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Nano-Targeted Drug Delivery in Breast Cancer: Advances, Challenges and Clinical Perspective

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ABSTRACT

Breast cancer remains the most frequently diagnosed malignancy among women worldwide and continues to be a leading cause of cancer-related mortality. Although conventional treatment strategies such as surgery, chemotherapy, radiotherapy, endocrine therapy, targeted therapy and immunotherapy have significantly improved patient outcomes, their clinical effectiveness is often limited by systemic toxicity, poor tumor selectivity, multidrug resistance, and unfavorable pharmacokinetic properties. These limitations emphasize the need for advanced drug delivery systems that can enhance therapeutic efficacy while minimizing adverse effects. In recent years, nanotechnology-based drug delivery systems have emerged as promising approaches for improving breast cancer treatment. Nanocarriers, generally ranging from 10 to 200 nm in size, possess unique physicochemical properties that enhance drug solubility, prolong systemic circulation and promote preferential accumulation in tumor tissues through the enhanced permeability and retention (EPR) effect. In addition, surface modification and stimuli-responsive designs enable targeted and controlled drug release in response to tumor-associated conditions such as acidic pH, hypoxia, enzymatic activity and redox imbalance. Several nanomedicine formulations, including liposomal doxorubicin and albumin-bound paclitaxel, have already demonstrated clinical success in oncology. This review provides a comprehensive overview of different nanocarrier systems developed for breast cancer therapy, including liposomes, polymeric nanoparticles, dendrimers, polymeric micelles, solid lipid nanoparticles, nanostructured lipid carriers, metallic nanoparticles, mesoporous silica nanoparticles, carbon-based nanomaterials, quantum dots, exosomes and hybrid nanocarriers. Their structural features, preparation strategies, targeting mechanisms, advantages and limitations are discussed, along with current challenges in clinical translation. Overall, nanocarrier-based systems hold significant potential for advancing precision-based breast cancer therapy.

Keywords: Breast cancer, Nanocarriers, Novel drug delivery, Tumor targeting, Clinical perspective

1. INTRODUCTION

1.1 Breast Cancer Epidemiology

Breast cancer is the most prevalent malignancy among women worldwide and represents a leading cause of cancer-related mortality. Recent global cancer statistics estimate approximately 2.3 million new cases annually, accounting for nearly one in four cancers diagnosed in women, with more than 680,000 deaths reported each year [1,11]. In India, breast cancer constitutes nearly 27% of all female cancers, with increasing incidence particularly in urban populations due to lifestyle transitions, delayed screening practices, reproductive factors, and genetic predispositions including *BRCA1* and *BRCA2* mutations [12,13].

Breast cancer is a biologically heterogeneous disease characterized by variations in histology, molecular expression patterns and clinical outcomes [14].

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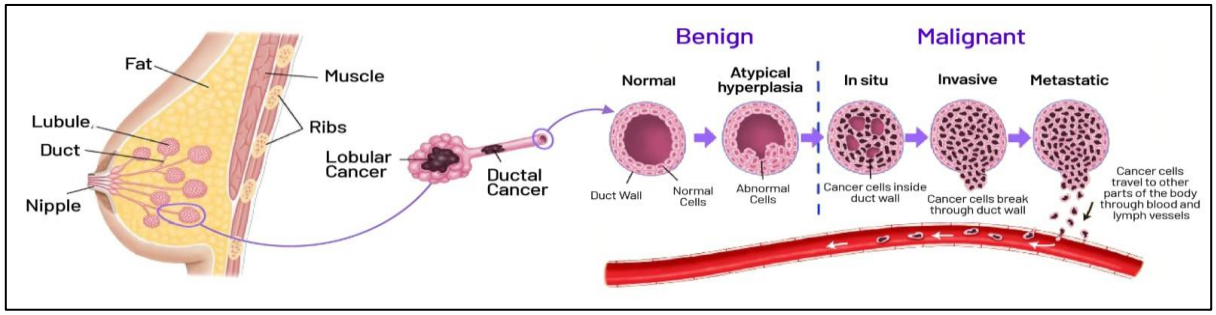

Fig.1 Progression of Breast Cancer

Histological classifications include:

- **Invasive ductal carcinoma (IDC):** Represents approximately 70–80% of cases.
- **Invasive lobular carcinoma (ILC):** Accounts for 10–15% and often demonstrates diffuse infiltration.
- **Special subtypes:** Including mucinous, tubular, papillary and medullary carcinomas with distinct prognostic characteristics.

Molecular classification based on hormone receptor status and HER2 expression guides therapeutic decision-making [15]:

- **Hormone receptor-positive (ER+/PR+):** ~70% of cases; responsive to endocrine therapy.
- **HER2-positive subtype:** Characterized by HER2 overexpression and responsiveness to HER2-targeted biologics.
- **Triple-negative breast cancer (TNBC):** Lacks ER, PR, and HER2 expression; associated with aggressive behavior and limited targeted therapies.
- **Gene-expression subtypes:** Luminal A, luminal B, basal-like and claudin-low categories provide additional prognostic insight.

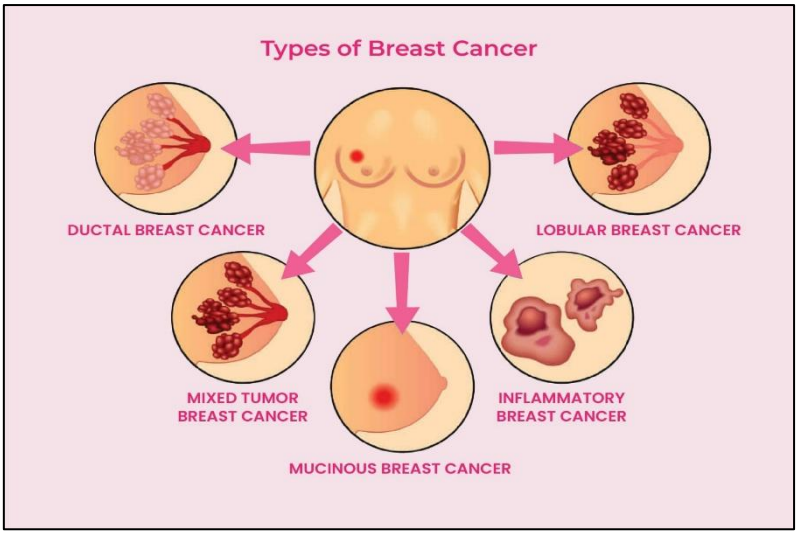

Fig.No.2 Types of Breast Cancer

1.2 Signs and Symptoms of Breast Cancer

Clinical presentation of breast cancer varies widely and may initially be subtle, contributing to delayed diagnosis. The most common manifestation is a painless breast mass, frequently located in the upper outer quadrant. Additional local features include nipple retraction, peau d'orange appearance, breast asymmetry, skin thickening and erythema [16].

Nipple discharge, particularly bloody or serous secretion, and eczema-like nipple changes may indicate malignancy. Regional metastasis may present as axillary or supraclavicular lymphadenopathy, whereas advanced disease can produce systemic symptoms such as bone pain, dyspnea, or neurological deficits due to distant metastases [17]. Early detection through screening mammography and clinical examination remains critical for improving survival outcomes.

1.3 Conventional Therapeutic Strategies

Breast cancer management involves multimodal treatment approaches including surgery, radiotherapy, chemotherapy, endocrine therapy, targeted therapy, and immunotherapy [18].

Surgical procedures such as lumpectomy or mastectomy remain primary interventions for localized disease, while radiotherapy reduces local recurrence rates. Endocrine therapies including tamoxifen and aromatase inhibitors are effective in hormone receptor-positive tumors [19].

Targeted biologics such as trastuzumab and pertuzumab have significantly improved outcomes in HER2-positive breast cancer. Standard chemotherapeutic regimens incorporate anthracyclines, taxanes, cyclophosphamide and capecitabine, often administered in neoadjuvant or adjuvant settings [20]. Recently, immune checkpoint inhibitors (e.g., pembrolizumab) and CDK4/6 inhibitors (e.g., palbociclib) have expanded treatment options for advanced disease [21].

Despite these advances, survival rates decline markedly in metastatic breast cancer, emphasizing the need for improved therapeutic delivery strategies.

1.4 Limitations of Conventional Therapies

Although conventional therapies improve survival, several limitations persist. Systemic chemotherapy demonstrates non-specific biodistribution, with less than 1% of administered drug typically reaching tumor tissue [22]. Hydrophobic drugs such as paclitaxel require toxic solubilizing agents, contributing to hypersensitivity reactions and systemic toxicity [23].

Multidrug resistance (MDR), mediated by ATP-binding cassette transporters such as P-glycoprotein, reduces intracellular drug accumulation and therapeutic efficacy [24]. Dose-limiting toxicities including anthracycline-induced cardiotoxicity and taxane-associated neuropathy further restrict treatment intensity [25]. Tumor heterogeneity and adaptive resistance mechanisms promote relapse and metastasis, particularly in TNBC [26].

Collectively, these challenges highlight the need for targeted drug delivery approaches capable of improving tumor selectivity while minimizing systemic adverse effects.

1.5 Nano-Targeted Drug Delivery Systems in Breast Cancer

Nano-targeted drug delivery systems (NDDS), typically 10–200 nm in size, have emerged as promising platforms to overcome limitations associated with conventional therapies [4,5]. These systems exploit the enhanced permeability and retention (EPR) effect resulting from abnormal tumor vasculature and impaired lymphatic drainage, enabling passive tumor accumulation.

Active targeting strategies involve ligand conjugation toward overexpressed receptors such as HER2, EGFR, folate receptor-α, and CD44, enhancing receptor-mediated endocytosis and intracellular drug delivery [27]. Stimuli-responsive nanocarriers further enable controlled drug release in response to tumor-specific triggers including acidic pH, redox gradients, enzymatic activity, and hypoxia [6].

Surface PEGylation imparts stealth properties that reduce opsonization and prolong circulation time [28]. Multifunctional nanocarriers integrating imaging components allow theranostic applications, enabling simultaneous diagnosis and therapy monitoring [29].

Clinically approved nanomedicines including liposomal doxorubicin (Doxil®/Caelyx®), albumin-bound paclitaxel (Abraxane®), and polymeric micellar paclitaxel (Genexol-PM®) validate the translational feasibility of nanotechnology in breast cancer therapy [8–10].

2. NANOCARRIER SYSTEMS FOR BREAST CANCER THERAPY

2.1 Liposomes

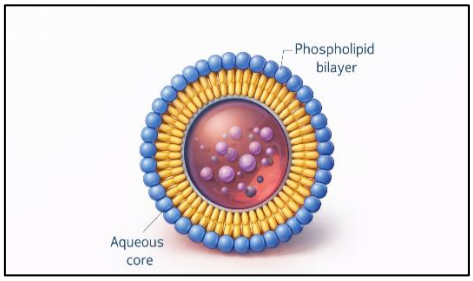

Fig.No.3 liposomes

Liposomes are spherical vesicular nanocarriers composed of one or more phospholipid bilayers enclosing an aqueous core, enabling simultaneous encapsulation of hydrophilic and hydrophobic therapeutic agents. Hydrophilic drugs are localized within the aqueous interior, whereas hydrophobic compounds partition into the lipid bilayer, providing versatile drug-loading capability [30]. Common phospholipids used in liposomal formulations include phosphatidylcholine, dipalmitoylphosphatidylcholine, and distearoylphosphatidylcholine, frequently combined with cholesterol to enhance membrane rigidity and stability.

Liposomes are typically prepared using techniques such as thin-film hydration, reverse-phase evaporation, ethanol injection, freeze–thaw cycling, and microfluidic-based fabrication methods. These preparation approaches influence vesicle size, lamellarity, encapsulation efficiency and long-term stability [31]. Drug loading may occur passively during vesicle formation or actively via transmembrane pH or ion gradients, significantly improving drug encapsulation efficiency.

Tumor targeting occurs through both passive accumulation via the enhanced permeability and retention (EPR) effect and active targeting through surface conjugation of ligands such as antibodies, peptides, or folate molecules that promote receptor-mediated endocytosis [27]. PEGylated liposomes exhibit prolonged circulation by reducing opsonization and clearance by the mononuclear phagocyte system [28].

Clinically approved formulations such as liposomal doxorubicin (Doxil®/Caelyx®) demonstrate reduced cardiotoxicity compared with conventional anthracycline therapy while maintaining antitumor efficacy [8]. Targeted immunoliposomes directed toward HER2 receptors have shown enhanced uptake in HER2-positive breast cancer models. Additionally, pH-sensitive and folate-modified liposomes improve intracellular drug delivery and cytotoxicity in breast cancer cell lines [32].

Despite their advantages—including biocompatibility and formulation flexibility—liposomes face limitations such as physical instability, drug leakage during storage, high manufacturing costs, and restricted penetration within dense tumor matrices [33].

2.2 Solid Lipid Nanoparticles (SLNs)

Solid lipid nanoparticles (SLNs) are submicron colloidal carriers composed of physiologically compatible lipids that remain solid at room and body temperature, forming a rigid lipid matrix suitable for encapsulating hydrophobic chemotherapeutic agents [34]. Common lipid materials include glyceryl monostearate, stearic acid, tripalmitin, and Compritol® 888 ATO, stabilized using surfactants such as Tween 80, lecithin, or Poloxamer 188.

SLNs are commonly produced using high-pressure homogenization, ultrasonication, solvent emulsification–evaporation, or microemulsion-based techniques. Drug release occurs via diffusion from the lipid matrix or gradual lipid erosion [35].

These systems primarily exploit passive targeting through the EPR effect; however, surface modification with ligands such as hyaluronic acid enables receptor-specific targeting toward CD44-overexpressing breast cancer cells. Paclitaxel-loaded SLNs have demonstrated enhanced antitumor activity in xenograft models, while tamoxifen-loaded SLNs improve oral bioavailability and reduce systemic toxicity [36].

Advantages of SLNs include biocompatibility, protection of labile drugs, controlled drug release and scalability of production. Nevertheless, limitations include polymorphic transitions of lipids, drug expulsion during storage, and potential aggregation over time [37].

2.3 Nanostructured Lipid Carriers (NLCs)

Nanostructured lipid carriers (NLCs) represent second-generation lipid nanoparticles developed to overcome limitations associated with SLNs. They incorporate both solid and liquid lipids, generating an imperfect crystalline matrix that enhances drug-loading capacity and minimizes drug expulsion during storage [38].

Typical formulations combine solid lipids such as glyceryl monostearate or cetyl palmitate with liquid lipids including oleic acid or medium-chain triglycerides (e.g., Miglyol® 812). NLCs are generally prepared using hot or cold high-pressure homogenization methods, producing nanoparticles with controlled particle size and sustained release properties.

Drug release occurs via diffusion and matrix restructuring mechanisms, while tumor accumulation is mediated through the EPR effect. Surface functionalization with targeting ligands such as hyaluronic acid promotes receptor-mediated uptake, particularly in triple-negative breast cancer models expressing CD44 receptors [39].

NLC systems delivering paclitaxel or combination therapies (e.g., tamoxifen–curcumin co-delivery) demonstrate enhanced cytotoxicity and synergistic therapeutic effects in preclinical studies. Compared with SLNs, NLCs provide improved stability and higher drug loading; however, formulation complexity and long-term storage stability remain optimization challenges [40].

2.4 Polymeric Nanoparticles

Polymeric nanoparticles are biodegradable colloidal systems fabricated from polymers such as poly(lactic-co-glycolic acid) (PLGA), polycaprolactone (PCL), chitosan and polyethylene glycol (PEG). These carriers enable sustained drug release and extensive surface modification for targeted delivery [41].

Polymeric nanoparticles may exist as:

- **Nanospheres:** drug uniformly dispersed throughout the polymer matrix.
- **Nanocapsules:** core–shell structures encapsulating the drug.

Common preparation methods include emulsion–solvent evaporation, nanoprecipitation, ionic gelation, and microfluidic synthesis. These methods influence particle size distribution, drug encapsulation efficiency and release kinetics [42].

Passive targeting occurs through EPR-mediated accumulation, while active targeting is achieved through ligand conjugation, including antibodies, peptides or folate derivatives. Stimuli-responsive polymer systems enable site-specific drug release triggered by pH, redox gradients or enzymatic activity.

Examples include HER2-antibody-functionalized PLGA nanoparticles delivering doxorubicin and chitosan nanoparticles co-delivering paclitaxel with siRNA targeting multidrug resistance pathways. These systems demonstrate improved intracellular drug accumulation and enhanced cytotoxicity compared with free drugs [43].

Limitations include burst drug release and the requirement for complete removal of residual organic solvents during synthesis.

2.5 Polymeric Micelles

Polymeric micelles are self-assembled nanostructures formed from amphiphilic block copolymers consisting of a hydrophobic drug-solubilizing core and a hydrophilic corona that stabilizes the system in aqueous environments [44]. Common copolymers include PEG-PLA and PEG-PCL.

Micelles are prepared via solvent displacement, dialysis, or direct self-assembly. Their nanoscale size enhances tumor penetration, while surface functionalization allows active targeting.

Drug release occurs through diffusion or micelle destabilization in response to environmental triggers such as pH or temperature changes. Paclitaxel-loaded polymeric micelles have demonstrated improved solubility, enhanced tumor accumulation and superior therapeutic efficacy in breast cancer models [45].

However, dilution-induced instability in systemic circulation may lead to premature drug release.

2.6 Dendrimers

Dendrimers are highly branched, monodisperse macromolecules characterized by a central core, repeating internal layers, and multiple terminal functional groups that enable high drug-loading capacity and precise surface engineering [46].

Polyamidoamine (PAMAM) and polypropylene imine (PPI) dendrimers are among the most widely investigated systems. Drugs may be encapsulated within internal cavities or covalently conjugated to surface groups for controlled release.

Surface functionalization with targeting ligands such as folate or trastuzumab enhances receptor-mediated uptake in breast cancer cells. Dendrimer-based delivery of methotrexate and doxorubicin has demonstrated improved tumor accumulation and cytotoxicity in preclinical studies [47].

Despite their advantages, higher-generation dendrimers may exhibit cytotoxicity, and large-scale synthesis remains technically demanding.

2.7 Mesoporous Silica Nanoparticles (MSNs)

Mesoporous silica nanoparticles possess highly ordered porous structures with large surface areas and tunable pore sizes, allowing high drug-loading capacity and controlled release [48].

Drugs are loaded within mesopores and can be sealed using stimuli-responsive gatekeepers responsive to pH or redox conditions. Surface modification with PEG or targeting ligands enhances circulation stability and cellular uptake.

In breast cancer models, doxorubicin- and paclitaxel-loaded MSNs demonstrate improved cytotoxicity and reduced systemic toxicity. However, concerns regarding biodegradability and long-term biosafety remain barriers to clinical translation [49].

2.8 Quantum Dots (QDs)

Quantum dots are semiconductor nanocrystals exhibiting size-dependent fluorescence properties, making them valuable for imaging-guided therapy and theranostic applications [50].

Drug-conjugated quantum dots enable simultaneous tumor imaging and therapeutic delivery. Although promising for real-time tracking of drug distribution, concerns regarding heavy metal toxicity and long-term accumulation limit clinical applicability.

2.9 Carbon-Based Nanomaterials

Carbon-based nanomaterials including carbon nanotubes, graphene oxide, nanodiamonds, and fullerenes offer large surface areas and photothermal properties suitable for combination cancer therapy [51].

Surface functionalization improves solubility and targeting efficiency. Preclinical studies demonstrate enhanced tumor inhibition and drug delivery efficiency. However, biodegradability and systemic safety remain key challenges.

2.10 Exosomes and Biomimetic Nanocarriers

Exosomes are naturally derived extracellular vesicles capable of transferring biomolecules between cells while exhibiting excellent biocompatibility and immune evasion properties [52].

Engineered exosomes can deliver chemotherapeutics, siRNA, or miRNA directly to breast tumors. Biomimetic systems, including cell membrane-coated nanoparticles, mimic endogenous cells to evade immune clearance and enhance targeting efficiency.

These systems show promising preclinical outcomes but face challenges related to scalable isolation, heterogeneity and reproducibility.

2.11 Hybrid Nanocarriers

Hybrid nanocarriers combine organic, inorganic or biomimetic materials to achieve multifunctional delivery systems. Lipid–polymer hybrid nanoparticles integrate polymer stability with lipid biocompatibility, enabling controlled drug release and active targeting [53].

Hybrid systems support co-delivery of drugs and imaging agents, facilitating theranostic applications. Preclinical breast cancer studies report enhanced tumor accumulation and reduced systemic toxicity, although regulatory complexity and scalable manufacturing remain challenges.

Table 1. FDA-Approved Nanomedicines for Cancer Therapy

Nanomedicine	Active Drug	Nanocarrier Type	Approved Indication	Approval Authority
Doxil®	Doxorubicin	PEGylated liposome	Breast cancer, ovarian cancer, Kaposi sarcoma	FDA
Myocet®	Doxorubicin	Non-PEGylated liposome	Metastatic breast cancer	EMA
Abraxane®	Paclitaxel	Albumin-bound nanoparticle	Breast cancer, lung cancer, pancreatic cancer	FDA
Onivyde®	Irinotecan	Liposomal formulation	Pancreatic cancer	FDA
Marqibo®	Vincristine	Liposomal formulation	Acute lymphoblastic leukemia	FDA
DaunoXome®	Daunorubicin	Liposomal formulation	Kaposi sarcoma	FDA
Vyxeos®	Daunorubicin + Cytarabine	Liposomal combination	Acute myeloid leukemia	FDA
Genexol-PM®	Paclitaxel	Polymeric micelle	Breast cancer	MFDS (Korea)
Mepact®	Mifamurtide	Liposomal formulation	Osteosarcoma	EMA
DepoCyt®	Cytarabine	Liposomal formulation	Lymphomatous meningitis	FDA

3. Design Principles of Nanocarriers

The rational design of nanocarriers for breast cancer therapy requires careful optimization of physicochemical, biological, and functional parameters to achieve efficient tumor targeting while minimizing systemic toxicity. Nanoparticle size represents one of the most critical determinants influencing biodistribution, circulation time, tumor penetration, and cellular uptake. Nanocarriers within the size range of 10–200 nm are considered optimal for exploiting the enhanced permeability and retention (EPR) effect, enabling preferential tumor accumulation through leaky tumor vasculature and impaired lymphatic drainage [54]. Particles smaller than 10 nm undergo rapid renal clearance, whereas larger particles (>200 nm) are more susceptible to uptake by the mononuclear phagocyte system (MPS), reducing therapeutic efficiency.

Surface charge also plays a significant role in nanoparticle behavior in biological environments. Neutral or slightly negative surface charges reduce nonspecific protein adsorption and opsonization, thereby prolonging circulation time. In contrast, positively charged nanoparticles may enhance cellular internalization due to electrostatic interaction with negatively charged cell membranes but are often associated with increased cytotoxicity and rapid clearance [55].

Surface functionalization is widely employed to enable active targeting. Ligands such as monoclonal antibodies, peptides, aptamers, and small molecules are conjugated to nanoparticle surfaces to recognize receptors overexpressed in breast cancer cells, including HER2, epidermal growth factor receptor (EGFR), folate receptor-α and CD44 [56]. PEGylation remains a commonly used stealth strategy that improves systemic stability and reduces immune recognition. However, excessive PEG density may hinder ligand–receptor interactions and reduce cellular uptake if not carefully optimized [57].

Drug-loading strategies further influence therapeutic performance. Drugs may be incorporated through encapsulation within carrier matrices, surface adsorption, or covalent conjugation. These approaches affect drug stability, release kinetics, and pharmacokinetics. Stimuli-responsive nanocarriers have gained considerable attention because they enable spatiotemporally controlled drug release in response to tumor-associated triggers such as acidic pH, elevated glutathione levels, enzymatic activity or hypoxic conditions [58].

Additionally, multifunctional nanocarriers integrating therapeutic agents with imaging modalities enable theranostic applications, allowing simultaneous diagnosis, drug delivery, and treatment monitoring. Considerations of biodegradability, biocompatibility, reproducibility, and large-scale manufacturability are essential for clinical translation. A balanced integration of these design parameters is therefore critical for developing next-generation nanomedicines with improved pharmacokinetics and therapeutic outcomes in breast cancer therapy [59].

4. Biological Barriers To Nanocarrier Delivery

Despite advances in nanocarrier engineering, multiple biological barriers significantly limit effective drug delivery to breast tumors. Tumor vasculature exhibits structural abnormalities characterized by irregular blood vessel architecture, heterogeneous

permeability, and elevated interstitial fluid pressure (IFP), which restrict uniform nanoparticle extravasation and distribution within tumor tissues [60].

Following extravasation, dense extracellular matrix (ECM) components including collagen fibers and proteoglycans impede nanoparticle diffusion beyond perivascular regions. Consequently, drug delivery to hypoxic tumor cores remains inadequate, reducing therapeutic efficacy. Cellular uptake further depends on endocytic pathways and many nanoparticles become trapped within endosomes or lysosomes, limiting cytoplasmic drug availability unless carriers incorporate endosomal escape mechanisms such as pH-responsive polymers or membrane-disruptive peptides [61].

Multidrug resistance (MDR) represents another major obstacle. Efflux transporters belonging to the ATP-binding cassette (ABC) family, particularly P-glycoprotein (P-gp) and multidrug resistance-associated proteins (MRPs), actively expel chemotherapeutic agents from cancer cells, lowering intracellular drug concentrations and contributing to treatment failure [62].

Systemically administered nanoparticles also encounter immune clearance mechanisms. The mononuclear phagocyte system, particularly macrophages in the liver and spleen, rapidly removes foreign particles from circulation. Strategies such as PEGylation, biomimetic coatings and surface charge optimization have been developed to minimize immune recognition and prolong circulation time [63].

Furthermore, the tumor microenvironment characterized by acidic pH, hypoxia, oxidative stress, and abnormal enzymatic activity can influence nanoparticle stability and drug-release behavior. Overcoming these barriers requires integrated strategies combining optimized particle size, active targeting ligands, stimuli-responsive materials and enhanced penetration mechanisms. Preclinical studies demonstrate that such approaches significantly improve tumor retention and therapeutic efficacy in breast cancer models [64].

5. Clinical Translation and Challenges

Although numerous nanocarrier systems have demonstrated encouraging preclinical outcomes, successful clinical translation remains limited. Currently, only a small number of nanomedicine formulations have achieved regulatory approval, including liposomal doxorubicin (Doxil®/Caelyx®), albumin-bound paclitaxel (Abraxane®) and polymeric micellar paclitaxel (Genexol-PM®), which validate the clinical feasibility of nanotechnology-based drug delivery [8,65].

Several additional nanoformulations including HER2-targeted immunoliposomes, polymeric nanoparticles and lipid-based nanocarriers are undergoing clinical evaluation and have shown promising safety and preliminary efficacy in advanced breast cancer patients. Nevertheless, multiple translational barriers persist.

Manufacturing scalability remains a major challenge due to sensitivity of nanoparticle properties to process parameters, resulting in batch-to-batch variability. Large-scale production requires strict control of particle size distribution, surface characteristics and drug-loading consistency, which increases manufacturing complexity and cost [66].

Regulatory approval pathways also remain challenging because standardized characterization methods for nanomedicines are still evolving. Parameters such as biodistribution, degradation behavior, immunogenicity and long-term toxicity must be thoroughly evaluated, often requiring extensive preclinical and clinical datasets [67].

Pharmacokinetic variability among patients represents another limitation. Tumor heterogeneity including differences in vascular permeability, receptor expression and microenvironmental conditions results in inconsistent nanoparticle accumulation and therapeutic response. Long-term safety concerns, particularly for inorganic and hybrid nanocarriers, further complicate clinical adoption [68].

Future directions emphasize multifunctional and biomimetic nanocarriers capable of personalized drug delivery. Integration of artificial intelligence, imaging-guided therapy and patient-specific tumor profiling may enable precision nanomedicine approaches that optimize carrier design and dosing strategies. Advances in biodegradable materials, scalable manufacturing technologies and harmonized regulatory frameworks are essential to bridge the gap between laboratory innovation and clinical implementation [69].

6. Future Perspectives

Despite significant progress in nanotechnology-based drug delivery systems for breast cancer therapy, several challenges remain before these systems can achieve widespread clinical application. Future research should focus on the development of multifunctional nanocarriers capable of combining targeted drug delivery, controlled release and diagnostic imaging within a single

platform. Such theranostic systems could enable simultaneous disease detection, monitoring, and treatment, thereby improving therapeutic precision and clinical outcomes.

Advancements in surface modification strategies, including ligand conjugation, antibody targeting, and receptor-mediated delivery, are expected to enhance the specificity of nanocarriers toward breast cancer cells while minimizing off-target toxicity. In addition, stimuli-responsive nanocarriers that release drugs in response to specific triggers such as pH, temperature, enzymes or redox conditions within the tumor microenvironment represent an emerging area of interest.

Another important direction involves the integration of nanotechnology with personalized medicine approaches. The use of genomic profiling, biomarkers and patient-specific tumor characteristics may allow the design of customized nanomedicine platforms tailored to individual patients. Furthermore, advances in artificial intelligence and computational modeling could facilitate the optimization of nanoparticle design, drug loading efficiency and targeting capability.

However, for successful clinical translation, future efforts must also address issues related to large-scale manufacturing, reproducibility, regulatory approval and long-term safety of nanocarriers. Comprehensive toxicological studies and standardized evaluation methods will be essential to ensure the safe implementation of nanomedicine in clinical oncology.

Overall, continued interdisciplinary collaboration among nanotechnologists, pharmacologists, oncologists and regulatory agencies will play a critical role in advancing nanocarrier-based drug delivery systems toward more effective and personalized breast cancer therapies.

7. Conclusion

Nanocarrier-based drug delivery has become an important strategy for improving breast cancer treatment by enhancing the delivery efficiency and therapeutic performance of anticancer drugs. Different nanosystems such as liposomes, polymeric nanoparticles, dendrimers and lipid-based carriers offer advantages including improved drug stability, prolonged circulation, and better tumor targeting. These features can help reduce the limitations of conventional chemotherapy, particularly systemic toxicity and poor selectivity. Although several nanomedicine formulations are currently available for clinical use, further research is necessary to address challenges related to safety, large-scale production, and regulatory considerations. Continued advancements in nanotechnology are expected to support the development of more effective and personalized therapeutic approaches for breast cancer management.

Abbreviation Table

Abbreviation	Full Term
ABC	ATP-Binding Cassette
ACS	American Chemical Society
ADME	Absorption, Distribution, Metabolism, and Excretion
ADME-Tox	Absorption, Distribution, Metabolism, Excretion and Toxicity
ATP	Adenosine Triphosphate
BC	Breast Cancer
BCRP	Breast Cancer Resistance Protein
BBB	Blood–Brain Barrier
CD	Cluster of Differentiation
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
DLS	Dynamic Light Scattering
DNA	Deoxyribonucleic Acid
DOX	Doxorubicin
EPR	Enhanced Permeability and Retention
FDA	Food and Drug Administration
HER2	Human Epidermal Growth Factor Receptor 2
HPLC	High-Performance Liquid Chromatography
IC50	Half Maximal Inhibitory Concentration
MDR	Multidrug Resistance
mRNA	Messenger Ribonucleic Acid
MRI	Magnetic Resonance Imaging
NLC	Nanostructured Lipid Carriers

NP	Nanoparticles
PEG	Polyethylene Glycol
PEGylation	Surface modification with polyethylene glycol
PDI	Polydispersity Index
PDT	Photodynamic Therapy
PLGA	Poly(lactic-co-glycolic acid)
PTX	Paclitaxel
RES	Reticuloendothelial System
RNA	Ribonucleic Acid
ROS	Reactive Oxygen Species
SLN	Solid Lipid Nanoparticles
TEM	Transmission Electron Microscopy
TNBC	Triple-Negative Breast Cancer
VEGF	Vascular Endothelial Growth Factor

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