



Targeted Drug Delivery in Cancer Therapy Using Nanotechnology(Breast Cancer).

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ABSTRACT:

Breast cancer is one of the most common cancers affecting women worldwide and remains a major health problem. Conventional chemotherapy is widely used for treatment, but it can cause serious side effects because anticancer drugs may affect both cancerous and healthy cells. Targeted drug delivery using nanotechnology offers a promising approach to improve the effectiveness and safety of breast cancer treatment. Nanoparticles can carry anticancer drugs and deliver them more selectively to tumor tissues. Passive targeting mainly uses the enhanced permeability and retention (EPR) effect, while active targeting uses specific molecules such as antibodies, peptides, or ligands to recognize receptors present on cancer cells. Different nanocarriers, including liposomes, polymeric nanoparticles, dendrimers, solid lipid nanoparticles, micelles, gold nanoparticles, and biomimetic nanoparticles, can be used for drug delivery. Molecular targets such as HER2, EGFR, CD44, folate receptors, and integrins may improve selective drug delivery. Stimuli-responsive nanoparticles can also release drugs in response to pH, enzymes, temperature, or other tumor-related conditions. Recent developments include smart nanoparticles, biomimetic systems, theranostics, personalized nanomedicine, and combination therapy. However, challenges such as tumor heterogeneity, poor tumor penetration, toxicity, manufacturing complexity, cost, and regulatory issues remain. Nanotechnology therefore has strong potential for developing safer, more precise, and effective breast cancer therapy.

1.Introduction

Breast cancer (BC) is the most common and the main cause of death in women. It is challenging to manage BC because of tumor recurrence, metastasis, or spread [1]. Cancer is one of the most serious diseases threatening human health and remains a leading cause of death worldwide. [2] Approximately 310,720 new BC cases were expected to be diagnosed in 2024, and the disease was predicted to cause 42,250 deaths in women [3]. There are four primary subtypes of this heterogeneous form of cancer: luminal A, luminal B, HER2-positive, and basal-like or triple-negative breast cancer (TNBC) [4] TNBC is a high-grade tumor with an increased tendency to spread, lacks hormone receptor expression, and is significantly more aggressive than other types of cancer [5,6]

1.1.Global Burden of Cancer

Cancer is one of the major global public-health challenges and a leading cause of morbidity and mortality worldwide. It comprises a large group of diseases characterized by uncontrolled growth of abnormal cells, invasion of surrounding tissues, and, in many cases, metastasis to distant organs. The global cancer burden is influenced by population growth, ageing, urbanization, lifestyle changes, environmental exposures, infections, and unequal access to prevention, screening, diagnosis, and treatment. [7] According to the International Agency for Research on Cancer (IARC) GLOBOCAN 2022, an estimated 19.98 million new cancer cases and 9.74 million cancer deaths occurred worldwide in 2022. Approximately 53.5 million people were living within five years of a cancer diagnosis. Overall, about 1 in 5 people develop cancer during their lifetime. [8] Global Incidence and Mortality The GLOBOCAN 2022 estimates demonstrate substantial differences in cancer incidence and mortality between geographical regions. The global age-standardized incidence rate was approximately 196.9 per 100,000 population, while the age-standardized mortality rate was approximately 91.7 per 100,000 population. [9]

1.2.Limitations of conventional anticancer therapy

Conventional cancer treatment primarily involves surgery, radiotherapy, chemotherapy, hormonal therapy, targeted medicines, immunotherapy, or combinations of these approaches depending on tumour type and stage. [10] Although these treatments have significantly improved cancer outcomes, several limitations continue to restrict their therapeutic effectiveness. A major limitation of conventional chemotherapy is poor selectivity, because many cytotoxic drugs cannot adequately distinguish malignant cells from rapidly dividing normal cells. Consequently, treatment may damage healthy tissues and produce adverse effects such as myelosuppression, gastrointestinal toxicity, alopecia, mucositis, nephrotoxicity and cardiotoxicity. [11]

1.3.Need for Targeted Drug Delivery

The limitations of conventional treatment have created a strong need for targeted drug-delivery systems capable of transporting therapeutic agents preferentially to tumour tissues or cancer cells. The fundamental objective of targeted delivery is to increase the concentration of a therapeutic agent at

the desired site while reducing its exposure to healthy tissues[12]. The limitations of conventional treatment have created a strong need for targeted drug-delivery systems capable of transporting therapeutic agents preferentially to tumour tissues or cancer cells. The fundamental objective of targeted delivery is to increase the concentration of a therapeutic agent at the desired site while reducing its exposure to healthy tissues.[13]

1.4.Introduction to Nanotechnology In Cancer Therapy

In cancer therapy, nanotechnology has emerged as an important platform for developing drug-delivery systems capable of modifying the pharmacokinetic, biodistribution and therapeutic characteristics of anticancer agents.[14] Several nanomedicines have progressed into clinical oncology, demonstrating that nanotechnology has moved beyond a purely experimental concept. Examples include liposomal and albumin-bound formulations designed to modify the distribution and toxicity profiles of established anticancer drugs.[15]

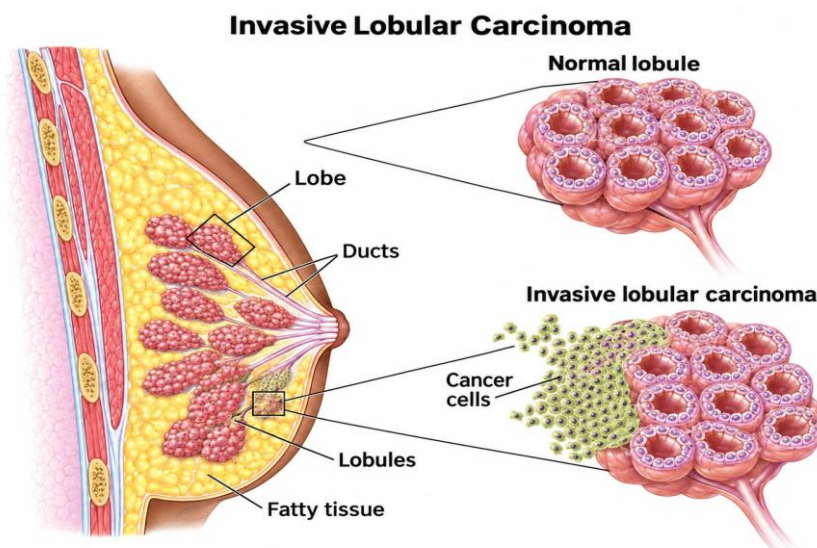


Fig.1.Invasive Lobular Carcinoma.

1.5.Aim

The aim of this review is to critically examine the role of nanotechnology-based targeted drug-delivery systems in cancer therapy, with particular emphasis on their ability to improve tumour targeting, therapeutic efficacy, pharmacokinetic behaviour and safety compared with conventional anticancer drug delivery.[16]

Scope.

Limitations of conventional anticancer therapies and the rationale for developing targeted delivery approaches.

Major nanocarrier systems, including liposomes, polymeric nanoparticles, micelles, dendrimers, lipid nanoparticles, nanogels and inorganic nanoparticles.[17]

Passive and active tumour-targeting strategies, including the EPR effect and ligand-mediated targeting.

Stimuli-responsive and controlled-release nanocarriers for tumour-specific drug release.

Delivery of chemotherapeutic agents, biological molecules and combination therapies using nanoscale systems.[18]

2.Fundamental of Targeted Drug Delivery

Targeted drug delivery is an important application of nanotechnology in breast cancer therapy. Conventional anticancer drugs circulate throughout the body and may damage both malignant and healthy cells. Nanocarrier-based targeted delivery aims to increase drug accumulation at the tumor site, improve therapeutic efficacy, control drug release, and reduce systemic toxicity.[19]

2.1.Definition and Concept

Targeted drug delivery is a drug-delivery approach in which a therapeutic agent is preferentially transported to the tumor tissue or cancer cells, with the objective of increasing drug concentration at the desired site while reducing exposure of healthy tissues. In breast cancer, nanocarriers such as liposomes, polymeric nanoparticles, micelles, dendrimers, metallic nanoparticles and protein-based nanoparticles can encapsulate anticancer drugs and modify their pharmacokinetic and biodistribution properties[20].

The fundamental concept can be represented as:

Anticancer drug → Nanocarrier → Prolonged circulation → Tumor accumulation → Drug release → Cancer-cell destruction

2.2. Passive Targeting

Passive targeting is based primarily on the enhanced permeability and retention (EPR) effect. Rapidly growing breast tumors develop abnormal and highly permeable blood vessels. These vessels may contain larger inter-endothelial gaps, while tumor lymphatic drainage is often inadequate. [21]. Consequently, appropriately designed nanoparticles can extravasate from the circulation and become retained within tumor tissue.

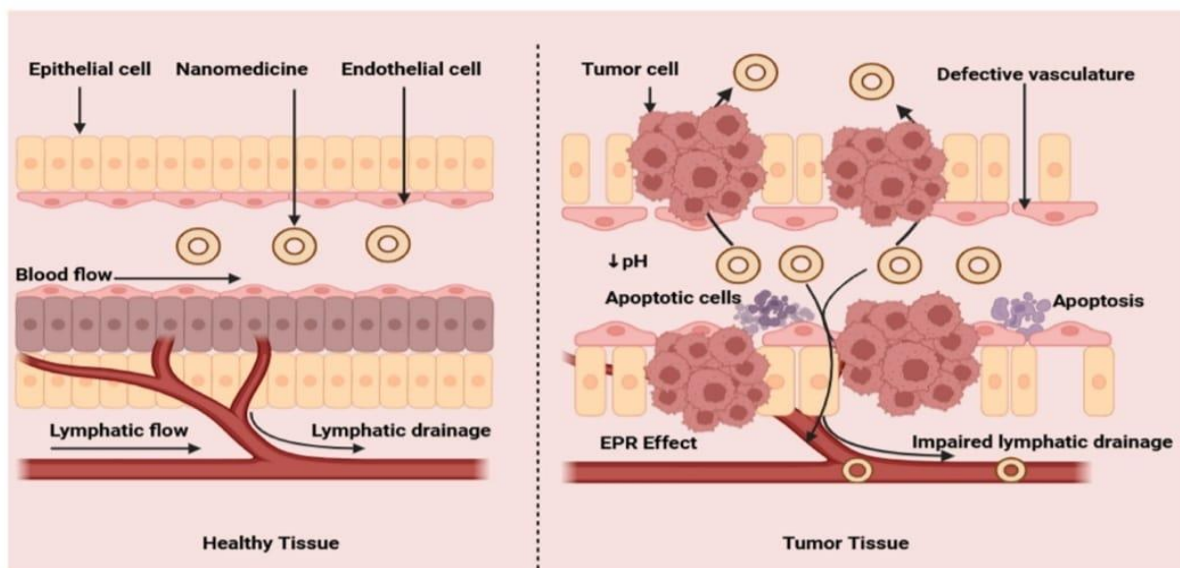
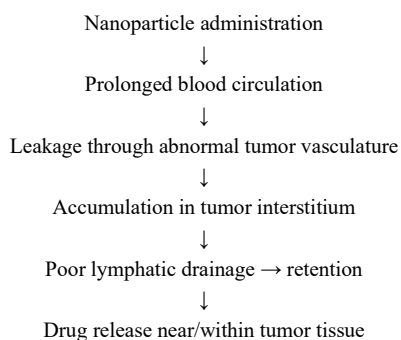


Figure.2. Passive Targeting in cancer Tissue.

Mechanism of passive targeting



Importance in breast cancer

Passive targeting can increase the local concentration of encapsulated drugs while decreasing exposure to some normal tissues. Pegylated liposomal doxorubicin (Doxil/Caelyx) is an important clinical example of a nanomedicine used in breast cancer; compared with conventional free doxorubicin, liposomal delivery can reduce cardiotoxicity while retaining anticancer activity.[22].

2.3. Active targeting:

Nanoparticles are modified with targeting molecules such as antibodies, peptides, folate or other ligands that recognize receptors or biomarkers overexpressed by cancer cells.[23]

Principle

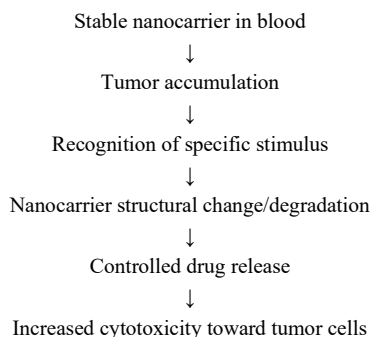
The general mechanism is:

Nanoparticle + targeting ligand → circulation → recognition of tumor receptor → ligand–receptor binding → cellular internalization → drug release

2.4. Stimuli Responsive Targeting

Stimuli-responsive drug delivery involves designing nanocarriers that remain relatively stable during circulation but release their drug preferentially after encountering a particular stimulus at the tumor site. This provides more controlled and localized drug release.[24].

Concept



2.4. Advantages Over Conventional Drug Delivery

Targeted nanocarrier systems offer several potential advantages over conventional administration of anticancer drug.

Improved tumor localization: Nanocarriers can increase drug accumulation in tumor tissue through passive targeting and, where appropriate, additional targeting mechanisms.[25].

Reduced systemic toxicity: Encapsulation and controlled delivery can reduce exposure of healthy tissues to free cytotoxic drugs.

Improved pharmacokinetics: Nanocarriers can prolong circulation and alter drug distribution, potentially improving drug exposure at the tumor site[26].

Controlled drug release: Stimuli-responsive systems can release their payload in response to tumor-associated or externally applied stimuli.[27].

3. Nanocarriers Used for Targeted Drug Delivery in Breast Cancer

Nanocarriers are nanosized delivery systems that transport anticancer drugs toward tumor tissue or specific breast-cancer cells. They can improve drug solubility, stability, cellular uptake and controlled release. Surface modification with antibodies, peptides, folic acid or other ligands can provide active targeting to receptors expressed by cancer cells.

3.1. Liposomes

Liposomes consist of a phospholipid bilayer surrounding an aqueous core. They can carry both hydrophilic and lipophilic drugs. Their surface can be modified with antibodies, peptides or other ligands for active targeting.

Example: Doxorubicin-loaded liposomes.

3.2. Polymeric nanoparticles

These are made from biodegradable polymers such as PLGA and related materials. Drugs can be encapsulated inside the polymer matrix, allowing controlled release.[28]

Examples: Paclitaxel, Docetaxel, Doxorubicin.

Polymeric nanoparticles can also be functionalized with targeting ligands.

3.3. Polymeric micelles

Micelles are generally formed from amphiphilic polymers and contain a hydrophobic core and hydrophilic outer shell. They are particularly useful for poorly water-soluble drugs such as paclitaxel. Their surfaces can be modified to improve tumor-cell targeting.

3.4. Dendrimers

Dendrimers are highly branched, three-dimensional nanosized polymers. Drugs can be incorporated into their internal cavities or attached to their surface. Their large number of surface functional groups allows attachment of targeting ligands and therapeutic molecules. They have been investigated for

overcoming drug resistance and improving delivery in breast cancer.

3.5. Solid lipid nanoparticles and NLCs

Solid lipid nanoparticles (SLNs) use a solid lipid matrix, while nanostructured lipid carriers (NLCs) contain both solid and liquid lipids. They can improve the solubility and bioavailability of poorly soluble anticancer drugs and provide controlled release.

3.6. Magnetic nanoparticles

Superparamagnetic iron oxide nanoparticles (SPIONs) can be used as drug carriers and can also provide magnetic resonance imaging functionality. A magnetic field can potentially help concentrate nanoparticles at a selected location, while their magnetic properties also make them useful for imaging and theranostic applications.

3.7. Gold nanoparticles

Gold nanoparticles can be functionalized with drugs, antibodies, peptides or nucleic acids. In addition to drug delivery, their optical properties make them useful for photothermal therapy and imaging. They are therefore particularly interesting for theranostic breast-cancer systems.

4. Targeting strategies in nanotechnology-based breast cancer therapy.

Nanotechnology-based drug delivery uses nanoparticles or nanocarriers to improve the delivery of anticancer drugs to breast tumors while reducing exposure of healthy tissues. Current strategies can broadly be divided into passive targeting, active targeting, tumor-microenvironment targeting, stimuli-responsive targeting, and biomimetic/cell-based targeting.

4.1. Passive targeting — EPR effect

Passive targeting does not require a specific ligand on the nanoparticle. Nanoparticles can accumulate in tumors because tumor blood vessels are often abnormal and more permeable, while lymphatic drainage is impaired. This phenomenon is called the Enhanced Permeability and Retention (EPR) effect.[29]

Mechanism:

Nanoparticle in blood → leaky tumor blood vessels → accumulation in tumor → drug release.

Examples:

PEGylated liposomes

Polymeric nanoparticles

Polymeric micelles

Dendrimers

Breast-cancer example: Doxil®, a pegylated liposomal doxorubicin formulation, uses passive tumor accumulation and has been used clinically in breast cancer.

Limitation: The EPR effect varies considerably between tumors and patients, so passive targeting alone may not provide sufficient tumor specificity.

4.2. Active targeting — receptor/ligand-mediated targeting

In active targeting, nanoparticles are modified with a targeting ligand that recognizes a receptor or antigen expressed at a higher level on cancer cells. This can increase cellular binding and internalization.

For example, HER2-targeted nanocarriers can use antibodies such as trastuzumab to recognize HER2-positive breast cancer cells and facilitate receptor-mediated uptake.

5. Tumor-microenvironment (TME) targeting

Instead of targeting only cancer cells, nanoparticles can target characteristics of the tumor microenvironment, such as:

Low/acidic pH

Hypoxia

Tumor-associated enzymes

Abnormal tumor vasculature

Cancer-associated stromal cells

This approach can improve drug release or accumulation specifically within the tumor environment.

Example: Nanoparticles can be designed to remain relatively stable during circulation but release their drug when exposed to the acidic environment of a tumor.[30]

5.1. Stimuli-responsive targeting

These are often called “smart nanoparticles.” They release their therapeutic payload when exposed to a specific stimulus.

Internal stimuli:

pH-responsive: responds to acidic tumor/endosomal conditions.

Enzyme-responsive: activated by enzymes that are elevated in tumors.

Redox-responsive: responds to differences in reducing conditions.

External stimuli:

Temperature

Light

Magnetic field

Ultrasound

Stimuli-responsive systems are being investigated to provide more controlled spatial and temporal drug release in breast cancer.

5.2. Breast-cancer-subtype-specific targeting

Breast cancer is biologically heterogeneous, so targeting can be designed according to molecular subtype.

HER2-positive breast cancer → HER2-targeted nanoparticles

Hormone-receptor-positive breast cancer → estrogen-receptor/hormone-related targeting approaches

Triple-negative breast cancer (TNBC) → alternative targets such as EGFR, integrins, CD44 and tumor-microenvironment targets are being investigated. Recent reviews emphasize that subtype-specific nanomedicine is an important direction because breast cancer subtypes differ in molecular characteristics and treatment responses.

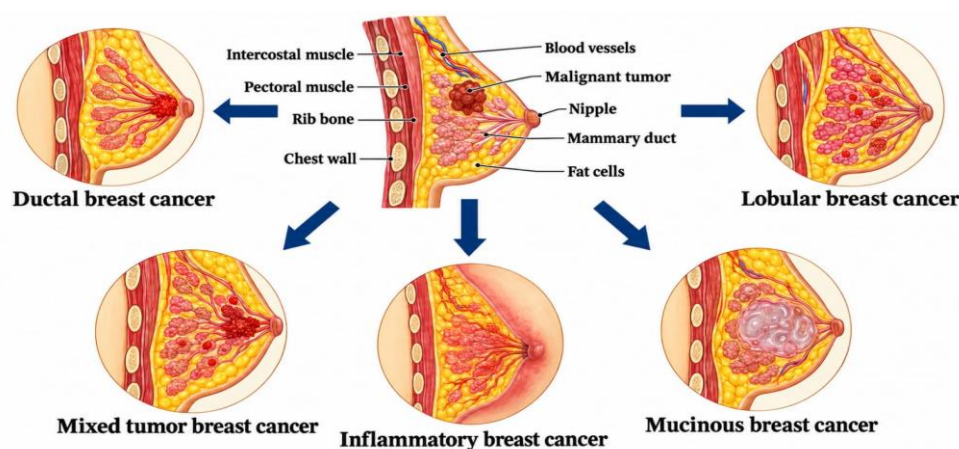


Figure.3.Types Of Breast Cancer.

5.3. Cancer stem-cell targeting

Cancer stem cells may contribute to tumor recurrence, metastasis and treatment resistance. Nanoparticles can be functionalized with ligands directed toward markers associated with breast cancer stem cells, including CD44 and CD133, among others. This is an active research area rather than a universally established clinical strategy.

5.4. Biomimetic targeting

In biomimetic nanotechnology, nanoparticles are designed or coated with biological materials such as cell membranes or exosome-like systems to improve biological compatibility and targeting. Exosomes are particularly interesting because naturally occurring extracellular vesicles can possess biological targeting properties; their potential application has been investigated in breast cancer, including triple-negative breast cancer.[31]

6. Molecular targets for breast cancer–targeted nanoparticles

In breast cancer nanomedicine, molecular targets are receptors, antigens, or other molecules that are overexpressed on breast cancer cells or in the tumor microenvironment. Nanoparticles can be surface-functionalized with antibodies, peptides, folic acid, hyaluronic acid, transferrin, or other ligands to recognize these targets and enhance cellular uptake.

6.1. HER2 — major molecular target

HER2 (human epidermal growth factor receptor 2) is one of the most extensively studied targets in breast-cancer nanomedicine. HER2-targeted nanoparticles can be decorated with trastuzumab or HER2-binding peptides, allowing the nanocarrier to bind HER2 and undergo receptor-mediated internalization. This approach has been investigated for delivery of chemotherapeutics, nucleic acids and imaging agents.[32]

Example= HER2-targeting ligand → HER2 receptor → nanoparticle binding → endocytosis → intracellular drug release

6.2. EGFR

Epidermal growth factor receptor (EGFR/HER1) is another important target, particularly in breast cancers where EGFR is overexpressed. Nanoparticles have been functionalized with antibodies and peptides such as GE11 to improve delivery to EGFR-expressing cells.

6.3. Folate receptor (FR)=

It can be targeted using folic acid, which is relatively small and easy to conjugate to nanoparticle surfaces. Folic-acid-functionalized nanocarriers have been investigated for improving uptake of anticancer drugs into folate-receptor-expressing breast cancer cells.[33]

6. 4. Transferrin receptor (TfR/CD71)

TfR1/CD71 is particularly interesting because rapidly proliferating cancer cells have a high requirement for iron. Transferrin-functionalized nanoparticles can bind TfR and undergo receptor-mediated endocytosis. A 2026 review specifically highlights TfR as an emerging target for breast-cancer nanotechnology.

6.5. CD44

CD44 is a cell-surface receptor associated with hyaluronic acid and is investigated as a target in breast cancer, including cancer stem-cell populations. Hyaluronic acid (HA) can be attached to nanoparticles to facilitate CD44-mediated uptake.

6.6. Integrin $\alpha\beta3$

$\alpha\beta3$ integrin is associated with tumor cells and tumor-associated blood vessels. RGD (Arg-Gly-Asp) peptides are commonly used as targeting ligands because they recognize integrins. RGD-functionalized nanoparticles have therefore been investigated for targeted drug delivery and imaging.

6.7. Targets particularly investigated in TNBC

Triple-negative breast cancer (TNBC) lacks ER, PR and HER2, so researchers have investigated alternative molecular targets. These include:[34]

These ligand–receptor interactions can promote selective nanoparticle binding, receptor-mediated endocytosis and intracellular delivery of anticancer drugs or genetic therapeutics.[35]. Nanotechnology for targeted drug delivery of different therapeutic agents in breast cancer

7. Nanotechnology for Targeted Drug Delivery of Different Therapeutic Agents in Breast Cancer.

Nanotechnology-based drug delivery systems use nanoparticles or nanocarriers to transport therapeutic agents more selectively toward breast-cancer

cells. Nanocarriers can improve drug solubility, stability, circulation time and tumor accumulation, while surface modification with ligands can promote uptake by cells expressing specific receptors such as HER2, EGFR, folate receptor and transferrin receptor. [36]

7.1. Chemotherapeutic agents

Conventional chemotherapy can affect both cancerous and healthy rapidly dividing cells. Nanocarriers can encapsulate or conjugate chemotherapeutic drugs and provide controlled or targeted release.

Examples:

Doxorubicin (DOX) – commonly incorporated into liposomes and polymeric nanoparticles.

Paclitaxel (PTX) – delivered using albumin nanoparticles, liposomes, polymeric nanoparticles and micelles.

Docetaxel – investigated in HER2-targeted nanoparticles.

Cisplatin – investigated using lipid/polymeric nanoparticles.

7.2. Hormonal therapeutic agents

Nanocarriers have also been investigated for drugs used against hormone-receptor-positive breast cancer.

Examples:

Tamoxifen

Exemestane

Other estrogen-related therapeutic agents

Nanoformulation can improve the solubility and bioavailability of poorly water-soluble drugs and may help provide sustained drug exposure. Studies have investigated exemestane and tamoxifen in lipid and other nanoparticulate systems. [37]

7.3. Monoclonal antibodies and targeted biological agents

Nanoparticles can carry or be decorated with biological targeting molecules.

Examples:

Trastuzumab (Herceptin) – targets the HER2 receptor.

Antibodies or antibody fragments can be attached to nanoparticles to increase receptor-mediated uptake.

The nanoparticle acts as a carrier while the antibody provides recognition of the target receptor. HER2-targeted nanocarriers have been extensively investigated for breast cancer.

7.4. Small interfering RNA (siRNA)

siRNA can silence specific genes involved in tumor growth, angiogenesis or drug resistance. However, free siRNA is unstable and has poor cellular uptake. Nanoparticles can protect siRNA and facilitate its delivery into cancer cells.

Nanoparticles have therefore been investigated as carriers for both anticancer drugs and gene-silencing molecules.

7.5. microRNA and nucleic-acid therapeutics

Nanocarriers can deliver microRNAs (miRNAs), mRNA and other nucleic acids to tumor cells. These approaches aim to modify abnormal gene-expression pathways involved in proliferation, metastasis, apoptosis and drug resistance. A major advantage of nanocarriers is protection of nucleic acids from degradation and improved cellular delivery. [38]

7.6. Immunotherapeutic agents

Nanotechnology can be used to deliver immune-modulating molecules, such as immune checkpoint-related agents, cytokines or tumor-antigen-related components. The objective is to modify the tumor microenvironment and stimulate an antitumor immune response while concentrating the therapeutic payload near the tumor. Recent reviews describe nanoparticle-mediated immunotherapy as an emerging area in breast-cancer nanomedicine..

7.7. Combination therapy

One important development is co-delivery, where a single nanocarrier transports two or more therapeutic agents.

Examples include:

Chemotherapy drug + siRNA

→ chemotherapy kills cancer cells while siRNA may suppress a resistance-related pathway.

Chemotherapy + P-glycoprotein inhibitor

→ investigated to help overcome multidrug resistance.[39]

How targeted nanodelivery works

Therapeutic agent → Nanocarrier loading → Surface modification → Blood circulation → Tumor accumulation → Receptor recognition → Cellular uptake → Controlled drug release → Cancer-cell death.

8. Nanotechnology-Based Theranostics in Breast Cancer

Theranostics combines therapy + diagnostics in a single platform. In breast cancer, nanotheranostic systems are designed to detect/visualize the tumor, deliver treatment specifically to tumor cells, and monitor the response to treatment. A typical nanotheranostic nanoparticle may contain a targeting ligand, therapeutic drug and imaging/contrast agent.

8.1. Basic concept

Nanoparticle + Targeting ligand + Imaging agent + Therapeutic agent → Breast-cancer targeting → Imaging + Treatment + Monitoring

Nanoparticles can be engineered with small size, high surface area and functionalized surfaces. Targeting molecules such as antibodies, peptides, aptamers or other ligands can help recognize receptors that are overexpressed on particular breast-cancer cells.[40]

8.2. Diagnostic applications

Nanotechnology can improve breast-cancer detection and tumor visualization through several imaging approaches: Fluorescence imaging: fluorescent dyes, quantum dots and other optical probes can help visualize cancer cells.

MRI: magnetic nanoparticles, particularly iron-oxide-based systems, can act as contrast-enhancing agents. CT imaging: high-atomic-number nanoparticles such as gold nanoparticles can provide contrast. PET/SPECT: nanoparticles can be associated with suitable radioactive imaging agents. Photoacoustic imaging: nanoparticles that absorb light can generate signals useful for tumor imaging.[41]

8.3. Therapeutic applications

The same nanoplatform can carry therapeutic agents to the tumor:

Nanotechnology approach	Therapeutic function
Drug-loaded nanoparticles	Deliver anticancer drugs to tumor cells
Gene-delivery nanoparticles	Deliver siRNA, miRNA or other genetic therapeutics
Gold nanoparticles	Can support photothermal therapy
Magnetic nanoparticles	Can be used for imaging and, in some designs, magnetic/thermal treatment
Upconversion nanoparticles	Can support imaging, photodynamic and photothermal approaches
Polymeric/lipid nanoparticles	Encapsulate and control release of anticancer drugs

These approaches have been investigated for chemotherapy, gene therapy, photothermal therapy, photodynamic therapy, radiotherapy and combination treatments.[42]

8.4. Targeting of breast-cancer cells

Targeting can be achieved by attaching specific molecules to the nanoparticle surface.

Examples:

..Target selection is important because breast cancer is molecularly heterogeneous; a target expressed in one subtype may not be equally useful in another.

Targeted nanoparticle → tumor accumulation → receptor recognition → cellular uptake → imaging → drug release → therapeutic action → response monitoring

8.5. Importance in breast cancer

Nanotheranostics is being investigated to address several limitations of conventional cancer treatment, including nonspecific drug distribution, difficulty in monitoring drug delivery and treatment response, and therapeutic resistance. However, many multifunctional nanotheranostic systems remain at the preclinical or research stage, and issues such as biodistribution, toxicity, manufacturing, scalability and regulatory approval remain important challenges.[43,44]

9.Applications of Nanotechnology in Breast Cancer.

Nanotechnology has several applications in breast-cancer diagnosis, targeted drug delivery, therapy, imaging, and theranostics. Nanoparticles can be engineered to carry drugs or imaging agents and can be functionalized to recognize specific molecules on cancer cells.

9.1. Targeted drug delivery

Nanocarriers such as liposomes, polymeric nanoparticles, dendrimers and micelles can deliver anticancer drugs to tumor tissue. Targeting ligands such as antibodies, peptides and aptamers can be attached to nanoparticles to improve recognition of cancer cells.

Example: HER2-targeted nanoparticles have been investigated for delivering therapeutic agents to HER2-positive breast-cancer cells.[45]

9.2. Cancer imaging and diagnosis

Nanoparticles can improve tumor visualization in different imaging techniques:

- MRI: magnetic nanoparticles can act as contrast agents.
- CT: gold nanoparticles can enhance imaging contrast.
- Fluorescence imaging: fluorescent nanomaterials can help visualize cancer cells.
- Photoacoustic imaging: light-absorbing nanoparticles can assist tumor imaging.

9.3. Photothermal therapy

Some nanoparticles, particularly gold-based nanomaterials, absorb light and convert it into heat. The generated heat can damage or kill tumor cells.

Nanoparticle → light irradiation → heat generation → tumor-cell damage

This approach has been investigated as a potential breast-cancer treatment.[46]

9.4. Photodynamic therapy

Nanoparticles can carry or enhance delivery of photosensitizers. After activation by suitable light, reactive oxygen species are produced, which can damage cancer cells.

9.5. Gene therapy

Nanoparticles can be used as carriers for siRNA, miRNA, DNA or other nucleic-acid therapeutics. This can help regulate genes involved in tumor growth, invasion, drug resistance and apoptosis.

9.6. Combination therapy

A single nanocarrier can potentially carry two or more therapeutic agents, such as a chemotherapeutic drug plus a gene therapeutic, allowing combination treatment and controlled delivery.

10.Theranostics

Theranostics = Therapy + Diagnostics

A multifunctional nanoparticle can contain both an imaging component and a therapeutic component. It can therefore help visualize the tumor, deliver treatment and potentially monitor treatment response.

10.1.Overcoming multidrug resistance

Nanocarriers are being investigated to improve intracellular drug delivery and co-deliver drugs with agents that modulate mechanisms associated with multidrug resistance. This is an important research application in breast cancer.

10.2.Controlled and stimuli-responsive drug release

Nanoparticles can be designed to release their drug in response to conditions such as pH, temperature, enzymes or light. This may provide more controlled drug exposure at the tumor site.[47]

10.3.Personalized breast-cancer treatment

Because breast cancer contains different molecular subtypes and targets, nanotechnology can be designed around specific biomarkers, potentially supporting more individualized diagnosis and treatment strategies. However, many advanced nanotheranostic approaches remain under investigation and require further clinical validation.

11.Recent advance in breast cancer

Breast cancer treatment has changed rapidly in recent years because of advances in molecular classification, targeted therapy, antibody–drug conjugates (ADCs), immunotherapy, endocrine therapy, liquid biopsy and personalized medicine. Treatment is increasingly selected according to biomarkers such as ER, PR, HER2, PD-L1, PIK3CA and ESR1, rather than using the same treatment for all patients. Recent 2025–2026 evidence shows important progress in both early-stage and metastatic breast cancer. [48]

11.1. Antibody–drug conjugates (ADCs)

One of the most important recent advances is the development of antibody–drug conjugates, which combine a monoclonal antibody with a potent cytotoxic drug. The antibody recognizes a specific antigen on cancer cells and helps deliver the drug preferentially to the tumor.

Trastuzumab deruxtecan (T-DXd) has become an important treatment for HER2-positive breast cancer. In May 2026, the FDA expanded T-DXd use to HER2-positive stage II–III early breast cancer in the neoadjuvant setting and for patients with residual invasive disease after neoadjuvant therapy.[49].

11.2. Immunotherapy

Immune checkpoint inhibitors, particularly PD-1/PD-L1 inhibitors, have become an important component of treatment for selected TNBC patients. Current research is focusing on combining immunotherapy with ADCs and other targeted treatments to overcome resistance.

11.3. Advances in HER2-targeted therapy

HER2-positive breast cancer has benefited greatly from targeted treatment. In addition to trastuzumab and pertuzumab, newer agents include T-DXd, tucatinib and other HER2-directed therapies.

The DESTINY-Breast09 results supported T-DXd plus pertuzumab as a new first-line treatment option for HER2-positive metastatic breast cancer, demonstrating the growing importance of ADC-based treatment in this subtype.

The 2026 ESMO guideline provides updated treatment algorithms for HER2-positive metastatic breast cancer and incorporates newer HER2-directed therapies and treatment sequencing.

11.4. CDK4/6 inhibitors and endocrine therapy

For hormone receptor-positive/HER2-negative (HR+/HER2–) breast cancer, endocrine therapy remains the foundation of treatment. CDK4/6 inhibitors such as abemaciclib, ribociclib and palbociclib are increasingly used in appropriate patients to delay disease progression or reduce recurrence risk.

11.5. Oral SERDs and treatment of ESR1-mutated breast cancer

Another important development is the introduction of oral selective estrogen receptor degraders (SERDs). These drugs are particularly relevant to patients with ESR1-mutated HR-positive breast cancer, in whom resistance to conventional endocrine therapy can develop.

Recent clinical evidence with agents such as imlunestrant supports the concept of using molecular information to select endocrine treatment and overcome acquired resistance. [50]

11.6. Liquid biopsy and ctDNA-guided treatment

Circulating tumor DNA (ctDNA) is becoming an important tool for precision oncology. A blood sample can be analyzed for tumor-derived DNA, potentially allowing clinicians to identify molecular changes before they become clinically apparent.

The 2025 SERENA-6 findings highlighted a new approach in which ctDNA detection of emerging ESR1 mutations can be used to switch endocrine therapy before radiological disease progression. This represents a move from treating visible progression to molecularly predicted progression.

11.7. Molecularly targeted therapy:

A major recent development in 2026 is gedatolisib, a PI3K/mTOR pathway inhibitor, which received FDA approval in combination with fulvestrant, with or without palbociclib, for a defined population of HR-positive/HER2-negative advanced breast cancer patients without a detected PIK3CA mutation after prior endocrine therapy.[51]

11.8. Personalized and precision medicine

Modern breast cancer management is moving toward personalized treatment, in which therapy is selected according to:

This approach can reduce unnecessary treatment and help identify patients who are most likely to benefit from specific targeted or immune-based therapies. The latest ASCO guideline specifically recommends integrating clinicopathologic features, genomic assays, patient preferences, treatment tolerability and recurrence risk into treatment decisions.

11.9. New approaches in early breast cancer

Recent advances are not limited to metastatic disease. T-DXd has now moved further into early HER2-positive breast cancer, including neoadjuvant treatment and treatment of residual disease after neoadjuvant therapy.

11.10. Future directions

Current research is focusing on:

- Next-generation antibody–drug conjugates
- Bispecific antibodies
- New immune checkpoint targets
- AI-assisted diagnosis and treatment selection
- Novel oral endocrine therapies
- PROTAC-based protein degraders
- Combination of ADCs with immunotherapy
- More precise treatment of treatment-resistant disease
- The major goal is to develop treatments that are more effective, more selective and less toxic, while improving quality of life.[52,53]

12.Overcoming biological barrier in breast cancer

Overcoming Biological Barriers in Breast Cancer Using Nanotechnology In breast cancer, therapeutic drugs must cross several biological barriers before reaching cancer cells. These include the protein corona, abnormal tumor vasculature, dense extracellular matrix (ECM), high interstitial fluid pressure, tumor-cell membrane, intracellular barriers, and—especially in breast cancer brain metastasis—the blood–brain barrier (BBB) and blood–tumor barrier (BTB). These barriers can reduce drug accumulation and penetration into tumors. [54,55]

12.1. Overcoming the protein-corona barrier

When nanoparticles enter the bloodstream, plasma proteins rapidly adsorb onto their surface, forming a protein corona. This can alter nanoparticle targeting and promote clearance. Surface modification, particularly with hydrophilic polymers and biomimetic materials, can help control these interactions.

12.2. Improving tumor penetration

Breast tumors have abnormal vasculature and a heterogeneous extracellular matrix. Therefore, simply reaching the tumor does not guarantee penetration into its deeper regions. Recent research emphasizes that the traditional EPR (enhanced permeability and retention) effect alone is insufficient for uniform nanoparticle delivery. Active transport through tumor vessels and interactions with tumor components are also important.

12.3.Overcoming the microenvironment.

The breast-cancer tumor microenvironment contains abnormal pH, hypoxia, reactive oxygen species (ROS), enzymes, stromal cells and dense ECM.

Stimuli-responsive nanocarriers can be designed to remain relatively stable in normal tissues but release their drug in response to tumor-associated stimuli such as low pH, ROS, enzymes or hypoxia.

For example:

Nanoparticle → tumor accumulation → acidic/ROS/enzyme-rich environment → nanoparticle activation → controlled drug release → cancer-cell killing

12.4. Overcoming cellular barriers

After reaching the tumor, nanoparticles still need to enter cancer cells and release their therapeutic cargo. Ligands such as antibodies, peptides or other targeting molecules can be attached to nanoparticles to recognize receptors overexpressed on breast-cancer cells. Once internalized, pH- or redox-responsive systems can facilitate intracellular drug release and, where needed, endosomal escape.[56]

12.5. Overcoming BBB/BBB in breast-cancer brain metastasis

This is particularly important in HER2-positive and other breast cancers that metastasize to the brain. The BBB and BTB restrict many therapeutic agents from reaching brain metastases. Nanoparticles can be engineered to exploit receptor-mediated transport pathways or use biomimetic carriers such as exosomes.[56,57,58]

13.Safety, Toxicity and Pharmacokinetic Considerations in Breast Cancer Nanomedicine.

In breast-cancer treatment, especially nanotechnology-based targeted drug delivery, safety, toxicity and pharmacokinetics are important because nanoparticles can change the distribution, metabolism, clearance and tissue accumulation of anticancer drugs. Nanoparticle properties such as size, shape, surface charge, composition and surface area can influence cellular uptake and toxicity.

13.1. Safety considerations

The major safety considerations for breast-cancer nanomedicines include:

- **Biocompatibility:** Nanocarriers should be compatible with blood and tissues and should not cause unacceptable inflammation or immune reactions.
- **Particle characteristics:** Size, shape, surface charge and composition should be carefully controlled because they affect biodistribution, cellular uptake and toxicity.
- **Long-term accumulation:** Some poorly degradable nanoparticles may accumulate in organs such as the liver and spleen.
- **Immunological effects:** Nanoparticles may interact with immune cells and plasma proteins, potentially causing unwanted immune responses.
- **Manufacturing consistency:** Particle size, drug loading, surface characteristics, purity and stability should remain consistent between batches.
- **Drug release:** The drug should be released at the intended site and at an appropriate rate to avoid excessive systemic exposure.
- **Regulatory evaluation:** FDA recommends adequate characterization of nanomaterials and understanding how their physicochemical properties affect quality, safety, efficacy, pharmacokinetics and in-vivo drug release.[59,60]

13.2. Toxicity considerations

Nanotechnology can potentially reduce non-specific systemic toxicity by improving drug delivery to tumors, but the nanocarrier itself can also introduce toxicity concerns. Recent breast-cancer reviews identify biodistribution, safety and regulatory challenges as important barriers to clinical translation.

Important toxicity concerns include:

A. Hepatotoxicity

Nanoparticles may accumulate in the liver and can affect hepatic cells or liver function.

B. Nephrotoxicity

Small nanoparticles or released drug molecules may be eliminated through the kidneys and can potentially produce renal toxicity.

C. Cardiotoxicity

This is particularly important for some breast-cancer therapies. For example, trastuzumab-associated cardiac dysfunction is a clinically important toxicity requiring monitoring.

D. Hematological toxicity

Anticancer drugs can cause myelosuppression, including neutropenia, anemia and thrombocytopenia.

E. Immunotoxicity and inflammation

Some nanomaterials can activate immune pathways or cause inflammatory responses.

F. Oxidative stress

Certain nanoparticles may generate reactive oxygen species (ROS), potentially damaging cellular components.

Therefore, toxicity evaluation should include cytotoxicity, hemocompatibility, immunotoxicity, oxidative stress, organ toxicity and long-term biodistribution, depending on the nanocarrier.[61]

13.3. Pharmacokinetic considerations

Pharmacokinetics describes what happens to the drug/nanocarrier in the body:

Absorption → Distribution → Metabolism → Excretion (ADME)

Nanocarriers can substantially modify these processes compared with conventional anticancer drugs.

A. Absorption

For orally administered nanomedicines, nanoparticles can influence drug solubility, intestinal absorption and bioavailability. For intravenous formulations, absorption is less relevant because the drug enters systemic circulation directly.

B. Distribution

Nanoparticle size and surface properties strongly influence distribution. Nanomedicine can potentially increase accumulation in tumors and decrease exposure of healthy tissues. In breast cancer, nanocarrier properties influence tissue penetration, tumor accumulation and cellular uptake.

C. Metabolism

Nanocarriers may alter the metabolism of their encapsulated drug by changing where and when the drug is released. Therefore, conventional pharmacokinetic parameters of the free drug cannot always be directly applied to the nanoparticle formulation.

D. Elimination

Clearance may occur through the liver/biliary system, kidneys or uptake by the reticuloendothelial system depending on the formulation.

Example=Trastuzumab.

Trastuzumab illustrates why pharmacokinetics is important in breast cancer. It has a relatively long half-life, approximately 28 days, with low systemic clearance and a relatively small volume of distribution.

For newer breast-cancer antibody–drug conjugates (ADCs) such as trastuzumab emtansine, trastuzumab deruxtecan and sacituzumab govitecan, both the antibody and cytotoxic payload contribute to their PK/PD behavior. These ADCs generally show two-compartment distribution, and their elimination involves antibody-related pathways with predominantly biliary/fecal rather than urinary elimination.[62]

14. Clinical translation and regulatory perspectives in breast cancer.

Clinical translation refers to the process of converting promising laboratory findings—such as targeted nanoparticles, nanocarriers, biomarkers, and novel drug-delivery systems—into safe and effective treatments for breast cancer patients. Breast cancer treatment is increasingly based on molecular characteristics such as ER, PR, HER2 and specific genetic alterations, allowing more personalized therapy.

14.1. Clinical translation

The translation of nanotechnology-based breast cancer therapies generally progresses through:

Laboratory research → Preclinical studies → Clinical trials → Regulatory approval → Clinical use

Preclinical stage: Nanocarriers are evaluated for drug loading, particle size, stability, drug release, cellular uptake, toxicity, pharmacokinetics and anti-cancer activity.

- Phase I trials: Mainly assess safety, tolerability, pharmacokinetics and an appropriate dose.
- Phase II trials: Evaluate preliminary efficacy and further characterize safety.
- Phase III trials: Compare the new treatment with standard therapy in larger patient populations.[63]

14.2.Regulatory perspectives for nanotechnology

For nanotechnology-based breast cancer formulations, regulatory evaluation must consider both the drug and the nanomaterial. FDA's guidance states that nanomaterials can be active ingredients, inactive ingredients, or drug carriers, and their nanoscale properties may produce characteristics requiring additional examination.

Important regulatory considerations include:

- Particle size and size distribution
- Surface characteristics and morphology
- Chemical composition and purity
- Drug loading and encapsulation efficiency
- Stability and degradation
- Drug-release profile
- Pharmacokinetics and biodistribution
- Immunogenicity and toxicity
- Reproducibility and manufacturing consistency
- Quality control and GMP compliance[64]

14.3.Regulatory approval and clinical implementation

A promising breast cancer nanomedicine must demonstrate an appropriate balance of quality, safety and efficacy before regulatory approval. FDA already has experience with oncology nanomedicines; examples include Doxil® (liposomal doxorubicin) and Abraxane® (albumin-bound paclitaxel), demonstrating that nanotechnology can successfully reach routine clinical practice. [63,64].

14.4. Major challenges in clinical translation

- The major barriers include: Difference between animal models and human tumors
- Tumor heterogeneity
- Variable nanoparticle accumulation in tumors
- Difficulty predicting long-term toxicity
- Complex manufacturing and scale-up
- High development costs
- Need for validated biomarkers
- Regulatory complexity of combination products
- Need for well-designed clinical trials
- Reproducibility of nanomedicine formulations

15.Challenges and limitations in breast cancer

Breast cancer is a highly heterogeneous disease, and although screening, surgery, chemotherapy, hormonal therapy, targeted therapy and immunotherapy have improved outcomes, several biological and clinical challenges remain.

15.1. Tumor heterogeneity

- Breast cancer is not a single disease; it contains different molecular subtypes such as HR+/HER2–, HER2+, and triple-negative breast cancer (TNBC).
- Even within the same tumor, different cancer-cell populations may have different genetic characteristics.
- This heterogeneity can produce different responses to the same treatment and contribute to treatment failure.

15.2. Development of treatment resistance

- Cancer cells can become resistant to chemotherapy, endocrine therapy, targeted therapy and other treatments. Resistance may be primary (present before treatment) or acquired after an initial response.
- Molecular changes such as ESR1 mutations and alterations in PI3K/AKT/PTEN and cell-cycle pathways can contribute to resistance. [65]

15.3. Metastasis and recurrence

- Breast cancer can spread to the bone, liver, lungs and brain.
- Metastatic breast cancer is generally more difficult to treat and is usually considered incurable, although modern therapies can prolong survival.
- Differences between the primary tumor and metastatic tumors can make treatment selection difficult. [66]

15.4. Limitations of conventional chemotherapy

- Chemotherapy can damage both cancerous and rapidly dividing normal cells.
- Common problems include fatigue, nausea, hair loss, myelosuppression and other toxicities.
- Some tumors may show little response or develop resistance.

15.5. Limitations of targeted therapy

- Targeted treatments require the presence of a specific molecular target.
- Target expression can vary between tumor cells and may change during disease progression.
- Loss or reduction of the target can contribute to resistance to targeted therapies, including antibody–drug conjugates.

15.6. Immunotherapy limitations

- Immunotherapy does not work equally well in all breast cancer patients.
- The immunosuppressive tumor microenvironment and other mechanisms can reduce immune-cell activity.
- Resistance to immunotherapy can develop and remains an important research challenge.

15.7. Difficulty in personalized treatment

- Breast cancer treatment increasingly depends on molecular and genetic characteristics.
- However, tumor characteristics can change during progression and after treatment.
- Therefore, a treatment that works initially may become less effective after recurrence or metastasis.

15.8. challenges in nanotechnology-based breast cancer therapy

For a nanotechnology-focused review, additional limitations include:

- Difficulty achieving selective accumulation of nanoparticles in tumors.
- Variable tumor blood flow and abnormal vasculature can reduce nanoparticle delivery.
- Uptake by the reticuloendothelial system can remove nanoparticles before they reach the tumor.
- Possible toxicity or immune reactions depending on the nanomaterial.
- Difficulty maintaining reproducible particle size, surface properties, drug loading and stability during large-scale manufacturing. [67,68]

16. Future Perspectives of Breast Cancer

Breast cancer research is moving toward early detection, precision medicine, targeted therapy, immunotherapy, and personalized treatment. Important future perspectives include:

16.1. Personalized and precision medicine

Future treatment will increasingly be selected according to the patient's tumor subtype, genetic mutations, biomarkers, and treatment response rather than using the same treatment for all patients. [69]

16.2. Liquid biopsy and ctDNA monitoring

Circulating tumor DNA (ctDNA), circulating tumor cells, and other liquid-biopsy markers may allow minimally invasive detection of residual disease, treatment resistance, and recurrence. Dynamic ctDNA monitoring is also being investigated to change therapy before clinical or radiological progression becomes evident.

16.3. Advanced antibody–drug conjugates (ADCs)

Next-generation ADCs are expected to provide more selective delivery of anticancer drugs to tumor cells while reducing systemic toxicity. Research is focusing on improved antibodies, linkers, payloads, and combinations with other therapies.

16.4.Improved immunotherapy

Immunotherapy is expected to become more personalized, particularly for difficult-to-treat subtypes such as triple-negative breast cancer (TNBC). Future research will focus on identifying biomarkers that can predict which patients will respond to immune-based treatments.

16.5.artificial intelligence (AI) in diagnosis and treatment

AI and digital pathology may improve breast-image interpretation, tumor classification, risk prediction, biomarker identification, and treatment selection. Combining AI with multi-omics information could support more accurate personalized treatment.

16.6.Nanotechnology-based drug delivery

Future nanocarriers may improve targeted delivery of anticancer drugs, reduce toxicity, increase drug accumulation in tumors, and enable combination delivery of drugs, genes, or other therapeutic agents.[70]

16.7.Combination therapies

Combining targeted therapy, hormone therapy, chemotherapy, immunotherapy, and ADCs may help overcome treatment resistance and improve outcomes. Research is also investigating rational combinations of ADCs with targeted drugs and immune checkpoint inhibitors.

16.8.Early detection and screening

Greater emphasis will be placed on detecting breast cancer at an earlier stage through improved imaging, biomarkers, liquid biopsy, and accessible screening programs. Early diagnosis remains one of the most important approaches for improving survival.

16.9.Overcoming drug resistance and recurrence

Future studies will focus on understanding why breast cancers become resistant to endocrine therapy, targeted therapy, immunotherapy, and ADCs, with the goal of developing strategies that prevent or overcome resistance.

16.10.Reducing global treatment inequalities

Future breast-cancer care must also focus on affordable screening, timely diagnosis, access to effective medicines, and patient-navigation programs, particularly in low- and middle-income countries. WHO's Global Breast Cancer Initiative aims to reduce global breast-cancer mortality through early detection, timely diagnosis, and comprehensive treatment.[71,72]

REFERENCE:-

- [1].. Surg. Oncol., 128 (6) (Nov. 2023), pp. 959-966, 10.1002/JSO.27459
- [2]Bray F, Laversanne M, Weiderpass E, Soerjomataram I. The ever-increasing importance of cancer as a leading cause of premature death worldwide. *Cancer*. 2021;127(16):3029-3030. doi:10.1002/cncr.33587
<https://doi.org/10.1002/cncr.33587>
- [3]M.Z. Afzal, L.T. Vahdat Evolving management of breast cancer in the era of predictive biomarkers and precision medicine
- [4]ny characteristics used to classify breast cancer are interdependent. For instance, TNBC is a high-grade tumor with an increased tendency to spread, lacks hormone receptor expression, and is significantly more aggressive than other types of cancerK. Asleh, N. Riaz, T.O. NielsenHeterogeneity of triple negative breast cancer: current advances in subtyping and treatment implications
- [5]V.B. Varzaru, T. Vlad, R. Popescu, C.S. Vlad, A.E. Moatar, I.M. CobecTriple-negative breast cancer: molecular particularities still a challenge*Diagnos*tics 2024, 14 (17) (Aug. 2024), p. 1875,
<https://doi.org/10.3390/diagnostics14171875>
- [6]A.M. Karim, et alTriple-negative breast cancer: epidemiology, molecular mechanisms, and modern vaccine-based treatment strategies*Biochem. Pharmacol.*, 212 (Jun. 2023), Article 115545, 10.1016/J.BCP.2023.115545
<https://doi.org/10.1016/j.bcp.2023.115545>
- [7]Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74(3):229-263. doi:10.3322/caac.21834.
<https://doi.org/10.3322/caac.21834>

- [8]International Agency for Research on Cancer (IARC). Global Cancer Observatory: GLOBOCAN 2022, World Fact Sheet.
- [9]World Health Organization. Cancer. WHO Fact Sheet, 3 July 2026.
- [10]World Health Organization. Cancer. WHO. Cancer treatment includes surgery, radiotherapy and systemic therapies, with treatment selected according to cancer type and individual patient characteristics.
- [11]Bhatia S. Nanoparticles in cancer therapy: limitations of conventional cancer treatment and potential role of nanotechnology. Relevant literature describes nonspecific distribution and toxicity as major limitations of conventional approaches.
- [12] Nanoparticles for Cancer Therapy: Current Progress and Challenges. *Frontiers/PMC*. Discusses nonspecificity, cytotoxicity and multidrug resistance as important limitations of conventional cancer treatment.
- [13] Recent progress on nanoparticle-based drug delivery systems for cancer therapy. *International Journal of Nanomedicine*. Nanoparticle systems can address limitations including nonspecific biodistribution, poor solubility and limited bioavailability.
- [14]Nano-biotechnology in tumour and cancerous disease: A perspective review. Discusses tumour barriers, conventional drug-delivery limitations and the potential of nanoparticles for improved tumour delivery.
- [15]Targeted therapy using nanotechnology: focus on cancer. Discusses nanoparticle physicochemical properties, biodistribution, passive targeting and active targeting strategies.
- [16]Nanotechnology in oncology: advances in biosynthesis, drug delivery, and theranostics. Discusses EPR-mediated accumulation, active targeting and stimuli-responsive delivery
- [17]Nanotechnology-Driven Cancer Therapies for Precision Oncology: Advances and Clinical Outlook. Reviews nanocarriers, active/passive targeting, biomimetic systems, stimuli-responsive delivery and clinical translation.
- [18] Multifunctional Nanomaterials and Their Applications in Drug Delivery and Cancer Therapy. Discusses multifunctional nanoparticles capable of integrating targeting, imaging and therapeutic functions and delivering multiple agents.
- [19]Cutting-edge approaches for targeted drug delivery in breast cancer: beyond conventional therapies. *PMC*.
- [20] Breast Cancer Targeted Treatment Strategies: Promising Nanocarrier Approaches. *Curr Pharm Des*. 2019. DOI: 10.2174/1871520619666191022175003.
<https://doi.org/10.2174/1871520619666191022175003>
- [21]Kumar S, Rathaur S, Maity D, Varshney P, Gayen JR. Nanotechnology based targeted drug delivery systems for breast cancer: challenges, recent advancement and future perspectives. *Nanomedicine*. 2026;21(7):1027-1048.
<https://doi.org/10.1080/17435889.2026.2637591>
- [22].Nanomedicine-Based Drug-Targeting in Breast Cancer: Pharmacokinetics, Clinical Progress, and Challenges. *ACS Omega*. 2024. DOI: 10.1021/acsomega.3c07345.
<https://doi.org/10.1021/acsomega.3c07345>
- [23].Kumar S, Rathaur S, Maity D, Varshney P, Gayen JR. Nanotechnology based targeted drug delivery systems for breast cancer: challenges, recent advancement and future perspectives. *Nanomedicine*. 2026.
<https://doi.org/10.1080/17435889.2026.2637591>
- [24]Bourang S, et al. Application of nanoparticles in breast cancer treatment: a systematic review. *Naunyn-Schmiedeberg's Archives of Pharmacology*. 2024;397:6459-6505.
<https://doi.org/10.1007/s00210-024-03082-y>
- [25].Tumor Microenvironment-Stimuli Responsive Nanoparticles for Anticancer Therapy. *International Journal of Molecular Sciences*.
- [26].Emerging Applications of Nanoparticles in the Diagnosis and Treatment of Breast Cancer. 2024.
- [27].Bourang S, et al. Application of nanoparticles in breast cancer treatment: a systematic review. *Naunyn-Schmiedeberg's Archives of Pharmacology*. 2024.
<https://doi.org/10.1007/s00210-024-03082-y>

- [28] Nanotechnology based targeted drug delivery systems for breast cancer: challenges, recent advancement and future perspectives. *Nanomedicine*. 2026;21(7):1027-1048. DOI: 10.1080/17435889.2026.2637591.
<https://doi.org/10.1080/17435889.2026.2637591>
- [29] Breast Cancer Targeted Treatment Strategies: Promising Nanocarrier Approaches. *Current Drug Delivery. Nanocarriers for Diagnosis and Targeting of Breast Cancer*. BioMed Research International.
- [30] Nanomedicine applications in the treatment of breast cancer: current state of the art.
- Actively Targeted Nanomedicines in Breast Cancer: From Pre-Clinical Investigation to Clinic.
- [31] Cutting-edge approaches for targeted drug delivery in breast cancer: beyond conventional therapies. *Nanoscale Advances*. 2024.
- [32] Receptor-Mediated Targeted Delivery of Surface-Modified Nanomedicine in Breast Cancer: Recent Update and Challenges. *Pharmaceutics*. 2021.
- [33] Nano-pharmaceutical formulations for targeted drug delivery against HER2 in breast cancer. *Current Pharmaceutical Design*.
- [34] Targeting the transferrin receptor in breast cancer: nanotechnology-based drug delivery strategies. *Nanomedicine*. 2026;21(6):853-867.
<https://doi.org/10.1080/17435889.2026.2628237>
- [35] Actively Targeted Nanomedicines in Breast Cancer: From Pre-Clinical Investigation to Clinic. Emerging targeted therapeutic strategies for the treatment of triple-negative breast cancer. *Journal of Drug Targeting*. 2023.
- [36] Kumar S, et al. Nanotechnology based targeted drug delivery systems for breast cancer: challenges, recent advancement and future perspectives. *Nanomedicine*. 2026;21(7):1027-1048.
<https://doi.org/10.1080/17435889.2026.2637591>
- [37] Wang T, et al. Nanotechnology-driven drug delivery systems for breast cancer: A review. *Biomaterials Advances*. 2026.
<https://doi.org/10.1016/j.bioadv.2026.214725>
- [38] Nanoparticles Targeting Receptors on Breast Cancer for Efficient Delivery of Chemotherapeutics. *PMC. Nanomedicine-Based Drug-Targeting in Breast Cancer: Pharmacokinetics, Clinical Progress, and Challenges*. PMC.
- [39] Nanoparticle-mediated targeted drug delivery for breast cancer treatment. *PMC*.
- [40] Arshad R, et al. Nano-Based Theranostic Platforms for Breast Cancer: A Review of Latest Advancements. *Bioengineering*. 2022;9(7):320. *Nanotheranostics for Diagnosis and Treatment of Breast Cancer*. PubMed. 2023.
<https://doi.org/10.3390/bioengineering9070320>
- [41] Emerging Applications of Nanoparticles in the Diagnosis and Treatment of Breast Cancer. 2024. *Current State of Breast Cancer Diagnosis, Treatment, and Theranostics*. PMC.
- [42] Nanoparticles for imaging and treatment of metastatic breast cancer. *PMC*.
- [43] Engineered upconversion nanocarriers for synergistic breast cancer imaging and therapy: Current state of art. 2022.
- [44] Breast cancer epidemiology, diagnostic barriers, and contemporary trends in breast nanotheranostics and mechanisms of targeting. 2024.
- [45] Arshad R, et al. Nano-Based Theranostic Platforms for Breast Cancer: A Review of Latest Advancements. *Bioengineering*. 2022;9(7):320.
<https://doi.org/10.3390/bioengineering9070320>
- [46] Current State of Breast Cancer Diagnosis, Treatment, and Theranostics. *PMC*.
- [47] Nanoparticles for imaging and treatment of metastatic breast cancer. *PMC*.
- [48] de Azambuja E, et al. Metastatic breast cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Annals of Oncology*. 2026;37(9):1203-1219.
<https://doi.org/10.1016/j.annonc.2026.05.707>

- [49]Caswell-Jin JL, et al. Medical Therapy for Hormone Receptor-Positive, HER2-Negative Stage I-III Breast Cancer: ASCO Living Guideline, Version 2026.1.0. *Journal of Clinical Oncology*. 2026.
<https://doi.org/10.1200/JCO-26-02034>
- [50]Wang JM, Zhou Y, Ding Y, et al. Recent advances in immunotherapy for breast cancer: An updated review. *Critical Reviews in Oncology/Hematology*. 2026;226:105498.
<https://doi.org/10.1016/j.critrevonc.2026.105498>
- [51]O'Sullivan CC. Cyclin-Dependent 4/6 Kinase Inhibitors for Treatment of HER2-Positive Breast Cancer: 2026 Update. *Cancers*. 2026;18(3):533.
<https://doi.org/10.3390/cancers18030533>
- [52]A Systematic Review of Major Advances in Breast Cancer Therapeutics in 2025. 2026.
- [53]U.S. FDA. FDA approvals of trastuzumab deruxtecan, datopotamab deruxtecan, sacituzumab govitecan and gedatolisib for specific breast cancer populations, 2026.
- [54]López-Estévez AM, et al. Personalized Cancer Nanomedicine: Overcoming Biological Barriers for Intracellular Delivery of Biopharmaceuticals. *Advanced Materials*. 2024;36:e2309355. DOI: 10.1002/adma.202309355.
<https://doi.org/10.1002/adma.202309355>
- [55]The mechanisms of nanoparticle delivery to solid tumours. *Nature Reviews Bioengineering*. 2024;2:201-213.
<https://doi.org/10.1038/s44222-024-00154-9>
- [56]Tumor microenvironment-responsive nanoformulations for breast cancer. 2024 review.
- [57]Mhaske A, et al. Receptor-Assisted Nanotherapeutics for Overcoming the Blood-Brain Barrier. *Molecular Neurobiology*. 2024;61:8702-8738. DOI: 10.1007/s12035-024-04015-9.
<https://doi.org/10.1007/s12035-024-04015-9>
- [58]Lim SH, Yee GT, Khang D. Nanoparticle-Based Combinational Strategies for Overcoming the Blood-Brain Barrier and Blood-Tumor Barrier. *International Journal of Nanomedicine*. 2024;19:2529-2552. DOI: 10.2147/IJN.S450853.
<https://doi.org/10.2147/IJN.S450853>
- [59]Nanomedicine-Based Drug-Targeting in Breast Cancer: Pharmacokinetics, Clinical Progress, and Challenges. *ACS Pharmacology & Translational Science*. 2024.
- [60]Bourang S, et al. Application of nanoparticles in breast cancer treatment: a systematic review. *Naunyn-Schmiedeberg's Archives of Pharmacology*. 2024;397:6459-6505. DOI: 10.1007/s00210-024-03082-y.
<https://doi.org/10.1007/s00210-024-03082-y>
- [61]pharmacokinetics and pharmacodynamics of antibody-drug conjugates for the treatment of patients with breast cancer. 2024. DOI: 10.1080/17425255.2024.2302460.
<https://doi.org/10.1080/17425255.2024.2302460>
- [62]Leyland-Jones B, et al. Pharmacokinetics, safety, and efficacy of trastuzumab administered every three weeks in combination with paclitaxel. *Journal of Clinical Oncology*. 2003;21:3965-3971.
<https://doi.org/10.1200/JCO.2003.12.109>
- [63]U.S. Food and Drug Administration (FDA). Drug Products, Including Biological Products, that Contain Nanomaterials: Guidance for Industry. 2022.
- [64]U.S. Food and Drug Administration (FDA). Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology: Guidance for Industry. 2014.
- [65]Ganguly A, et al. Factors affecting heterogeneity in breast cancer microenvironment: A narrative mini review. *International Review of Cell and Molecular Biology*. 2024;385:211-226.
<https://doi.org/10.1016/bs.ircmb.2024.01.002>
- [66]Khan MM, et al. Recent strategies to overcome breast cancer resistance. *Critical Reviews in Oncology/Hematology*. 2024;197:104351.
<https://doi.org/10.1016/j.critrevonc.2024.104351>

- [67]Will M, et al. Therapeutic resistance to anti-oestrogen therapy in breast cancer. *Nature Reviews Cancer*. 2023;23:673-685.
<https://doi.org/10.1038/s41568-023-00604-3>
- [68]Bianchini G, et al. Triple-negative breast cancer: challenges and opportunities of a heterogeneous disease. *Nature Reviews Clinical Oncology*. 2016;13:674-690.
<https://doi.org/10.1038/nrclinonc.2016.66>
- [69]Valle I, et al. Antibody-drug conjugates in breast cancer: mechanisms of resistance and future therapeutic perspectives. *npj Breast Cancer*. 2025;11:102.
<https://doi.org/10.1038/s41523-025-00829-5>
- [70]Davis AA, et al. Novel treatment approaches utilizing antibody-drug conjugates in breast cancer. *npj Breast Cancer*. 2025;11:42.
<https://doi.org/10.1038/s41523-025-00743-w>
- [71]Sanjari Moghaddam A, et al. Biomarker prediction of immunotherapy response in breast cancer: from single markers to multi-omics integration. *npj Breast Cancer*. 2026;12:10.
<https://doi.org/10.1038/s41523-025-00873-1>
- [72]Medford AJ, Wander SA. SERENA-6: dynamic ctDNA assessment and the future of precision cancer medicine. *Nature Reviews Clinical Oncology*. 2025;22:804-805.
<https://doi.org/10.1038/s41571-025-01066-2>