Clinical Translation and Regulatory Considerations

Several nanomedicines have achieved regulatory approval, validating the clinical feasibility of nanocarrier-based delivery [9]. However, reproducibility, scale-up manufacturing, batch consistency, and long-term toxicity remain regulatory concerns [10]. Standardized characterization methods and predictive in vivo models are essential to accelerate translation [11].

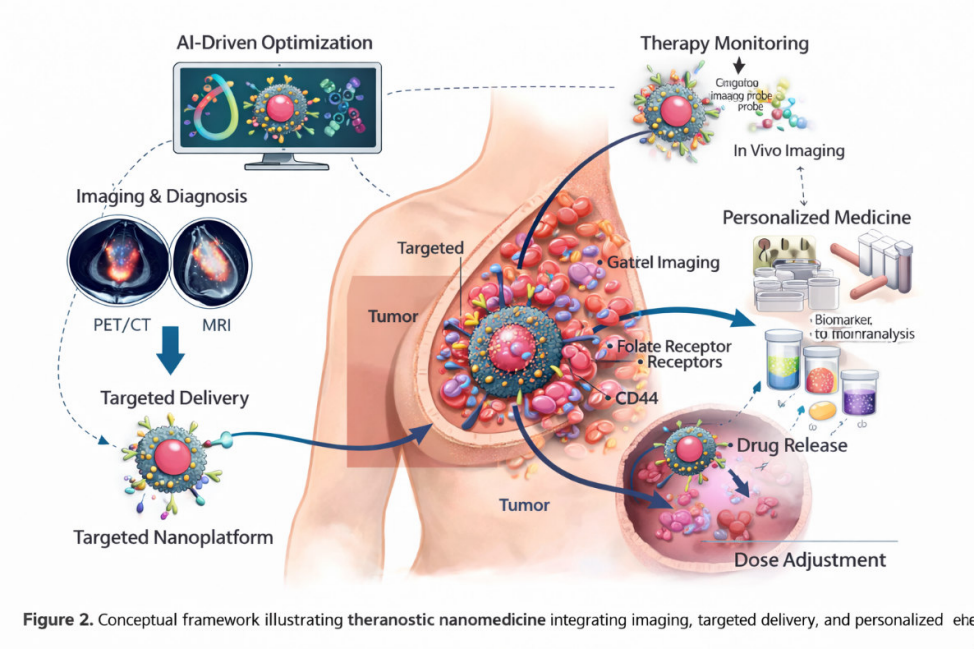
Table 2. Selected nanomedicines evaluated for breast cancer therapy

Product	Nanocarrier	Drug	Clinical Status	Key Benefit
Doxil®	Liposome	Doxorubicin	Approved	Reduced cardiotoxicity
Abraxane®	Albumin NP	Paclitaxel	Approved	Improved bioavailability
MM-302	HER2 liposome	Doxorubicin	Phase II	Enhanced targeting
BIND-014	Polymer NP	Docetaxel	Phase I/II	Ligand targeting

Emerging Trends and Theranostic Integration

Integration of diagnostics and therapeutics within a single nanoplatform enables real-time monitoring of treatment response and biodistribution [8]. Quantum dots, iron oxide nanoparticles, and gold nanostructures support imaging-guided therapy and personalized dose adjustment [21]. Artificial intelligence–driven optimization of nanoparticle design accelerates predictive modeling and clinical translation [18].

Figure 2. Conceptual framework illustrating theranostic nanomedicine integrating imaging, targeted delivery, and personalized therapy.



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Conclusion

Targeted drug delivery systems based on nanomedicine represent a paradigm shift in breast cancer therapy by enabling precise modulation of pharmacokinetics, tumor specificity, and therapeutic efficacy. Advances in carrier engineering, ligand-based targeting, and stimuli-responsive mechanisms have significantly improved intracellular drug delivery and reduced systemic toxicity. Clinically validated formulations demonstrate tangible benefits, supporting the feasibility of nanotechnology-driven precision oncology. Nevertheless, challenges related to biological variability, long-term safety, regulatory harmonization, and manufacturing scalability continue to limit widespread adoption. Future progress will depend on standardized characterization frameworks, integration of artificial intelligence–guided design, and robust clinical validation across diverse patient populations. Multidisciplinary collaboration between materials scientists, oncologists, pharmacologists, and regulatory experts will be essential to translate innovative nanoplatforms into routine clinical practice. As personalized medicine advances, nanomedicine-based targeted delivery is poised to become a cornerstone in optimizing therapeutic outcomes and improving quality of life for breast cancer patients.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020. CA Cancer J Clin. 2021;71(3):209–49. doi:10.3322/caac.21660.

2. Chabner BA, Roberts TG. Chemotherapy and the war on cancer. Nat Rev Cancer. 2005;5(1):65–72. doi:10.1038/nrc1529.

3. Gottesman MM, Fojo T, Bates SE. Multidrug resistance in cancer. Nat Rev Cancer. 2002;2(1):48–58. doi:10.1038/nrc706.

4. Ferrari M. Cancer nanotechnology. Nat Rev Cancer. 2005;5(3):161–71. doi:10.1038/nrc1566.

5. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an emerging platform for cancer therapy. Nat Nanotechnol. 2007;2(12):751–60. doi:10.1038/nnano.2007.387.

6. Danhier F, Feron O, Préat V. To exploit the tumor microenvironment. J Control Release. 2010;148(2):135–46. doi:10.1016/j.jconrel.2010.08.027.

7. Perou CM, Sørlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumours. Nature. 2000;406(6797):747–52. doi:10.1038/35021093.

8. Muthu MS, Leong DT, Mei L, Feng SS. Nanotheranostics. Theranostics. 2014;4(6):660–77. doi:10.7150/thno.8694.

9. Barenholz Y. Doxil®—the first FDA-approved nano-drug. J Control Release. 2012;160(2):117–34. doi:10.1016/j.jconrel.2012.03.020.

10. Tinkle S, McNeil SE, Mühlebach S, Bawa R, Borchard G, Barenholz Y, et al. Nanomedicines. Nat Nanotechnol. 2014;9(9):707–10. doi:10.1038/nnano.2014.190.

11. Blanco E, Shen H, Ferrari M. Principles of nanoparticle design. Nat Biotechnol. 2015;33(9):941–51. doi:10.1038/nbt.3330.

12. Maeda H, Wu J, Sawa T, Matsumura Y, Hori K. Tumor vascular permeability. J Control Release. 2000;65(1–2):271–84. doi:10.1016/S0168-3659(99)00248-5.

13. Sapra P, Allen TM. Ligand-targeted liposomal anticancer drugs. Prog Lipid Res. 2003;42(5):439–62. doi:10.1016/S0163-7827(03)00032-8.

14. Ruoslahti E. Peptides as targeting elements. Adv Drug Deliv Rev. 2017;110–111:3–12. doi:10.1016/j.addr.2016.03.002.

15. Varkouhi AK, Scholte M, Storm G, Haisma HJ. Endosomal escape pathways. J Control Release. 2011;151(3):220–8. doi:10.1016/j.jconrel.2010.11.004.

16. Mura S, Nicolas J, Couvreur P. Stimuli-responsive nanocarriers. Nat Mater. 2013;12(11):991–1003. doi:10.1038/nmat3776.

17. Torchilin VP. Multifunctional nanocarriers. Nat Rev Drug Discov. 2014;13(11):813–27. doi:10.1038/nrd4333.

18. Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles. Nat Rev Drug Discov. 2021;20(2):101–24. doi:10.1038/s41573-020-0090-8.

19. Kamaly N, Yameen B, Wu J, Farokhzad OC. Degradable polymeric nanoparticles. Chem Rev. 2016;116(4):2602–63. doi:10.1021/acs.chemrev.5b00346.

20. Kesharwani P, Jain K, Jain NK. Dendrimer drug delivery. Prog Polym Sci. 2014;39(2):268–307. doi:10.1016/j.progpolymsci.2013.07.005.

21. Huang X, Jain PK, El-Sayed IH, El-Sayed MA. Gold nanoparticles in cancer therapy. Lasers Med Sci. 2008;23(3):217–28. doi:10.1007/s10103-007-0470-x.

22. Fang RH, Kroll AV, Gao W, Zhang L. Cell membrane coating. Adv Mater. 2018;30(23):e1706759. doi:10.1002/adma.201706759.

23. Park JW, Hong K, Kirpotin DB, Colbern G, Shalaby R, Baselga J, et al. Anti-HER2 immunoliposomes. Clin Cancer Res. 2002;8(4):1172–81. doi:10.1158/1078-0432.CCR-01-0120.

24. Lu Y, Low PS. Folate-mediated delivery. Adv Drug Deliv Rev. 2012;64(11):342–52. doi:10.1016/j.addr.2012.09.012.

25. Misra S, Hascall VC, Markwald RR, Ghatak S. Hyaluronan–CD44 interactions. Front Immunol. 2015;6:201. doi:10.3389/fimmu.2015.00201.