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Review

Enhanced drug delivery with nanocarriers: a comprehensive review of recent advances in breast cancer detection and treatment

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Abstract
Breast cancer (BC) remains a leading cause of morbidity and mortality among women worldwide, with triple-negative breast cancer (TNBC) posing significant treatment challenges due to its aggressive phenotype and resistance to conventional therapies. Recent advancements in nanocarrier technology offer promising solutions for enhancing drug delivery, improving bioavailability, and increasing drug accumulation at tumor sites through targeted approaches. This review delves into the latest innovations in BC detection and treatment, highlighting the role of nanocarriers like polymeric micelles, liposomes, and magnetic nanoparticles in overcoming the limitations of traditional therapies. Additionally, the manuscript discusses the integration of cutting-edge diagnostic tools, such as multiplex PCR-Nested Next-Generation Sequencing (mPCR-NGS) and blood-based biomarkers, which are revolutionizing early detection and molecular profiling of BC. The convergence of these technologies not only enhances therapeutic outcomes but also paves the way for personalized medicine in BC management. This comprehensive review underscores the potential of nanocarriers in transforming BC treatment and emphasizes the critical importance of early detection in improving patient prognosis.

Keywords Breast cancer · Nanocarriers · Tumor location · Diagnostic

1 Introduction

In women, breast cancer (BC) is the most prevalent form of cancer. Early-stage, non-metastatic cases of this cancer are treatable in around 70–80 percent of individuals [1]. The term "breast cancer" denotes the presence of malignant growths originating in breast tissue, frequently emerging from the lobules responsible for milk production in the ducts or from the inner lining of the milk ducts [2]. Men generally experience poorer outcomes because of delays in detection, despite the fact that BC is about 100 times more common in women than in men. Cancer cells possess DNA and RNA that bear similarities (though not identical) to the cells of the organism from which they originated. This resemblance is a key reason why they are often able to evade detection by the immune system, particularly when the immune system is already compromised

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[3]. Globally, there exists a notable contrast in BC survival rates, where developed nations boast an estimated 5-year survival rate of 80%, while underdeveloped nations struggle with a survival rate of less than 40%. In developing countries, challenges related to limited resources and infrastructure hinder the pursuit of enhancing BC outcomes through early detection, diagnosis, and treatment [2]. The regulation of BC and the progression of metastases is governed by various mechanisms. BC is categorized into three main subtypes, distinguished by molecular markers—specifically, human epidermal growth factor 2 (ERBB2, formerly known as HER2), progesterone receptor (PR), and estrogen receptor (ER). These markers play a crucial role in classifying tumors as ERBB2-positive (15%-20%), hormone receptor-positive/ERBB2-negative (constituting approximately 70% of patients), and triple-negative (15%), the latter term indicating tumors that do not express any of the three common molecular indicators. Advancements in understanding the biological activity of HER-2, PRs and ERs for different subtypes of BC have been made [4, 5]. Chemotherapy remains the most frequently used and effective treatment for BC. However, a major drawback is its low selective site-specificity, leading to toxic effects on normal, healthy cells. Consequently, the use of nanocarrier systems is employed to mitigate the numerous drawbacks associated with standard care for BC [6].

To increase the therapeutic effectiveness of anticancer medications, several nanocarriers have been developed, including polymeric micelles, liposomes, dendrimers and quantum dots [7]. According to studies, the utilization of nanocarriers for combinational delivery has shown encouraging outcomes in addressing BC [8]. Traditional treatment methods pose risks to non-targeted areas, causing harm to normal cells. Consequently, there is a growing inclination towards developing chemotherapeutic approaches that inflict minimal or no damage to patients while actively or passively targeting malignant cells. Employing NPs holds promise in delivering customized drugs directly to tumor cells, resulting in an increased concentration of medication within cancer cells through active or passive targeting strategies [9].

2 Human BC and its stages

As per a report from breastcancer.org, the stage of BC is determined by factors such as the size, shape, and depth of carcinoma cell invasion into the breast tissues. Stage zero is assigned to non-invasive tumors, while Stage 1 signifies incurable BC with the potential for microscopic penetration. In Stage 2, tumors may vary in size from less than 2 cm to over 5 cm. Stage 3 is characterized by inflammatory BC, involving the tumor has expanded to 10 or more lymph nodes in the axillary region, impacting lymph nodes above and below the collarbone. Lymph nodes above and below the collarbone are affected in stage 4. Refer to Fig. 1 below for a visual representation of all BC stages [2].

BRCA gene germline mutations are identified as the cause of 5–10% of BC cases [10]. Approximately 70% of BC cases are classified as sporadic. About 30% of patients have familial BC, which is frequently seen in families with a high prevalence of the condition. Several high-, moderate-, and low-penetrance susceptibility genes are linked to familial BC [11].

The Tumor-Node-Metastasis (TNM) system, pioneered by Pierre Denoix in 1942, was formulated to categorize cancer based on crucial visual characteristics of malignant tumors believed to impact the prognosis of the disease. This categorization takes into account variables like the size of the original tumor (T), if local lymph nodes (N) are involved, and whether distant metastases (M) are present. The American Joint Committee on Cancer (AJCC) incorporated the TNM clinical BC classification system into their first cancer stage manual in 1977, after the International Union Against Cancer (UICC) developed one in 1958. Updates have since been implemented to align with advancements in diagnosis and treatment. Notably, the 1987 revision addressed disparities between the AJCC and UICC versions of the TNM system. For instance, data from the National Cancer Database (NCDB) reveals a rise in the percentage of US patients initially diagnosed as Stage 0 or Stage I from 42.5% in 1985 to 56.2% in 1995, with a concurrent decrease in patients diagnosed as Stage III or Stage IV from 18.3% to 11.6% during the same period [12]. Recent advancements in clinical research are reflected in adjustments to the new TNM/AJCC classification. The axillary node status additions are the most significant. The terms "micrometastasis" and "isolated tumor cells" have been modified, as have the various sentinel lymph node biopsy detection techniques [13].

3 Recent advancements in detection of breast cancer

Analyzing the factors that have influenced the changes in the occurrence and fatality rates of BC over recent decades provides crucial insights into the significance of BC identification, the extensive use of adjuvant medications and the changing landscape of risk factors [16]. Detecting BC at an early stage is associated with improved outcomes for individuals undergoing treatment, as small, non-metastatic (early) diseases can be effectively managed, potentially leading to a 5-year survival rate increase. Employing BC screening measures is crucial for enhancing patient outcomes. Additionally,

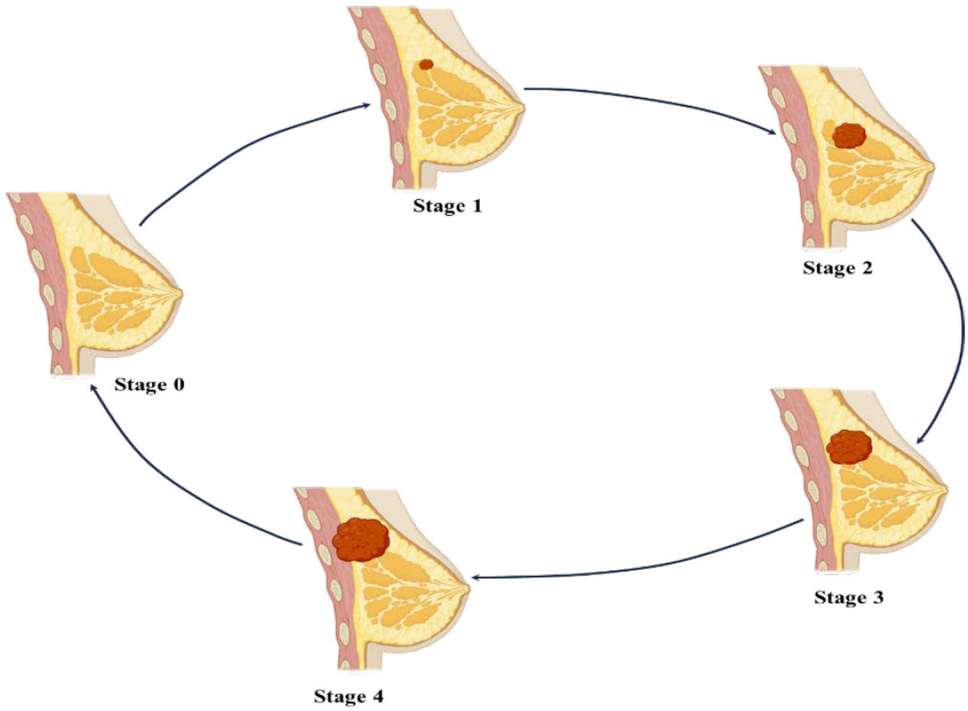

Fig. 1 The stages of breast cancer

early detection and treatment of BC contribute to an improved quality of life for women by enabling the use of less invasive surgical interventions [17].

Furthermore, the initial recognition and treatment of BC enhance the quality of life for women by facilitating the adoption of less invasive surgical interventions. After selecting adjuvant therapy, the subsequent challenge lies in identifying the most effective treatment or combination of therapies tailored to an individual patient. Prognostic biomarkers play a crucial role in resolving the initial challenge, while predictive biomarkers contribute to addressing the second. Key molecular markers such as HER-2, PRs and ERs and the Mib1/Ki-67 proliferation index are highly significant in the context of BC (BC) and undergo thorough validation in the routine care of both primary and recurrent, as well as metastatic BC patients [18]. Many sensitivity-enhancement procedures have been applied to date with a diverse range of NPs and nanomaterials to increase the threshold and precision of analyte detection in the production of innovative aptasensors [19]. The plasma of cancer patients harbors circulating cell-free DNA (cfDNA) derived from tumors. Assays are in the process of being developed to identify prevalent cancer mutations in cfDNA, spanning across various types of cancer. Pretreatment breast cfDNA was found with an 80% sensitivity and 97% specificity in individuals with localized illness. In the creation of cutting-edge Strong molecular tumor profiles and the disease's metabolic activity have been associated with increased levels of cfDNA in the breast. Breast cfDNA levels significantly decreased after receiving neoadjuvant therapy [20]. The process of diagnosing breast tumors frequently entails examining a number of characteristics in mammography pictures. One of the most prevalent markers is the existence of tiny calcium deposits known as microcalcifications. These microcalcifications could frequently be the only observable sign of a BC [21]. Yue Miao and Siyuan Tang developed a novel approach for mammography lump segmentation. The investigation into clinically high-risk BRCA1/2 mutant carriers demonstrated the sensitivity and specificity of genetic mutation locations with the use of mPCR-NGS sequencing. In comparison to conventional Sanger sequencing various methods for testing target sequences, the mPCR-NGS sequencing technology demonstrated benefits including ease of use, rapid processing times, and cost-effectiveness. [22]. Multiplex PCR-Nested Next-Generation Sequencing (mPCR-NGS) is a sophisticated genetic analysis method that merits in-depth exploration and contrast with the conventional Sanger sequencing approach. Several investigations have undertaken this comparison, shedding light on the advantages of mPCR-NGS. For instance, a study conducted by Li and colleagues in 2019 demonstrates the increased sensitivity and the ability to detect low-frequency mutations offered by mPCR-NGS when compared to Sanger sequencing. Additionally, research by Jones et al. in 2018 emphasizes the cost-effectiveness and the comprehensive mutation profiling capabilities of mPCR-NGS as opposed to Sanger sequencing. These studies underscore the benefits of using mPCR-NGS for genetic analysis [14, 15]. Biomarkers can be used to identify BC in both indirect and direct ways. Proteomics and gene expression profiling approaches are anticipated to become major cancer

diagnosis tools in the future. The most advanced frontier in biomarker development is centered around blood-based markers, with the potential to lead to early detection approaches in the form of proteins or RNA [23] (Fig. 2).

3.1 Recent developments in treatment of BC

The current approach to managing metastatic BC (MBC) centers on customizing the patient's care based on specific features of their BC, disease burden, including prognostic indicators and molecular subtype. Furthermore, their clinical history, which includes co-morbidities, prior treatments, and social circumstances, is taken into account. Targeted treatment with anti-angiogenic drugs exhibits clinical action, but the trade-off between effectiveness, toxicity, and cost is still up for dispute, highlighting the unmet need for a biomarker that can predict how well a patient would respond to this type of medication. Inhibitors of poly (ADP ribose) polymerase (PARP) seem to be therapeutically effective against BRCA germline mutant BC. It is yet unclear how PARP inhibitors act in various subsets of BC [24]. The targeting of the HER2 by Trastuzumab stands out as a highly effective instance of targeted treatment in metastatic MBC. For HER2-positive BC resistant to trastuzumab, the simultaneous and irreversible targeting of the HER2 receptor, similarly the suppression of downstream resistance mechanisms, looks to be promising. Targeted treatment with antiangiogenic drugs exhibits clinical action, but the trade-off between effectiveness, toxicity, and cost is still up for dispute, highlighting the unmet need for a biomarker that can predict how well a patient would respond to this type of medication [25]. The effective selection of patients for immunotherapy research and its integration into clinical practice may be shaped by the incorporation of various potential biomarkers and the evaluation of dynamic markers indicating early response or resistance [26]. The immune system has an intricate function in tumor detection and eradication, as well as progression. Inhibitors of checkpoints and chimeric antigen receptor T cell treatment have now been used in clinical settings, with impressive

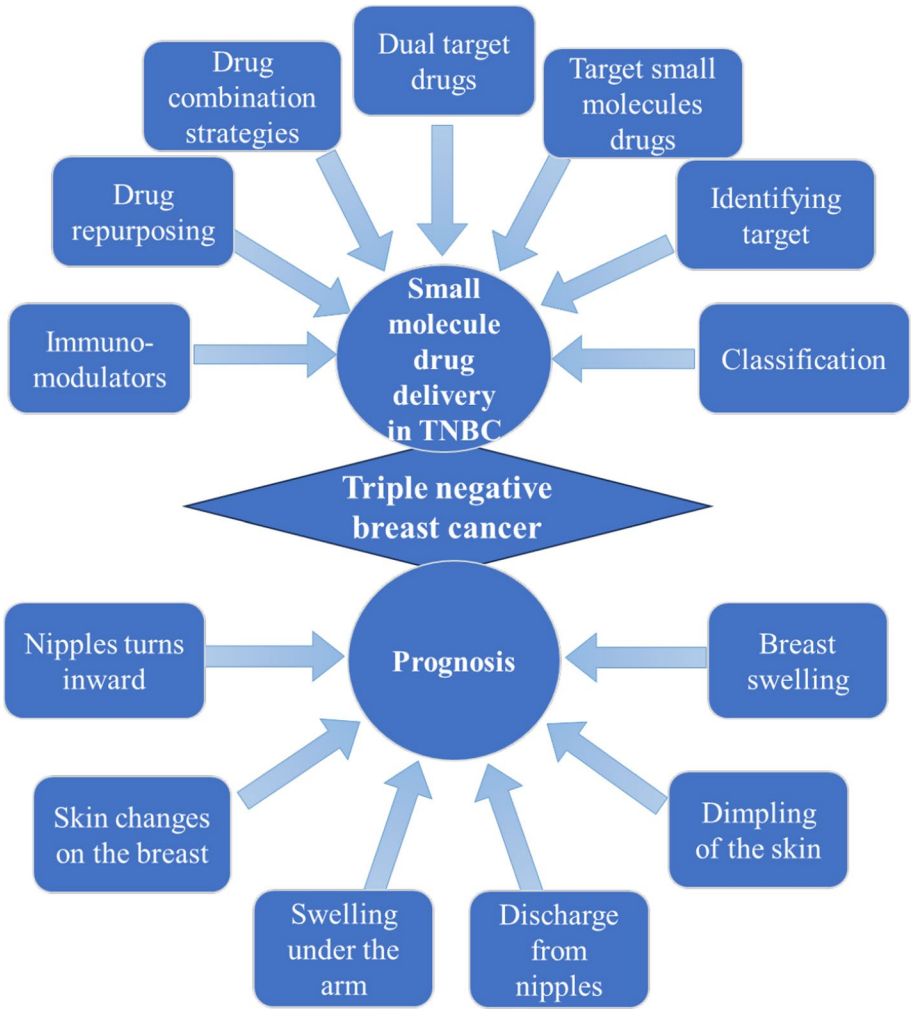

Fig. 2 Symptoms for prognosis and small molecule drug delivery process in Triple-negative breast cancer

and long-lasting clinical responses across a wide spectrum of tumor types [27]. To target and visualize metastatic BC, researchers have developed both macroscopic and microscopic NPs, classified in Fig. 3. In this context, these NPs must possess tumor-specific ligands to enhance the detectability of imaging modalities. It is possible to choose certain ligands for the identification of probable metastases with the right molecular profiling of tumor tissues [28]. Neoadjuvant chemotherapy may be given via combination treatments. In a phase II neoadjuvant research, docetaxel and epirubicin were used to examine the effectiveness and safety of treating individuals with inflammatory BC as well as those with operable, substantial, or regionally advanced (Stage III) BC. The trial's findings revealed a 76.7% observed response rate [29]. The most difficult BC subtype to treat is triple-negative BC (TNBC). Chemotherapy continues to be the gold standard of treatment since medicines that target particular molecular targets have only sometimes improved the outcomes of people with TNBC clinically meaningfully [30]. Pembrolizumab recently showed encouraging outcomes in early- stage TNBC, which may soon result in its approval in (neo) adjuvant settings [31]. Novel small-molecule medications designed to specifically target unique molecular characteristics of TNBC may offer a potential treatment for the disease.

There is still much work to be done to achieve perfection in the discovery of single-target drugs. Alternately, new developing approaches such medication repurposing, dual-targeting, and combination methods may offer fresh perspectives on how to enhance TNBC therapies as depicted in the Fig. 2 below [32–36].

3.2 Challenges with chemotherapy

Despite significant advancements in breast cancer treatment, achieving optimal therapeutic response remains challenging. Chemotherapy, often used alone or with other treatments like radiation or surgery, suffers from lack of specificity and multidrug resistance (MDR). This leads to reduced quality of life due to the need for frequent dosing. Common chemotherapeutic regimens face issues such as poor biodistribution, inadequate targeting, low bioavailability, high toxicity, and adverse effects. MDR development in breast cancer is linked to factors like ABC transporters, overexpression of P-glycoprotein (P-gp), MDR-associated protein (MRP1), breast cancer resistance protein (BCRP), microtubule alterations, enzyme changes, and p-53 gene mutations [107, 108]. Developing theranostic nanomedicines faces major challenges, including creating simple, controllable, and reproducible synthesis methods; achieving consistent batch-to-batch quality and high yields; understanding in vivo biochemical mechanisms, biodistribution, transformation, and metabolic pathways; and addressing chronic toxicity. Regulatory and safety guidelines also pose significant hurdles for market translation. Effective clinical application requires multidisciplinary expertise from pharmaceutical scientists, nanochemists, nanophysicists, nanotoxicologists, and clinicians to ensure safety and efficacy. The high heterogeneity of breast cancers complicates prognosis and treatment, highlighting the need for selectively targeting theranostic agents to cancer cells. Developing effective theranostic nanomedicine remains a complex endeavor [108]. The mTOR/PI3K/Akt pathway inhibitors, including pan-PI3K inhibitors buparlisib and pictilisib, target all PI3K isoforms but cause significant off-target effects. Clinical trials (BELLE-2, BELLE-3, BELLE-4, FERGI, PEGGY) showed modest improvements in progression-free survival (PFS) with buparlisib, but severe adverse effects were common. Pictilisib did not improve PFS and also caused severe side effects, leading to limited further research [109, 110]. mTORC1 inhibitors, such as everolimus, target

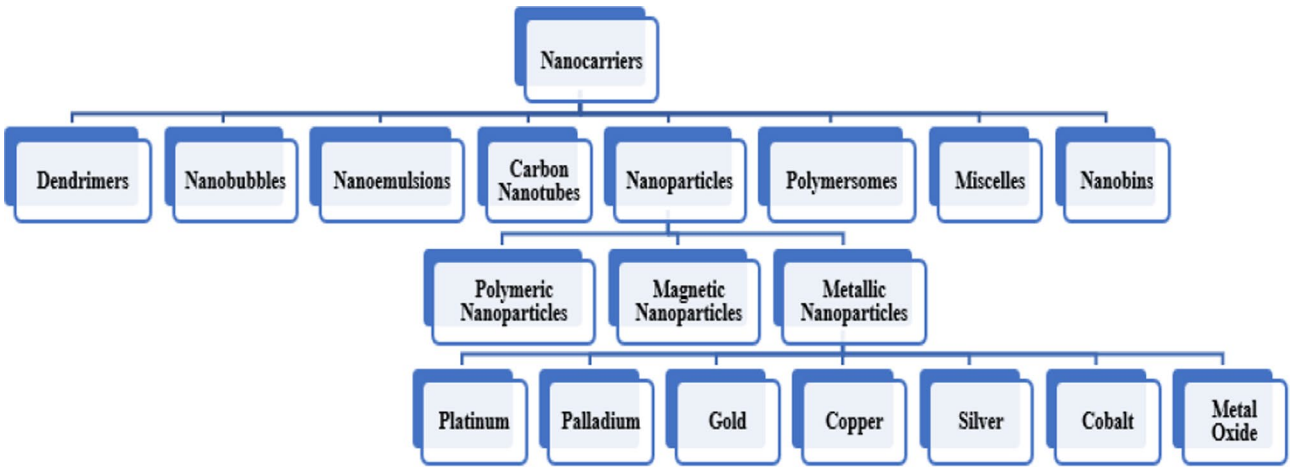

Fig. 3 Classification of nanocarriers

the mTORC1-dependent phosphorylation of s6k1. The BOLERO-2 phase III trial demonstrated that combining everolimus with exemestane improved progression-free survival (PFS) in AI-resistant ER + metastatic breast cancer (BC) patients. The TAMRAD phase II study showed that everolimus combined with tamoxifen improved overall survival (OS) in AI-resistant luminal A BC patients, leading to FDA approval of everolimus. Additionally, the PrE0102 phase II trial found that adding everolimus to fulvestrant enhanced PFS in patients with AI-resistant ER + BC compared to fulvestrant alone [111]. New tyrosine kinase inhibitors (TKIs), such as tucatinib and poziotinib, offer better efficacy and reduced toxicity in treating HER2 + metastatic breast cancer (BC). Tucatinib, highly selective for HER2, minimizes EGFR-related toxicities. A phase I trial showed its efficacy and tolerability in BC patients with HER2 + brain metastases. Tucatinib combined with TDM-1 demonstrated acceptable toxicity and antitumor activity in heavily pre-treated HER2 + metastatic BC patients. Approved by the FDA, tucatinib, when combined with trastuzumab and capecitabine, improved progression-free survival (PFS) and overall survival (OS) in advanced HER2 + metastatic BC, as shown in the phase II HER2CLIMB trial [112].

4 Treatment with nanocarriers

4.1 Dendrimers

Dendrimers represent promising drug delivery technologies capable of overcoming the limitations of current anticancer medications. They improve drug bioavailability, lessen the adverse effects of drugs, increase solubility of drugs, and address medication resistance. Dendrimers' sustained drug release characteristics in physiological conditions contribute to their low toxicity to healthy cells. Furthermore, under tumor settings, their fast drug release resulted in great cytotoxicity and absorption in BC cells [37]. The utilization of nanocarriers, specifically dendrimers, has showed promise as a strategy in drug delivery owing to their distinctive structural properties and versatile surface functionalities. Dendrimers, being highly branched macromolecules with precisely defined shapes and sizes, enable meticulous control over drug loading and release kinetics. These nanocarriers present several advantages, encompassing enhanced drug solubility, improved bioavailability, and targeted delivery to specific cells or tissues. The dendritic architecture of these nanocarriers enables the incorporation of various therapeutic agents, such as anticancer drugs, imaging agents, and gene therapeutics. Additionally, their modifiable surface chemistry allows for the attachment of ligands, facilitating targeted delivery and minimizing off-target effects. Notably, studies by Svenson and Tomalia have highlighted the potential of dendrimers in drug delivery, emphasizing their role in overcoming challenges associated with traditional drug formulations. Furthermore, the work of Wu et al. underscores the importance of dendrimers in enhancing the efficacy and safety of therapeutic agents, showcasing the significant strides made within the realm of nanomedicine through the application of dendrimer-based nanocarriers. The exploration of dendrimers as nanocarriers continues to evolve, indicating potential for innovative and potent solutions across various medical applications [38, 39]. Dendrimers, which are highly branched and well-defined large molecules, demonstrate distinct characteristics and potential applications across various domains. To grasp their fundamental principles, it is crucial to explore their structure and how they function. Recent research has revealed that dendrimers possess a tree-like design comprising a central core, branched arms, and functional end groups [40]. These nanoscale structures are painstakingly crafted, enabling precise manipulation of their size, shape, and surface attributes.

The functionality of dendrimers is multifaceted. They can enclose drugs or other substances within their interior, shielding them from degradation and improving delivery [41]. Moreover, thanks to their adjustable surface properties, dendrimers can target specific cells or tissues, making them highly promising for drug delivery applications [42]. The research delved into investigating the dynamics, pathways, and mechanisms of exocytosis in multidrug-resistant (MDR) cancer cells, focusing on polyamidoamine (PAMAM) dendrimers. Employing a multidrug-resistant human breast cancer cell model (MCF-7/ADR), researchers identified the potential for creating a surface-charged drug delivery system that targets tumors, exhibiting notable effectiveness in transfecting treatment-resistant cells. The administration of SiRNA-MVP or an inhibitor emerged as a strategy to reduce MVP-mediated nuclear efflux, thereby enhancing DNA transfection efficiency with PAMAM-NH2.

As a control, sensitive BC cells (MCF-7 cells) were used in comparative investigations. PAMAM-NH2 dendrimer intracellular transport, cellular uptake, and efflux were investigated in MDR BC cells (MCF-7/ADR cells). PAMAM-NH2 absorption rates from P-glycoprotein and MDR-associated protein were much lower in MCF-7/ADR cells, resulting in significantly increased exocytosis and lower endocytosis compared to MCF-7 cells. P-gp and MDR-associated protein were identified

as factors contributing to the observed differences in PAMAM-NH2 exocytosis and endocytosis between the two cell types, with macropinocytosis playing a more substantial role in subsequent cells.

In another study, NPs made of iron oxide (IONPs) were functionalized with fourth-generation (G4) PAMAM dendrimers and used to treat BC in BALB/c animals using magnetic hyperthermia. AMF exposure and incubation with G4@IONPs reduced the persistence of BC cells significantly, owing to apoptosis and an elevated Bax/Bcl-2 ratio. This study demonstrated that magnetic hyperthermia therapy reduced tumour angiogenesis and increased cancer cell apoptosis, both of which suppressed tumour growth [43]. Dendrimers, a group of highly branched polymers, can be meticulously designed to envelop both anti-cancer medications and targeting molecules, facilitating the precise delivery of drugs to cancerous regions. In 2018, a research conducted by Chauhan and collaborators demonstrates the enhanced capability of drug delivery systems based on dendrimers to selectively target tumors [44]. Dendrimers, with their highly branched structures, are advanced drug delivery systems that ensure precise drug loading, enhanced solubility, and targeted delivery. They improve drug bioavailability, reduce toxicity, and address drug resistance by rapidly releasing drugs in tumor settings, increasing cytotoxicity and absorption in cancer cells. Their benefits include drug encapsulation, modifiable surfaces for targeted delivery, and reduced off-target effects. Consequently, dendrimers enhance therapeutic outcomes and effectively treat multidrug-resistant cancer cells.

4.2 Nanoemulsion

Nanoemulsions comprise minuscule tiny particles of one liquid scattered in another medium that exhibit poor mixing tendencies, and their stability is maintained by surfactants or analogous molecules possessing both hydrophilic and hydrophobic properties. Nanoemulsions are highly adaptable and come with numerous benefits, such as improved solubility, bioavailability, and the stability of different substances.

The nanoemulsion structure comprises an oil phase that encapsulates lipophilic compounds, a water phase that solubilizes hydrophilic components in the continuous aqueous medium, and surfactants that encircle the oil droplets to inhibit coalescence. This arrangement operates by reducing droplet size to the nanometer scale, thereby increasing the surface area available for interaction with biological substrates. It enhances the solubility of hydrophobic substances within the oil phase, aiding in their delivery and promoting improved bioavailability through enhanced cellular uptake and absorption of the encapsulated contents. Additionally, surfactants serve a critical function in sustaining longer stability by inhibiting droplet aggregation, hence extending shelf life, as mentioned in references [45, 46]. In a previous investigation, researchers evaluated the antioxidative properties of a nanoemulsion containing elemene using Electron Spin Resonance (ESR) measurements and quantum mechanical simulations. To establish a mouse model for Triple-Negative Breast Cancer (TNBC), BalB/c mice were subcutaneously injected with the murine BC cell line 4T1 in the left fourth mammary fat pad. The therapeutic effectiveness of the elemene nanoemulsion on TNBC-infected mice was evaluated using various methods, such as immunohistochemical staining, Hematoxylin and Eosin (H&E) staining, Dihydroethidium (DHE) staining, and Western blot analysis. Due to its capacity to scavenge reactive oxygen species (ROS), the elemene nanoemulsion significantly inhibited the metastasis of BC cells to the liver and lungs. Consequently, their intervention prolonged the survival period of mice with TNBC [47]. Another study prepared an LAP-loaded nanoemulsion (NE- LAP) with the intention of testing its anticancer effectiveness. The nanoemulsion has been produced using a heated homogenization method, and its morphology was investigated using cryogenic transmission electron microscopy (cryo-TEM). The effective preparation and characterization of NE-LAP revealed the necessary characteristics to support intravenous delivery. The 30-day short-term potency of NE-LAP at 0.5 mg/mL was demonstrated, and drug release tests revealed an additional prolonged release profile. Studies on biodistribution and blood clearance support the hypothesis that longer blood circulation times result in preferential tumour absorption. These enhancements undoubtedly played a role in the increased antitumor activity seen for NE-LAP compared to LAP alone.Its positive performance, together with the lack of toxicity symptoms, encourages us to recommend NE-LAP as a successful cancer therapy method [48]. A folate-targeted nanoemulsion (FNEs) was generated employing high-pressure homogenization with a microfluidizer in a distinct research endeavor that used conventional nanoemulsion and integrated the notion of long-circulation targeting receptor mediation. This novel strategy has the potential to considerably improve the effectiveness of treatment of chemotherapy drugs used in cancer treatment, providing a useful reference for resolving the issue of chemotherapy's inadequate clinical efficacy [49]. In a separate study, researchers improved the composition of nanoemulsion to co-encapsulate paclitaxel and elacridar. The selected nanocarrier exhibited favorable qualities, as well as short-term stability, resulting in enhanced toxicity of paclitaxel. The presence of elacridar further enhanced this effect in both 3D and 2D models. Furthermore, elacridar demonstrated a reduction in the quantity of nanoemulsion needed to inhibit P-glycoprotein (P-gp) ATPase

function. The incorporation of hyaluronic acid (HA) in the modification of nanoemulsions extended the in vivo retention of rhodamine, which was integrated into NETri. These results suggest that the formulated nanoemulsion efficiently transports elacridar and paclitaxel to cancer cells, thereby augmenting the therapeutic effectiveness of paclitaxel, especially in triple-negative breast cancer cell lines. The significant application of the study lies in improving treatment outcomes for triple-negative BC, where therapy options are limited, offering new opportunities for research into novel therapeutic approaches for the condition [50]. Nanoemulsions, comprising extremely small droplets of oil dispersed in water or vice versa, can enhance drug solubility and stability. These tiny droplets have the ability to encapsulate medications and selectively target tumor tissues, thereby improving the precision of drug delivery. The research conducted by He and colleagues in 2020 underscores the promising prospects of nanoemulsions in the realm of targeted drug delivery [51]. In conclusion, nanoemulsions, with their ability to encapsulate drugs and enhance solubility and stability, offer significant advancements in targeted drug delivery. Their effectiveness in improving drug bioavailability, prolonging circulation times, and selectively targeting tumor tissues underscores their potential in cancer treatment. Research highlights their promising applications, particularly in treating challenging cancers like triple-negative breast cancer, marking a significant step forward in precision medicine. Lipid-based delivery platforms stood out among these nanocarriers as one of the best possibilities for cancer therapy because they enhanced the therapeutic efficacy and safety profile of encapsulated medicines. This research primarily focuses on discussing and elucidating the recent advancements in delivery systems designed for treating metastasis in BC. The emphasis is specifically on targeting prevalent metastatic locations in the bone, brain, and lungs. The work emphasizes the exceptional ability of liposomes and lipid-based NPs (LNPs) for delivery to cure BC metastases, outperforming systemic treatment [88]. Liposomes, nanoemulsions, solid lipid NPs (SLNs), nanostructured lipid nanocarriers (NLCs), and lipid-polymer hybrid NPs (LPH-NPs) have all been produced and intensively studied for cancer therapy [89]. Liposomes, for example, have therapeutic advantages over traditional methods and other NPs, such as higher stability, increased loading capacity, lower therapeutic dose and related toxicity, and decreased drug resistance. Moreover, LNPs overcome physiological barriers, leading to greater therapeutic accumulation at the targeted site.

The lipids utilized in LNP production, such as liposomes, nanoemulsions, SLNs, LPH-NPs and NLCs, were found to be non-toxic, biodegradable and biocompatible with minimal immunogenicity. Because of their capacity to form nanostructures, lipids have been widely researched as nanocarriers for cancer-targeted medication delivery systems. Furthermore, the drug delivery system can be improved by customizing the particle form, size, loading of drugs, trapping effectiveness and in in vitro release of drugs profile due to the physicochemical features of lipids [90].

However, the study also identified increased cytotoxicity and potential metastatic activity of lipid-based formulations against human breast cancer cells, suggesting significant promise for both pre-clinical and clinical applications. Another investigation emphasized the effectiveness of combining Artemether (ART) and docosahexaenoic acid (DHA) as a novel approach for breast cancer treatment. Additionally, the ART/DHA nanocarriers exhibited potential long-term effects on inhibiting colony formation and inducing apoptosis in MCF-7 cells, with minimal necrosis observed. Confocal microscopy and flow cytometry analyses illustrated the interaction of NE, NLC, and NC lipid nanocarriers with MDA-MB-231 and MCF-7 cells. These findings underscore ongoing research into the use of nanocarriers to address these challenges [91]. Researchers describe a novel class of hybrid nucleoside-lipid-based sorafenib-based NPs. Depending on the nucleoside-lipid charge, the solid lipid NPs (SLNs) displayed either positive or negative zeta potential values. Sorafenib-loaded SLNs revealed by transmission electron microscopy contained 200 nm parallelepiped NPs. Sorafenib-based SLNs show stronger anticancer characteristics than the free drug, according to studies on four distinct cell lines, comprising those from breast and liver cancers. These results highlight the potential of SLNs based on nucleoside-lipids as drug delivery vehicles. This is the first instance of a trial using sorafenib to treat luminal B breast tumors, and it demonstrates the efficacy of the SLN method. The facts provided here suggest that nucleoside-lipid-based SLNs could be employed as drug delivery platforms. The biocompatible nature of SLNs allows for the incorporation of a wide range of drugs and the treatment of numerous tumor types while overcoming cancer cells' resistance mechanisms. Moreover, SLNs are able to cross biological barriers and promote the cellular uptake of the medications via modulating passive, active, and co-transport processes [92].

To enhance the prolonged release and stability of drugs while utilizing non-toxic nanocarriers and improving bioavailability through pulmonary administration, a prior investigation aimed to formulate solid lipid NPs (SLNs) loaded with NRG (a poorly water-soluble medication). The selection of the optimal solid lipid matrix for SLN creation was initially determined using a group contribution technique. The NRG-SLNs were then synthesized via emulsification and low-temperature solidification, with an orthogonal experimental technique used for optimization. The findings suggest that SLNs are a viable pulmonary delivery method for increasing the bioavailability of water-insoluble medicines like NRG. The successful incorporation of NRG into SLNs by emulsification and low-temperature solidification was further

refined using a L9 (34) orthogonal design, demonstrating the promise of SLNs as a pulmonary delivery system for poorly water-soluble drugs such as NRG [93]. Therefore, Lipid-based nanocarriers, including liposomes, nanoemulsions, and solid lipid nanoparticles (SLNs), offer significant potential for enhancing cancer therapy, particularly in treating breast cancer metastasis. Their biocompatibility, ability to overcome physiological barriers, and improved drug stability and bioavailability highlight their effectiveness. Recent studies demonstrate their promise in pre-clinical and clinical applications, with SLNs showing potential for drug delivery, especially in pulmonary administration and treating resistant cancer types like luminal B breast tumors.

4.3 Carbon nanotubes

Carbon nanotubes (CNTs) are elongated carbon structures possessing extraordinary characteristics, and comprehending their fundamental principles is crucial. CNTs possess distinctive mechanical, electrical, and thermal properties due to their hexagonal lattice configuration. Single-walled carbon nanotubes (SWCNTs) are composed of a single layer of graphene rolled into a cylindrical shape, whereas multi-walled carbon nanotubes (MWCNTs) consist of multiple concentric layers. To exemplify the underlying principles and mechanisms, we can turn to recent research. For example, a study carried out by Liu et al. in 2021 provides insights into the growth processes of SWCNTs and MWCNTs, shedding light on catalytic mechanisms and the significance of catalyst NPs. Furthermore, the research conducted by Wang et al. in 2022 underscores the electronic structure and conductivity of CNTs, which are the foundations of their exceptional electrical characteristics [52, 53]. Through suitable functionalization, carbon nanotubes have been used as nanocarriers for carrying chemotherapeutic proteins, genes, and anticancer medicines. They've also been used as mediators for photothermal therapy (PTT) and photodynamic therapy (PDT) to directly kill cancer cells [54]. PTT, CNTs serve as agents that can be precisely directed to cancer cells and cause them to heat up when exposed to near-infrared light. This localized increase in temperature effectively harms and eliminates cancer cells. On the other hand, PDT involves the activation of photosensitizers, often connected to CNTs, using specific light wavelengths. This activation leads to the synthesis of reactive oxygen species, which can trigger cell death in targeted cancer cells. Recent research, exemplified by the work conducted by Yang et al. in 2021, underscores the promising potential of CNTs in PTT and PDT, highlighting their role as innovative approaches for treating cancer. In a previous study, a nanoconjugate made of SWCNT functionalized with carboxyl groups (SWCNT-COOH) and cisplatin (CDDP) was created in a prior study look into the possibility of blocking the PI3K/Akt signalling pathway. Inhibiting BC cell migration, downregulating PI3K/Akt signalling, and promoting cell death are all effects of CDDP conjugated with SWCNT-COOH that are highly potential and may help in the creation of new methods for the targeted treatment of BC that is both highly proliferative and metastatic. Conjugated single-walled carbon nanotubes (SWNT) are biocompatible, quickly excreted, and have little toxicity, making them potential for cancer-targeted accumulation.46 [54]. The focus of the study was to evaluate the developments in carbon nanotubes, particularly SWNT, for treating BC. Future tumour therapy with low drug doses may benefit from the great efficacy and minimal adverse effects of nanotube drug delivery systems. It demonstrates how we now understand the interaction between cells and their surroundings. CNTs, particularly SWNTs, have been shown to resemble the natural ECM, allowing cells to adhere to one another and influence gene expression. This field of study offers a brand-new approach to identifying and treating BC [55].

In a separate study, molecular dynamics simulations were utilized to explore the binding characteristics between SWNT and glycated chitosan. The radius of gyration, mean square displacement, radial distribution, and interaction energy function of the system comprised of SWNTs and glycated chitosan were investigated. Results from molecular dynamics simulations revealed a robust noncovalent association between glycated chitosan and SWNTs [56]. The fundamental goal of the research was to carefully select suitable SWNTs and GC polymers to build an efficient SWNT-GC for biomedical applications. The investigation focused on the SWNT-GC nanosystem's binding properties, considering SWNTs with diverse chiralities, diameters, and lengths, along with glycated chitosan of varying properties [56]. An experimental limitation encountered when investigating a functionalized SWNT system, particularly SWNT-GC, is the challenge of modifying the repeat unit (RU) length of the glycated chitosan (GC) polymer. DOX and paclitaxel PTX, two commonly used anticancer medications, have unique physicochemical characteristics and chemotherapeutic specificity. Initially, various SWCNT systems were simulated using all-atom molecular dynamics (MD) to study their interaction mechanisms, co-loading, and releasing processes from the SWCNTs. Subsequently, binding free energy calculations were performed using MM-PBSA. The results show that DOX and PTX co-loaded exothermically and spontaneously onto pure SWCNT.

Finally, the research reveals that simultaneous loading and subsequent release of DOX and PTX via functionalized SWCNT (f-SWCNT) is feasible [57].

In a previous study, a proposed dual-responsive smart carrier, sensitive to both pH and temperature, was composed of functionalized SWNT and single-walled carbon nanotubes grafted with dimethyl acrylamide-trimethyl chitosan (DMAA-TMC). Molecular simulations were employed to investigate the carrier's drug affinities and interaction energies with DOX and PAX. The carrier demonstrated selective and sensitive drug delivery for DOX and PAX in both healthy and malignant conditions, as evidenced by drug release and adsorption energy analysis. The interaction between DMAA-TMC, a biodegradable and biocompatible copolymer, and SWCNT revealed copolymer distortion during degradation in an acidic environment, promoting a smart release pathway in acidic cancerous tissues. This approach improved hydrophilicity, achieved an optimal nanoparticle size, and addressed concerns related to cell cytotoxicity [58].

In a separate investigation, MWCNTs were synthesized using lysine as a linker and functionalized with carbohydrate ligands. This method facilitated effective Dox delivery to BC cells through targeted mechanisms. MWCNTs, which are extended hollow cylindrical carbon nanotubes, have received interest in drug delivery since they have their expansive surface area and exceptional drug-loading capability. The use of lysine as a linker offers a low-cost method of functionalizing MWCNTs with carbohydrate ligands like galactose (GA), mannose (MA), and lactose (LA). Characterization techniques such as FT-IR, FE-SEM, Raman, XRD, and NMR were used to confirm the effective functionalization of MWCNTs loaded with Doxorubicin (Dox). Drug-loaded MWCNTs in BC cells underwent in vitro evaluation for drug loading, release, and cell toxicity. The findings revealed that carbohydrate-modified lysinated MWCNTs, specifically LyMWCNTs, exhibited a higher capacity for loading Dox compared to lysinated MWCNTs and carboxylated MWCNTs (COOHMWCNTs). Notably, LyMWCNTs displayed a sustained release profile of Dox, releasing more drug over 120 h at pH 5.0, indicative of their potential as candidates for targeted drug delivery in the tumor microenvironment [59]. CNTs exhibit distinct physicochemical characteristics that can be harnessed for drug delivery and imaging purposes. In the study conducted by Kostarelos and colleagues in 2018, they delve into the precise targeting of CNTs for treating tumors. Integrating these innovative therapeutic methods into your review paper will provide insight into their potential for targeted tumor therapy and the encouraging advancements in this field [60]. Hence, carbon nanotubes (CNTs), with their exceptional mechanical, electrical, and thermal properties, offer significant promise in drug delivery and cancer therapy. Their ability to be functionalized for targeted delivery, combined with advanced methods like photothermal and photodynamic therapies, enhances their effectiveness in treating cancer. Research highlights CNTs' potential in drug co-loading, smart drug delivery systems, and targeted therapy. These innovations demonstrate CNTs' capability to revolutionize cancer treatment and improve therapeutic outcomes through precise targeting and controlled release.

4.4 Nanoparticles

NPs, which are typically sized between 1 and 100 nm, possess unique characteristics at the nanoscale that have led to innovative approaches in the management of BC. These minuscule structures can be designed to transport and administer drugs with precision, offering several advantages. For example, drug delivery systems based on nanoparticles can enhance the ability to dissolve and remain stable of anticancer medications, extend their circulation in the body, and facilitate precisely targeted administration to cancerous tissue. This targeted drug delivery reduces unwanted adverse effects and boosts the functionality of BC treatments.

Recent research has underscored the potential of NPs in the context of BC therapy. For instance, in 2020, Wang et al. [61] explored the use of NPs to precisely transport chemotherapy drugs to BC cells, emphasizing the improved efficacy of the drugs and the reduction in side effects. Another investigation in 2021 by Guo et al. [62] delved into the utilization of NPs in photothermal therapy for BC, showcasing their efficiency in eradicating cancer cells. Traditionally, nanotechnology has been employed in cancer therapy to enhance the pharmacokinetics of chemotherapies and mitigate systemic toxicity. This is achieved by selectively targeting and delivering anticancer medicines to tumor tissues. Numerous studies utilize various types of NPs in conjunction with effective chemotherapy to treat various cancers, including BC. Previous research concentrated on targeting the epidermal growth factor receptor (EGFR) by conjugating bovine serum albumin (BSA) with cetuximab-valine-citrulline (vc)- DOX, enabling the targeted release of the medication specifically into tumor cells that overexpress EGFR. The results suggest that cetuximab-vc-DOX-loaded NPs present a viable strategy for targeted drug delivery, showcasing favorable tumor-targeting capabilities while minimizing toxicology at the systemic level. This research highlights the potential for therapy of cetuximab-vc-DOX-modified BSA NPs against EGFR-positive tumors [63].

An alternative and promising strategy for efficient chemotherapy involves combining a specific targeting antibody with an antitumor medication on a platform for NPs. By modifying BSA, for the controlled release and administration of

drugs, a stimuli-responsive system was created. The desolvation method was employed to effortlessly create DOX-loaded BSA NPs, which were further crosslinked using Schiff base bonds to yield pH-sensitive DOX-loaded systems (DOXs@BSA NPs). These resultant NPs demonstrated noteworthy drug loading capacity (21.4%), a size of approximately 130 nm, low polydispersity, and a strongly negative surface charge (−20.5 mV). Changes in size and charge observed after incubation at different pH levels provided evidence of the pH sensitivity of the DOXs@BSA NPs. The pH-sensitive characteristic of carbonate apatite (CA) particles allows for quick intracellular drug release, but they often exhibit heterogeneity and a tendency to self-aggregate [64]. In this study, the nano-carrier underwent modification through the partial substitution of Ca^{2+} with Mg^{2+} and Fe^{3+} in a foundational carbonate apatite (CA) framework, resulting in Fe/Mg-carbonate apatite (Fe/Mg-CA) NPs. These NPs demonstrated the ability to reduce self-aggregation, form a distinctive protein corona in the presence of serum, and effectively deliver the anti-cancer medication DOX into breast cancer (BC) cells. Fe/Mg-CA, predominantly forming a protein corona linked to transport proteins, may therefore serve as an effective BC therapeutic administration carrier. The nano-sized dimensions of both high and low Fe/Mg-CA NPs, together with their enhanced homogeneity and propensity to reduce self-aggregation, are noteworthy. This leads to enhanced drug binding, increased cytotoxic effect on cancer cells, and more effective cellular absorption of drug-loaded NPs. These findings align with protein corona analysis, demonstrating interactions between dysopsonins and DOX-loaded CA, low Fe/Mg-CA, and high Fe/Mg-CA NPs, extending their blood circulation times and preventing hepatic degradation of the drug cargo before reaching the tumor site. Fe/Mg-CA NPs, particularly those with high Fe/Mg ratios, show promise as a means of delivering anti-cancer medications, encompassing for the management of BC [65].

Another study used no toxic chemicals or chemical processes to create two new self-assembled NPs containing DOX. Although BC-DOX-NPs were made through BSA adsorption on the surface of BC-DOX-NPs, CS-DOX-NPs were created through interactions between positive and negative charges. In vitro, both formulations demonstrated improved dependability and long-term release, as well as excellent CD44 targeting and improved cell uptake. In a 4T1 mouse model, BC-DOX-NPs outperformed CS-DOX-NPs in terms of tumor-specific spread and invasion, resulting in increased antitumor effectiveness. It indicates the promise of BC-DOX-NPs for active targeted tumor therapy, and their ease of fabrication may make them more valuable for commercial applications [66].

In a recent study, the effective delivery of the anthracycline medication DOX into BC cells was successfully achieved using goose bone ash (GBA) as a pH-responsive carrier. Specifically, MCF-7 and MDA-MB-231 cells were targeted in this investigation. The characteristics of GBA, including size, shape, cellular internalization, functional groups, pH-responsive release of DOX, cytotoxicity, and analysis of the protein corona, were thoroughly examined in both its pure form and in suspension. The study revealed a dose-dependent increase in the binding affinity between DOX and GBA, indicating a heightened effectiveness with higher DOX concentrations. Notably, GBA particles exhibited no intrinsic toxicity, as evidenced by cell viability and cytotoxicity analyses. Qualitative and quantitative assessments of cellular absorption in two cell lines, MCF-7 and MDA-MB-231, indicated that the uptake of GBA-loaded DOX surpassed that of free DOX molecules. Furthermore, the findings suggested to this employing GBA as a carrier enhances cellular internalization and improves the effectiveness of drug binding. Importantly, in vitro cytotoxicity analysis confirmed the ability of DOX-loaded GBA particles to effectively halt the proliferation of BC cells, including MCF-7 and MDA-MB-231 cells. A key finding of the study highlighted the pH-responsive nature of GBA, releasing DOX under acidic conditions (endosomal/lysosomal pH: 6.5–5.5) while remaining stable at physiological pH (pH 7.5). This pH-responsive behavior contributes to the possibility of therapeutic efficacy of GBA in the targeted treatment of BC cells.

4.4.1 Polymeric nanoparticles

Several illness treatments have showed promise when using cell membrane as a surface covering. NPs with cell membrane coatings have improved immune-compatibility and longer circulation times. A targeted nano-therapy for combating cancer has been devised by employing NPs enveloped in human red blood cell (RBC) membranes, enhancing their targeting precision. The NPs consist of polymeric cores housing both chemotherapy agents and imaging substances. The naturally produced human RBC membranes have been modified with coupled targeting ligands to improve their targeting capabilities. The novel theranostic platform known as nature-inspired targeted polymeric nanoparticles (TT-RBC-NPs) coated on the membrane of red blood cells, demonstrates the ability to specifically adhere to cancer cells, facilitate the efficient delivery of doxorubicin (DOX), and enable visualization of targeted cancer cells, the use of epithelial cell adhesion molecule (EpCAM)-positive MCF-7 BC cells as a typical disease model exemplifies this point. The utilization of biomaterials characterized by low immunogenicity, exceptional biocompatibility, and drug delivery methods benefit from extended circulation durations as an excellent stealth barrier. evading immune system detection and generating

increasing interest in the field. The key characteristics and functioning of the membrane cells are more easily transferred to the core of the nanoparticle when they are coated with an RBC cell membrane [67].

In a recent study, the investigation of microRNA (miRNA, miR)-340-5p, LINC01094, and E2F transcription factor 3 (E2F3) expressions in BC tissues and cells utilized western blot and quantitative real-time polymerase chain reaction (qRT-PCR). LINC01094 was identified to modulate the miR-340-5p/E2F3 molecular axis, encouraging BC cell growth and progress cell cycle progression while suppressing apoptosis. Through its impact on the miR-340-5p/E2F3 molecular axis, LINC01094 facilitated cell cycle progression, stimulated BC cell proliferation, and hindered apoptosis. This study gives information that could be useful for early cancer detection, prognostication, and treatment using genes [68]. In another investigation, the functions of miR-16-5p and ANLN in BC were explored. The impact on various cellular processes, including proliferation, migration, invasion, cell cycle, and apoptosis, was evaluated through wound healing assays, MTT assays, flow cytometry, and transwell invasion assays, respectively. Results suggest that miR-16-5p modulates ANLN, suppressing migration, proliferation, and invasion while influencing the cell cycle and promoting apoptosis. These findings propose novel potential biomarkers for the detection and treatment of BC [69]. MicroRNA-135a-5p (miR-135a-5p) has been observed to influence the behavior of BC cells. In order to evaluate the expression levels of Bcl-2 Associated Athanogene (BAG3) and miR-135a-5p in BC tissues and cells, respectively, quantitative western blot and real-time PCR analyses were employed. The migration, proliferation, invasion, and cell cycle of BC cells were investigated using the cell counting kit-8 assay, wound healing and BrdU assay, flow cytometry, and transwell assay. In BC tissues, there was a noticeable increase in BAG3 expression and a corresponding decrease in miR-135a-5p expression. The impact of miR-135a-5p on the malignant characteristics of BC cells was nullified upon BAG3 overexpression. Elevated BAG3 expression activated the cell cycle, mTOR, and TGF-signaling pathways in BC cells. It was shown that miR-135a-5p regulates BAG3, As a result, BC's development, invasion, and advancement through the cell cycle are hampered [70].

4.4.2 Magnetic nanoparticles

Magnetic NPs have garnered significant attention as a promising means of delivering drugs precisely to cancer cells. They operate by responding to an external magnetic field. These NPs are often filled with chemotherapy drugs and, when subjected to a magnetic field, are directed to specific areas of interest, such as metastatic organs. Recent research, exemplified by Estelrich and colleagues in 2015, clarifies how magnetic NPs can be tailored to transport drugs and guide them to metastatic locations using magnetic fields. Once they arrive at the target, the NPs release their cargo, enabling localized drug delivery. This method reduces unintended side effects and increases the concentration of therapeutic agents at the tumor site, providing a more efficient and precisely targeted treatment approach. To demonstrate the efficacy of curcumin-naringenin loaded dextran-coated magnetic nanoparticles (CUR-NAR-D-MNPs) in tumor treatment, they were employed both as chemotherapy and in combination with radiation, which improved the effectiveness of cancer treatment. To determine how CUR- NAR-D-MNPs would work in conjunction with radiotherapy in the treatment of malignancies, they were created and put to the test in vitro and in vivo. With good biocompatibility, the nanomaterial can promote ROS, direct tumour cell death, and prevent tumour cell multiplication [71]. In a prior investigation, the safety and efficacy of novel nanoparticles facilitating the concurrent administration of DOX and curcumin for treating invasive B cell lymphoma were evaluated through in vitro and in vivo studies. The researchers utilized mPEG-b-P(Glu-co-Phe) polymer nanomaterials to co-deliver curcumin (CUR) and DOX, referred to as L-DOX + CUR. Using flow cytometry to quantify the DOX signal allowed researchers to assess the medicines' cellular penetration. Furthermore, confocal microscopy was used to directly view various cell enrichment locations. The study revealed that the high molecular weight mPEG-b-P(Glu-co-Phe) co-loaded with DOX and CUR demonstrated low toxicity and a strong anti-lymphoma effect. These findings support the utilization of polymeric NPs for delivering traditional chemotherapeutic agents, providing a conceptual basis for employing synergistic medications in lymphoma treatment [72]. To address a Balb/c mouse model of breast cancer, researchers developed a dual-function nanocomposite (NC) that integrates photodynamic therapy (PDT) and photothermal therapy (PTT). The nanostructure, silica coating, and immobilization of CUR on Fe3O4 NPs were confirmed using transmission electron microscopy, XRD FTIR, and UV–visible spectroscopy. In vivo experimentation with Fe3O4/SiO2-CUR in conjunction with PDT and PTT was conducted on a breast tumor mouse model. Immunohistochemistry (IHC) was utilized to evaluate the expression of apoptotic proteins Bax and Caspase3. Triple-negative breast cancer, chosen as the model for their study, is notably aggressive due to limited treatment options. Their findings indicate that the NC + PTT + PDT approach shows promise as an alternative to chemotherapy for treating triple-negative breast cancer.

These results suggest that this dual irradiation strategy could potentially replace current, more hazardous therapeutic treatments [73]. In another study, effective macrophage activation for anticancer immunotherapy has two main obstacles. Initially, cancer cells are shielded from phagocytosis by macrophages through the binding of signal regulatory protein alpha (SIRP) on macrophages to CD47, which serves as a "don't eat me" signal on cancer cells. Second, tumor-associated macrophages (TAMs) get polarised to a tumorigenic M2 phenotype by colony promoting substances released by cancer cells. Here, it is claimed that magnetic NPs with cell membrane coatings created through genetic engineering (gCM-MNs) can block both pathways. A combination of the MN core, which promotes M2 TAM repolarization, and the gCM shell, which has high affinity for SIRP variations, effectively inhibits CD47- The activation of the SIRP pathway has been observed to induce potent immune responses in macrophages [74, 75]. Using an approach consisting of membrane-based coating nanotechnology and genetic editing technologies to activate the immune system in the body for cancer immunotherapy has proven to be a dependable and efficient strategy. Sentinel lymph node biopsy (SLNB) is one of four major categories of magnetic NPs (MNPs) use in BC, medication delivery systems, magnetic hyperthermia, and imaging of primary and metastatic illnesses. There is increasing evidence supporting the application of MNPs in these areas, with emerging clinical uses, particularly in breast oncological surgery. MNPs have been employed through various methods, including imaging, medication administration, and magnetic hyperthermia, to detect nonpalpable lesions. These disciplines are still evolving rapidly. Yet, SLNB for BC and malignant melanoma is currently achieving the surgical uses of MNPs [76].

4.4.3 Metallic nanoparticles

4.4.3.1 Platinum Platinum NPs (PtNPs) were investigated for their potential as radiosensitizers in two BC cell lines, T47D and MDA-MB-231, which exhibit varying radiation sensitivities. Following PtNP ingestion, the NPs were localized in multivesicular bodies and lysosomes within the cells. Contrary to findings in a previous study involving cervical cancer HeLa cells under identical conditions, pre-exposure of T47D and MDA-MB-231 cells to PtNPs before radiation did not show any discernible enhancements in survival, mortality, clonogenicity, cell-cycle distribution, DNA double-strand breaks or oxidative stress. This underscores the substantial impact of cell type on the effectiveness of radio-enhancement by PtNPs. The study concludes that PtNPs exhibit a high degree of cell-dependent variability in their ability to enhance radiation effects, with no observable impact on the investigated BC cell lines. This research confirms how strongly cancer cells influence the success of combination therapies [79].

4.4.3.2 Palladium The use of an extract derived from a medicinal herb called Gloriosa superba tuber is presented in this study, which marks the first investigation into the anticancer properties associated with phytogenic PtNPs and palladium NPs (PdNPs) found in GSTE (Glorriosa superba tuber extract).The production of black dark and brown colors for PtNPs and PdNPs, respectively, as well as an increase in the highest intensity in the UV–visible spectrum, served as proof that the nanoparticle synthesis was completed in less than 5 h at 100 °C. These results support the efficacy of phytogenic manufacture of nanoscale platinum and palladium medications for the treatment and management of BC. Using G. superba tuber extract, monodispersed PtNPs and PdNPs were created, and they were reported to be consistently spherical and almost isodiametric. It was discovered that the synthesis was quick, effective, and safe for the environment. With regard to MCF-7 (human breast adenocarcinoma) cells, PtNPs and PdNPs both shown strong anticancer activity. The induction of apoptosis, which is characterised by phosphatidyl serine externalisation, membrane breakdown, and blebbing with chromosomal condensation, has been identified as the mechanism of cell death [80].

4.4.3.3 Gold Gold NPs (GNPs) have been employed to enhance the absorbed dose administered to malignant cells and sensitize them, with minimal impact on normal cells. Active targeting, specifically the conjugation of GNPs with the AS1411 aptamer (AS1411/GNPs), aims to achieve a targeted effect, increasing GNP uptake in tumor cells. The objective of this study was to explore the feasibility of cancer cells becoming radiosensitive exposed to 4 MeV electron beams using AS1411/GNPs. The AS1411 aptamer facilitated improved distribution of gold NPs within cancer cells, resulting in enhanced radiation-induced cancer cell death. Clonogenic assay results and Au cell uptake findings indicated that the AS1411 aptamer contributed to increased radiation-induced cell death by augmenting Au uptake. Notably, the enhanced sensitivity induced by AS1411 aptamer-conjugated GNPs rendered cells resembling cancer stem cells more responsive to 4 MeV electron beams. Gold NPs exhibit a unique capability to selectively target tumor cells over normal ones, referred to as active targeting. This selectivity can be attributed to several factors. To begin with, tumor cells tend

to display higher rates of cell division and increased blood vessel formation, resulting in leakier and more chaotic blood vessel structures. The effect of enhanced permeability and retention (EPR) in tumor blood vessels is the name given to this phenomenon, enables GNPs to accumulate more within the tumor's environment. Additionally, modifying the surface of GNPs by attaching targeting molecules like aptamers or antibodies can further improve their tumor cell affinity. These molecules enable the uptake of GNPs by cancerous cells by identifying particular markers that are overexpressed on the surface of cancer cells. For instance, research conducted by Li et al. in 2018 has demonstrated the potential of the AS1411 aptamer to increase GNP absorption by cancerous cells, leading to improved cell death when exposed to radiation. This active targeting approach leverages the unique features of tumor microenvironments and cancer cell surfaces to enhance the therapeutic effectiveness of GNPs while minimizing their impact on normal cells [81, 82].

4.4.3.4 Copper A safe, copper-depleting nanoparticle (CDN) that targets the mitochondria is created in a prior study and tested against triple-negative BC (TNBC). They demonstrate that CDNs trigger a metabolic switch to glycolysis, lower ATP synthesis, and decrease oxygen consumption and oxidative phosphorylation in TNBC cells. Apoptosis is brought on by this lack of energy, damaged mitochondrial membrane potential, and increased oxidative stress. In healthy mice, we show that CDNs are not harmful. The injection of CDN suppresses tumour growth and significantly increases survival in three mice models of TNBC. The effectiveness and safety of CDNs point to the potential clinical utility of this strategy.

4.4.3.5 Silver The purpose of this study was to see if silver NPs (AgNPs) could limit the metastatic capacity of BC cells by triggering epithelial-to-mesenchymal transition (EMT). Various methods, including the sulforhodamine B assay, wound healing test, measurement of reactive oxygen species (ROS) production, conventional cytofluorimetric analysis of the cell cycle, Western blot analysis for EMT marker proteins and MTA3 protein expression, calcium flux, and AgNPs' effects on MCF-7 cells were examined using histone deacetylase (HDAC) activity. In order to determine AgNPs' direct impact on mitochondria, the study also assessed how they affected the potential of the mitochondrial membrane. The results showed that MCF-7 cells were more mobile than control cells and that they were resistant to AgNPs' cytotoxic effects. Treatment with AgNPs led to increased ROS production, while no significant impact on the cell cycle was observed. Instead, it altered the expression of the MTA3 and EMT marker proteins. Results imply that AgNPs change BC cells' metabolism and activate a number of metastasis-related pathways by causing the production of reactive oxygen species [83, 84].

4.4.3.6 Cobalt Researchers have looked into the potential of magnetic NPs like cobalt ferrite (CFNPs) for cancer treatment in the context of clinical hyperthermia applications. These CFNPs include hydrophilic polyethylene oxide chains that operate as inhibitors for cobalt and iron precursors after thermal breakdown with the non-ionic surfactant Triton-X100. High-resolution transmission electron microscopy revealed monodispersed NPs measuring 10 nm in size. The study exposed triple-negative BC cells (TNBC) to microwaves when there is different CFNP doses (5 mg/mL to 40 mg/mL), resulting in enhanced cytotoxicity compared to CFNPs alone. To manufacture consistent CoFe2O4 NPs, a controlled thermal breakdown synthesis was used, where higher temperatures lowered oxygen solubility, resulting in a thinner oxide layer during synthesis and improved particle dependability [85].

4.4.3.7 Oxide Materials like zinc oxide (ZnO) and tin oxide (SnO2), known for their versatile physicochemical characteristics, offer promising solutions for addressing this challenge. Zinc oxide nanoparticles (ZnO NPs) show significant potential due to their adaptable properties. In contrast to pure ZnO NPs, the synthesis of reduced graphene oxide nanocomposites (SnO2-ZnO/rGO NCs) and SnO2-doped ZnO NPs has demonstrated enhanced anticancer activity and biocompatibility. SnO2-ZnO/rGO NCs exhibited superior biocompatibility and anticancer efficacy compared to SnO2-ZnO NPs and pure ZnO NPs. This study introduced a novel approach to enhancing the selectivity and anticancer properties of ZnO NPs. The hydrothermal synthesis method was employed to produce SnO2-ZnO/rGO NCs, ensuring the formation of hexagonal wurtzite ZnO in a single phase, as confirmed by XRD analysis. HRTEM and SEM mapping revealed uniform distribution of SnO2 and rGO within the ZnO NPs, showcasing high-quality lattice fringes without distortions. These findings suggest that modifying the physicochemical properties of ZnO could enhance its selectivity and anticancer effectiveness in human breast cancer cells [86]. The aim of this investigation was to enhance the efficacy of ZnO/ZrO_2/rGO nanocomposites (NCs) in combating cancer while preserving the integrity of healthy

cells. Various analytical techniques, TEM, scanning electron microscopy (SEM), photoluminescence (PL), dynamic light scattering (DLS), energy dispersive X-ray spectroscopy (EDS), and X-ray diffraction (XRD), were employed to validate the synthesis of pure ZnO NPs, ZnO/ZrO_2 NCs, and ZnO/ZrO_2/rGO NCs. XRD spectra revealed two distinctive sets of diffraction peaks for ZnO/ZrO_2/rGO NCs. Biologically, ZnO/ZrO_2/rGO NCs demonstrated approximately 3.5 times greater anticancer efficacy in human lung cancer (A549) and BC (MCF7) cells compared to ZnO NPs. A mechanistic investigation demonstrated that oxidative stress drove the anticancer response of ZnO/ZrO_2/rGO NCs, as evidenced by increased intracellular reactive oxygen species levels and decreased glutathione levels. According to the findings of this study, ZnO/ZrO_2/rGO NCs assisted by ginger extract could be a viable therapeutic agent for cancer treatment. [87].

In conclusion, nanoparticles represent a significant leap forward in breast cancer treatment, offering precise targeting and innovative drug delivery systems that enhance the efficacy of therapies while minimizing side effects. Through various nanoparticle-based approaches, such as polymeric, magnetic, and metallic NPs, the potential to improve chemotherapy, photothermal therapy, and immunotherapy is becoming increasingly evident. Metallic NPs, such as platinum, palladium, gold, copper, silver, cobalt, and oxide NPs, have been investigated for their potential in BC treatment. These NPs can enhance radiosensitivity, induce apoptosis, and target specific cancer cell markers.

4.4.4 Polymersomes

Researchers have developed a multifunctional nanovehicle to enhance drug delivery and cancer cell imaging, specifically for BC. This nanovehicle consists of gold nanorods combined with porous silicon NPs (composite NPs or cNPs), on a microfluidic system, double-emulsion templates were used to surround a hybrid polymersome. Administered intravenously in mice, the nanovehicle efficiently accumulates at the tumor site, demonstrating excellent capacity for loading for both hydrophilic and hydrophobic drugs. Notably, a triple-drug combination, delivered at total dosages of 5 and 2.5 mg/kg, reduces BCs by 94% and 87%, respectively. This research highlights the likelihood of the nanovehicle as a versatile drug delivery platform for combination therapy across various cancer types and biological targets associated with disease development [77]. In another study, researchers investigated the use of polymersomes as carriers for recoiling daughters of 225Ac, evaluating their therapeutic potential. Intravenous injection of 225Ac-containing vesicles in both healthy and tumor-bearing mice revealed the redistribution of free 213Bi in various organs. The study also examined the therapeutic efficacy of intratumorally injected 225Ac-containing vesicles, demonstrating no tumor-related fatalities in the treatment groups over 115 days. While 225Ac-containing polymersomes show promise for long-term tumor irradiation without considerable kidney damage, thorough analysis of the impact of daughter nuclides in localized alpha treatments is critical [78]. In conclusion, polymersomes demonstrate significant potential as versatile drug delivery vehicles for cancer treatment, particularly in breast cancer. Their ability to effectively deliver multiple drugs and radioactive isotopes while minimizing side effects highlights their promise for advancing combination therapies and localized tumor irradiation across various cancer types.

4.4.5 Micelles

In a previous investigation, researchers created a unique medication by linking a drug called DOX to a substance known as TPGS2000. This specialized medication, referred to as TPGS2000-DOX, exhibits enhanced effectiveness in treating tumors due to its ability to release the drug directly within the tumor, resulting in improved treatment outcomes, reduced adverse effects, and increased difficulty to establish medication resistance in tumor cells. To produce this unique medication, they established a robust chemical connection between DOX and TPGS2000. TPGS2000-DOX is encapsulated within minuscule particles referred to as micelles, which possess a remarkable capacity for locating and homing in on tumors. In experiments, these micelles demonstrated their capability to deliver the medication precisely to the tumor site. This novel approach to drug delivery using nano-sized particles has potential applications in both disease treatment and diagnosis. It holds particular promise for BC treatment due to its efficacy and selectivity in targeting BC cells [94].

The researchers utilized Pluronic F127 and Vitamin E TPGS to swiftly devise and evaluate a drug delivery approach for encapsulating resveratrol (res) and coumarin 6, yielding a fully soluble pharmaceutical formulation. The resulting

nanoparticle demonstrated effectiveness in selectively targeting invasive types of breast cancer (BC) while exhibiting low absorption by immortalized healthy epithelial cells. Additionally, the nanoparticle significantly reduced BC cell survival, with no observable adverse effects on immortalized breast cells. These findings suggest that the proposed nanoparticle could serve as a potentially beneficial platform for drug delivery to BC cells, catering to both diagnostic and therapeutic applications [95]. Recent research suggests that triple-negative BC treatment with HTPMs (Halofuginone hydrobromide-loaded TPGS PMs) has a great deal of clinical promise. The thin- film ultrasonic technique was successful in creating HTPMs. The improved HTPM demonstrated better suppression of TNBCs than free HF and PTX in addition to having a small size with restricted dispersion, superior stability, and prolonged release behaviour. Additionally, by destroying mitochondria and boosting ROS production, HTPM caused the death of BC cells. HTPM also showed good biocompatibility and significantly reduced in vivo tumour development in tumor-bearing animals.

The findings suggest that the use of thin-film hydration yielded successful creation of halofuginone (HF)-loaded TPGS polymeric micelles (HTPM), demonstrating promising therapeutic potential for triple-negative BCs (TNBCs) [96]. Intravenous administration of HTPM exhibited excellent anticancer effects on both subcutaneous xenografts and TNBC cells. Using subcutaneous and orthotopic mice models of TNBC, the study investigated the therapeutic effect and mechanism of oral HTPM alone and in conjunction with surgical therapy. In simulated gastrointestinal fluids, the as-prepared HTPM displayed excellent stability and sustained release behavior due to reduced diameters and uniform dispersion. TPGS polymeric micelles not only improved intestinal absorption by inhibiting P-gp efflux, but they also raised cellular permeability to HF substantially. When compared to HF, oral treatment of HTPM significantly reduced gastrointestinal toxicity in subcutaneous tumor animal models. Furthermore, gavage-administered HTPM substantially reduced TNBC lung metastasis and improved the therapeutic effectiveness of HF against remaining tissues in TNBC orthotopic xenografts after surgical resection. The findings underscore HTPM's potential as an oral anticancer therapy for TNBC [97].

The current study examined the cancer-preventing properties of an oral nanomicellar (NM) formulation of Honokiol against multiple TNBC cell lines in a separate study. The efficacy of the oral Honokiol NM formulation in reducing TNBC growth was proven by cytotoxicity, clonogenic activity, and wound healing assays. Studies on the permeability of Caco-2 in vitro revealed Honokiol was more readily absorbed. It proves that using a nanomicellar formulation is a better option than using other techniques when using anticancer substances like HNK. Their nanomicellar formulation methods open up new channels for therapeutic administration ways to enhance the efficacy of orally active, secure anticancer medications [98]. To increase docetaxel's effectiveness in treating triple-negative BC (TNBC), a novel delivery method was devised using RGD-modified PEGylated lipid-core micelles. The size, shape, zeta potential, encapsulation effectiveness, release kinetics, and targeted impacts of these micelles, which were created with TNBC tumors in mind were all carefully examined. Docetaxel-loaded nano-micelles were tested for anticancer activities in vitro using an MDA-MB-231 cell model and in vivo using an MDA-MB-231 xenograft model. The novel RGD-modified PEGylated Lipid-Core Micelle Delivery System greatly increased docetaxel's anticancer benefits while reducing its side effects. This technique shows promise as a potential therapy strategy for TNBC. To enhance the therapeutic effects of DTX on TNBC, they created a brand-new RGD-modified lipid micelle delivery method. RGD-DTX-straightforward M's preparation procedure made it possible to produce these formulations in large quantities. High encapsulation efficiency and qualities of long-term release in the produced RGD-DTX-M made it suitable for intravenous administration. According to the results of the pharmacokinetics study, RGD-DTX-M had a 3.2-times increased relative bioavailability when compared to DTX commercial injections, and it had a 5-times greater anticancer impact in mice with the MDA-MB-231 tumour. Its good safety was evidenced by preliminary safety results [99]. Hence, micelles show significant potential in targeted breast cancer therapy, particularly against triple-negative breast cancer (TNBC). Innovative formulations, such as TPGS2000-DOX, HTPM, and RGD-modified lipid-core micelles, enhance drug delivery, stability, and efficacy while minimizing side effects. These nano-sized carriers improve drug release at tumor sites, reduce resistance, and demonstrate promising therapeutic outcomes in both in vitro and in vivo models. The research highlights micelles as a promising platform for effective and safer cancer treatment.

4.4.6 Nanobubbles

The use of nanobubbles (NBs) that can target tumour cells in ultrasound (US) molecular imaging has enormous promise for more accurate diagnosis and treatment. However, the development of current targeted medicines is hampered by the absence of traditional biomarkers in TNBC. By capitalizing on the homotypic recognition of cancer cells, researchers

successfully created the inaugural nanobubbles (NBs) utilizing the triple-negative breast cancer (TNBC) tumor cell membrane, denoted as NBCCM. This tailored diagnostic agent exhibits specificity in interacting with cancer cells. A study sought to develop a microfluidic technique for producing NBCCM based on cell membranes' ability to self-assemble in aqueous liquids. Biomimetic bubbles enable for individualised treatment, which may provide the best possibilities for effective TNBC targeting when compared to traditional targeted UCA formulations. The cell membrane-based NBs demonstrated in this study, we feel, are only the initial stage of the fabrication of tailored UCAs with substantial oncological potential. This strategy could be employed for a variety of diagnostic and therapeutic objectives, including the development of tailored drug delivery systems, immunomodulatory medicines, and cancer vaccines [100]. Separate research is being conducted to see whether the "nanobubbles" created by lasers around NPs produce an immune response that can be utilized to treat cancer. A single 1064 nm nanosecond laser pulse induces micron-sized bubbles to form around gold nanorods in the cytoplasm of BC cells. Nanorod treatment and radiation caused cell death in some cells, but not in cells that had just been exposed to radiation. With simultaneous immunogenic cell death signalling and quick and highly specific tumour cell eradication, this treatment modality has promise as an immunotherapy combo approach. They discovered that nanosecond pulsed radiation from lasers provided a fast and highly focused strategy for eliminating tumor cells and activating immunogenic cell death markers. [41].

A prior article details the production of a DNA vaccine route of administration for the treatment of HER2 + BC utilizing particularly engineered chitosan-shelled nanobubbles (NBs). To make the NBs functional and target dendritic cells (DCs), anti-CD1a antibodies were added. The NB combinations are positively surface charged, have diameters of around 300 nm, and have good physical stability when stored at 4 °C for up to 6 months. This work successfully generated chitosan-coated NBs were loaded with DNA vaccine and delivered to DCs for the treatment of HER2-positive BC. With carefully regulated kinetics, this type of NBs can release DNA over an extended duration while loading it with good encapsulation efficiency. It displayed the ability to transfect DCs very specifically and activate them in both human and mouse cell lines [101]. Nanobubbles (NBs) offer promising advancements in cancer diagnosis and treatment, especially for TNBC and HER2 + breast cancer. They enable targeted imaging, personalized therapies, and potential immunotherapy approaches, highlighting their significant oncological potential for precise and effective treatment.

4.5 Nano bins

To enhance the fidelity of simulating the triple-negative BC (TNBC) tumor microenvironment in vitro, this recent study introduces a distinctive 3D co-culture spheroid model (3D TNBC). This model integrates color-coded murine tumor tissue analogs (TTA) by combining tumor cells, fibroblasts and endothelial cells. The implanted TTA in nude mice demonstrates heightened growth and rapid metastasis to distant locations, establishing a direct connection between in vitro and in vivo outcomes. This approach facilitates the assessment of both conventional and novel combined cancer nanotherapies [102]. Recent research indicates that stromal galectin-1 is more prevalent in clinical TNBC samples. Anginex-conjugated arsenic-cisplatin-loaded liposomes are being used to investigate stromal targeting of radiation-induced galectin-1. Employing a TNBC model with orthotopic tumors derived from 3D TTA, consisting of tumor cells, endothelial cells, and fibroblasts, the study demonstrates the prevention of tumor growth and metastasis through a multimodal nanotherapeutic strategy. The outcomes illustrate the utilization of therapeutically relevant radiation doses to facilitate concurrent receptor-mediated enhanced chemotherapeutic administration, while minimizing systemic toxicity [103–106]. The study presents a 3D TNBC spheroid model that simulates the tumor microenvironment, enhancing the evaluation of cancer therapies. It highlights the potential of stromal-targeted, multimodal nanotherapy to prevent tumor growth and metastasis while minimizing systemic toxicity in TNBC treatment.

4.6 Related toxicology

Nanoparticles can penetrate biological barriers, causing toxicity, primarily through oxidative stress and ROS release. Their shape, size, and charge are key toxicity factors. Surface modification or functionalization is a widely used strategy to reduce this toxicity, enhancing biocompatibility and altering protein binding and cytotoxicity. Effective, non-toxic functionalization is crucial for their safe biomedical application. The toxicity of carbon nanoparticles is influenced by their in vivo aggregation. Studies have shown that non-functionalized carbon nanotubes accumulate

in organs like the liver, lungs, and spleen, though no immediate toxicity was noted within the first 24 h. Research by Yang et al. found elevated serum markers indicating hepatic damage and oxidative stress in the liver and lungs. Additionally, Faczek et al. discovered that multi-walled carbon nanotubes (MWCNTs) form larger aggregates than single-walled carbon nanotubes (SWCNTs) [113]. The toxicity of carbon nanotubes depends on their purity, concentration, surface properties, and length, with single-walled carbon nanotubes (SWCNTs) preferred over multi-walled carbon nanotubes (MWCNTs) due to reduced aggregation and shorter lengths. Functionalizing SWCNTs can enhance their dispersibility in biological fluids, potentially reducing toxicity. In dendrimers, surface charge and terminal groups contribute to toxicity, with positively charged dendrimers causing cell lysis. Surface modifications like PEGylation can improve dendrimer biocompatibility and neutralize their charge [114]. Surface coating of metallic nanoparticles can reduce their toxicity, while quantum dots require secondary coatings to prevent the release of toxic metal ions and enhance biocompatibility. Choosing an effective coating agent is crucial, as a weak coating may degrade, exposing the metallic core and causing toxic effects. Additionally, nanoparticles' surface charge impacts their toxicity, making the charge of the coating agent important. Modifying nanoparticles with biological ligands can enhance target specificity and minimize non-target toxicity. However, ligand conjugation may still lead to off-target effects, as seen with transferrin or folic acid-coated nanoparticles, which can affect non-target organs like the pancreas, liver, and brain [115, 116]. The development and validation of methodologies to characterize various intrinsically defined characteristics and media-dependent external features of nanoparticles, as well as to describe their routes of exposure and various related hazards displayed by nanoparticles to environments and human health, have been given serious attention by regulatory and standardization authorities, such as the US-EPA, ISO, OECD, and FAA. To prevent false positives and negatives as well as misrepresentations of safety or toxicology data for the nanoparticle safety research, questions such as "which testing parameters are dependable for the identification of the possible health implications of nanoparticles" and "how the knowledge and comprehension can be translated in the context of regulatory requirements" need to be clarified [117]. In conclusion, as the field of nanotoxicology continues to evolve, REACH guidelines emphasize that risk evaluations for nanocarriers should adhere to the standards applied to conventional materials. The interaction of nanocarriers with biological cells is significantly influenced by their chemical and morphological properties. Therefore, understanding and assessing their toxicological effects through nanotoxicology is essential for ensuring their safety and efficacy [118]. (Table 1).

5 Conclusion and discussion

BC, especially TNBC, is becoming the focus of current research due to a lack of suitable TNBC therapy compared to other hormone-positive BCs. Researchers discovered that a thorough understanding of TNBC pathophysiology is the most important factor in producing better-functioning NPs. Tumor target-based techniques and controlled payload release are deemed essential for addressing any sort of malignancy. Polymeric nanocarriers stand out as a viable technique for TNBC therapy due to their physiochemical features and multifunctional nature. There are now combinations of chemotherapy with novel targeted drugs and molecular gene therapy that can help patients survive longer. To enhance clinical applicability in large populations, we know that innovative therapeutic techniques, such as molecular gene therapy, are necessary.

This review explores recent advancements in BC diagnosis and treatment, focusing on various nanocarriers such as dendrimers, carbon nanotubes, nanoemulsions, and different types of NPs like polymeric, magnetic NPs, metallic polymerase (such as palladium, platinum, copper, silver, gold, tin oxide, cobalt-doped), lipid-based nanocarriers, micelles, nanobins, and nanobubbles. NPs offer sophisticated and precise targeting of tumors, resulting in increased treatment effectiveness with reduced toxicity. These diverse nanoparticle formulations are currently utilized in therapeutic applications. Ongoing research efforts undertaken by scientists, healthcare professionals, and medical practitioners in the field of nanotechnology are continuously evolving, establishing a robust platform for NPs. In the foreseeable future, nanotechnology is poised not only to expand its role in cancer treatment but also to significantly enhance the landscape of medicine.

Table 1 Properties of Nanocarriers used in treatment of breast cancer

S.no	Nanocarriers	Application	Limitation
1	Dendrimers	There is a wide variety of dendrimers, each possessing biological properties such as multivalency, self-assembly, electrostatic interactions, chemical stability, low cytotoxicity, and solubility	Certain toxicity reduction approaches have been developed as a result of the toxicity of certain dendrimers, which limits their use in biomedicine and other treatments [119]
2	Nanoemulsion	Their small size gives them a large surface area per unit volume, which gives them useful properties such as robust stability, optically transparent appearance, and low production cost	They have less permeability and bioavailability of drug, low viscosity and spreadiblity, unpredictable absorption, and low oral bioavailability [120]
3	Carbon nanotubes	CNTs have high thermal conductivity and high aspect ratio electrical conductivity. CNTs are highly elastic, have very high tensile strength, high flexibility, and a low coefficient of thermal expansion	Due to very small size, it is difficult to work with them. Highly cost effective [55]
5	Polymeric NPs	It is easy to synthesize, inexpensive, biocompatible, biodegradable, non-immunogenic, non-toxic and water soluble	The accumulation of hazardous monomers, their leftover material, and the process of toxic degradation [121]
6	Magnetic nanoparticles	Electrons, holes, protons, and cations and anions	They cannot be condensed into a three-dimensional space [122]
7	Metallic Polymersome	Strong plasma absorption, enhanced Rayleigh scattering, surface-enhanced Raman scattering, determination of chemical information on nanoscale metallic substrates, and imaging of biological systems	Very susceptible to grinding conditions and susceptible to unwelcome milling medium and environment contamination [122]
9	Micelles	Particle size in the range of 5–100 nm	Poor physical stability in vivo, insufficient cellular contact of neutral micelles with malignant cells for absorption, and poor drug-loading efficiency [123]

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Declarations

Conflict of interest The authors declare no competing interests.

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