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Innovative Strategies and Challenges in Breast Cancer Therapy: Advances in Raloxifene, Curcumin, and Nanostructured Lipid Carriers

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ABSTRACT

In this narrative review, the authors discuss the emerging therapeutic applications of breast cancer with an emphasis on synergetic potential of raloxifene and curcumin, and use of nanostructured lipid carriers (NLCs) as novel drug delivery systems. Raloxifene with selective estrogen receptor modulator (SERM) activity and curcumin with polyphenolic compounds with anti-inflammatory, antioxidant, and anticancer effects possess good effectiveness in the case of hormone-sensitive breast cancer. They are however limited in their clinical application by low bioavailability, quick degradation and low absorption. NLCs used in combination of solid and liquid lipids provide an effective alternative since they stabilize the drugs as well as have the advantage of increasing absorption and specific tumor targeting. These carriers facilitate co-delivery of raloxifene and curcumin at low dose exposure and an increased therapeutic effect and reduced systemic toxicity. Using literature, this review also looks at breast cancer subtypes, their molecular characteristics and the inadequacy of the standard management like chemotherapy, radiotherapy and endocrine therapy. It covers the new focused treatment modality, e.g., PI3K/AKT/mTOR inhibitors, selective estrogen receptor degraders (SERDs), anti-HER2 therapies, and PARPI, particularly to aggressive forms of triple-negative breast cancer (TNBC). These approaches reveal the significance of individualized approaches of treatment with the inclusion of nanomedicine. In summation, this narrative review identifies the therapeutic potential of molecular targeting in combination with lipid-based nanocarriers to overcome the issue of resistance and enhance breast cancer treatments.

INTRODUCTION

Breast cancer has been the most common cancer in women in the world and still one of the causes of deaths to cancer. In 2020 alone there have been more than 2.3 million new cases and around 685,000 deaths throughout the entire world which shows the enormous load that this disease places on the health systems of society. (Jaman MS, *et al.,* 2018) The number of cases is increasing continuously, especially in low- and middle-income nations, because of urbanization, change of life, and late diagnosis. Breast cancer still represents almost a third of all female cancers regardless of the progress made in early detection and treatment. (Bhuiyan MRH, *et al.,* 2023) The existing treatment modalities, which include surgery, radiotherapy, chemotherapy, and endocrine therapy, have greatly increased the survival rate, particularly among the early-stage diagnosed patients. However, the modalities also face the problem of systemic toxicity, lack of specificity, drug resistance, and decreased the quality of life. (Sobuj DR, *et al.,* 2025) Specifically, chemoresistance and endocrine resistance are the factors that are associated with treatment failure and disease recurrence in numerous patients. In that regard, more efficient and less toxic treatment regimens are urgently needed. (Jaman MS, *et al.,* 2025) Breast cancer has been realized as a heterogeneous disease on a molecular scale. Depending on the status of the expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2), it consists of four principal subtypes: Luminal A, Luminal B, HER2-enriched, and triple-negative breast cancer (TNBC). Such molecular fingerprints play an important role in deciding treatment response and prognosis. Although endocrine agents can target hormone receptor-positive cancers, TNBC has aggressive response mechanisms, and they are unlikely to have specific targets, which involves significant challenges in treatment. (Maniruzzaman M *et al.,* 2025) In that regard, raloxifene, which is a selective estrogen receptor modulator (SERM), and curcumin, a plant polyphenol, have shown potential in breast cancer treatment. Raloxifene acts as an anti-estrogen in the breast by binding to the estrogen receptor and has such effects as it is effective in the case of hormone-sensitive cancers. (Jaman MS, *et al.,* 2023) Extensively studied because of their ant-inflammatory, antioxidant and pro-apoptotic activities, curcumin showed its anticancer activity in different models, including breast cancer. Nevertheless, the two agents face obstacles with regard to

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low bioavailability, low water solubility, and high rates of metabolism that limited their clinical usefulness. (Kashyap D, *et al.,* 2023) In line with these pharmacokinetic related issues, the introduction of nanostructured lipid carriers (NLCs) has come to the fore as an enhanced drug delivery platform. NLCs consist of solid and liquid lipid mixtures and these provide better drug encapsulation and extended release and greater entrapment of tumor tissue. NLCs can be used as a potential solution to administer more therapeutic benefits, resulting potentially in the overcoming of limitations of conventional administration, systemic toxicity reduction, and increased efficacy. This narrative review aims to First, to review the molecular and clinical aspects of breast cancer and focus on subtype-specific challenges relating to treatment. Second, evaluate the pharmacological mechanisms and limitations of raloxifene and curcumin as anticancer agents. (Jaman MS, *et al.,* 2023) Third, explore the design, advantages, and therapeutic utility of nanostructured lipid carriers (NLCs) for co-delivery of raloxifene and curcumin. Lastly, highlight the synergistic potential of integrating molecular targeting and nanotechnology to improve outcomes in breast cancer management. (Bhuiyan RH, *et al.,* 2022)

LITERATURE REVIEW

This narrative review summarizes the important literature on how current breast cancer treatments are limited and how raloxifene and curcumin may be used therapeutically through the use of nanostructured lipid carriers (NLCs). The manuscript has been organized to take the reader through the biological foundations of breast cancer, analyze the available traditional and new therapeutic modalities used in treating breast cancer and the justification and evidence of associating the delivery of these modalities to the use of novel nanocarrier based systems. An overview of the sections and their focal points is provided in Table 1.

Table 1: Overview of Review Sections and Key Themes

Section	Focus
Pathophysiology and Molecular Subtypes	Breast anatomy, ER/PR/HER2 status, clinical implications of subtypes
Conventional Therapies and Limitations	Surgery, chemotherapy, radiotherapy, endocrine therapy, and resistance
Raloxifene	Mechanism of action, clinical role in ER+ cancers, formulation challenges
Curcumin	Anti-cancer pathways, pharmacological limitations
Nanostructured Lipid Carriers (NLCs)	Design, delivery advantages, co-delivery rationale
Personalized and Targeted Therapy	NLCs' role in reducing toxicity and enhancing specificity
Conclusion	Synergistic potential, future directions

MATERIALS AND METHODS

This narrative review was conducted through focused searches on PubMed and Scopus up to June 2025, using keywords such as "breast cancer," "raloxifene," "curcumin," and "nanostructured lipid carriers." Included sources featured original research and relevant reviews that discussed preclinical or clinical findings related to the efficacy, pharmacology, formulation strategies, or delivery platforms involving raloxifene, curcumin, or NLCs. Many duplicate studies and non-English studies, backdated publications were eliminated from a total of 720 studies. The remaining titles and abstracts were checked and studies not relevant to the topics were excluded along with papers for which no full text could be accessed. The titles and abstracts of the remaining papers were examined and studies that were unrelated to the subject and publications for which there was no full text available were both eliminated. In total 64 studies matched our inclusion criteria and their findings are described in this review. However, the manuscript was organized topically—beginning with cancer biology and moving through conventional treatments, pharmacologic agents, and nanocarrier technology—to synthesize insights and identify translational gaps. Given its narrative nature, this review does not aim to be exhaustive or to perform quantitative synthesis; potential selection bias and study heterogeneity are acknowledged. We prepared the figures using Adobe Photoshop CS 13.0, and no additional AI-based tools were used for figure creation or data extraction. All figures were created by the authors based on their original ideas, and the relevant sources are properly cited in the manuscript.

RESULTS AND DISCUSSION

Breast Cancer: Pathophysiology And Subtypes

Breast cancer arises from the epithelial cells of the ducts and lobules in the mammary gland and is marked by uncontrolled proliferation, invasion, and potential metastasis. The normal breast is composed of glandular lobules, milk-carrying ducts, fibrous connective tissue, and adipose tissue, structurally supported by ligaments such as Cooper's ligaments. (Bonfill X, *et al.,* 2001) Malignant transformation involves genetic and epigenetic alterations that disrupt normal cell cycle regulation, leading to clonal expansion and tumor development (Doren A, *et al.,* 2018) A key determinant of breast cancer behavior and therapeutic response is its molecular subtype, classified based on immunohistochemical expression of estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor 2 (HER2). In addition to being prognostic, they have become therapeutic targets because these molecular markers guide the administration of endocrine or HER2-directed therapies Typically four major subtypes of breast cancers have been identified

based on the molecular classification of breast cancer namely Luminal A, Luminal B, HER2-enriched and triple-negative breast cancer (TNBC). (Sung H, etal 2021) All subtypes vary in the receptor profile, clinical aggressiveness, and response to treatment, which are summarized in Table 2.

Luminal A tumors represent the most common subtype and are associated with a relatively good prognosis due to their low proliferation rate and high sensitivity to endocrine therapy. Luminal B tumors, while also hormone receptor-positive, tend to grow more aggressively and may exhibit HER2 expression or high Ki-67, necessitating a combination of hormonal and cytotoxic treatments. HER2-enriched tumors overexpress the HER2 protein and are typically hormone receptor-negative. These cancers exhibit rapid growth and historically had poor

Table 2: Molecular Subtypes of Breast Cancer: Characteristics, Prognosis, and Therapy

Subtype	Receptor Status	Prognosis	Preferred Treatment	Reference
Luminal A	ER+, PR+, HER2-, low Ki-67	Favorable	Endocrine therapy (e.g., SERMs)	(Doren A, *et al.,* 2018)
Luminal B	ER+, PR+, HER2+ or -, high Ki-67	Intermediate	Endocrine therapy + chemotherapy	(Sung H, *et al.,* 2021)
HER2-Enriched	HER2+, ER-, PR-	Poor (without targeted therapy)	HER2-targeted agents + chemotherapy	(Parada H Jr, *et al.,* 2019)
Triple-Negative (TNBC)	ER-, PR-, HER2-	Very poor	Chemotherapy (limited targeted options)	(Gucalp A, *et al.,* 2019)

outcomes, but HER2-targeted therapies like trastuzumab and pertuzumab have significantly improved survival rates in this group. (Parada H Jr, *et al.,* 2019) Triple-negative breast cancer (TNBC), which lacks all three key receptors, presents the greatest clinical challenge. TNBC disproportionately affects younger women and is associated with high rates of recurrence, metastasis, and mortality. Lacking hormone and HER2 targets, TNBC is primarily treated with chemotherapy, but the response is often short-lived, and the five-year survival rate in metastatic cases remains low—around 12%. (Gucalp A, *et al.,* 2019) Understanding these molecular subtypes is essential not only for prognosis but also for tailoring therapies to maximize efficacy and minimize harm. However, aggressive subtypes like HER2-positive and TNBC continue to resist conventional treatments, driving interest in novel, targeted, and delivery-enhanced strategies.

Conventional Breast Cancer Therapies And Limitations

Breast cancer treatment has traditionally relied on a multimodal strategy that includes surgery, radiotherapy, chemotherapy, and endocrine therapy. These modalities have led to improved survival, particularly in early-stage disease, but are often constrained by toxicity, resistance, and lack of tumor specificity. (Azamjah N, *et al.,* 2019) Their limitations have prompted exploration of more targeted and less toxic alternatives, especially for aggressive subtypes and metastatic disease.

Surgery

Surgical resection remains the primary treatment for localized breast tumors. Depending on tumor size and spread, procedures may include breast-conserving surgery (lumpectomy) or mastectomy, often accompanied by sentinel lymph node biopsy or axillary dissection for staging. While surgery is potentially curative, it addresses only the primary tumor and is ineffective against micro metastases or systemic disease. (Roulot A, *et al.,* 2016)

Radiotherapy

Radiotherapy plays a crucial adjuvant role by targeting residual cancer cells in the breast, chest wall, or regional lymph nodes. It significantly reduces local recurrence and supports breast conservation approaches. However, radiation exposure to healthy tissues can cause long-term adverse effects such as fibrosis, cardiotoxicity, and lymphedema—particularly in left-sided tumors. (Prat A, *et al.,* 2015)

Chemotherapy

Chemotherapy remains a cornerstone of treatment for both early-stage and metastatic breast cancer. Agents such as taxanes, anthracyclines, and alkylating compounds disrupt DNA synthesis and cell division in rapidly proliferating cells. (Perou CM, *et al.,* 2000) Despite its broad efficacy, chemotherapy is associated with severe side effects including myelosuppression, neuropathy, alopecia, and gastrointestinal toxicity. Moreover, intrinsic or acquired resistance mechanisms—such as drug efflux pumps, apoptosis evasion, and DNA repair activation—can render chemotherapy ineffective over time. (McCart Reed AE, *et al.,* 2021)

Endocrine Therapy

For hormone receptor-positive tumors, endocrine therapy offers a less toxic and highly targeted alternative. Drugs such as tamoxifen, raloxifene, aromatase inhibitors, and SERDs inhibit estrogen signaling or reduce systemic estrogen levels. (Roux P, *et al.,* 2019) However, resistance may develop due to mutations in the estrogen receptor (e.g., ESR1), cross-talk with other growth pathways (e.g., PI3K/AKT/mTOR), or epigenetic alterations. (Cserni G. 2020)

Quality Of Life And Unmet Needs

The physical and psychological burden of conventional therapies—including fatigue, organ toxicity, immune suppression, and long-term endocrine effects often compromises patient quality of life. These challenges are magnified in metastatic or aggressive subtypes, where treatments fail to provide durable control. As summarized in Table 3, each modality has specific advantages but also significant limitations, which underline the critical need for innovative therapeutic approaches that enhance specificity, minimize toxicity, and overcome resistance.

Raloxifene: Mechanistic And Clinical Perspectives.

Mechanism of Estrogen Receptor Modulation

Raloxifene is a second-generation selective estrogen receptor modulator (SERM) that acts as an estrogen antagonist in breast tissue while maintaining agonistic effects in bone and cardiovascular systems. This is shown in Table 1, (Amir E, *et al.,* 2010) It binds competitively to estrogen receptors (ER), thereby inhibiting the transcription of estrogen-responsive genes associated with cellular proliferation and survival. (Baines CJ. 1992) This mechanism effectively halts the estrogen-driven growth of hormone receptor-positive breast cancer cells.

Table 2: Conventional Breast Cancer Treatments: Mechanisms, Benefits, and Limitations

Therapy	Mechanism	Advantages	Limitations	Reference
Surgery	Tumor excision	Curative in localized cases	Ineffective for systemic/metastatic disease	(Roulot A, *et al.,* 2016)
Radiotherapy	DNA damage via ionizing radiation	Reduces recurrence; breast conservation	Cardiopulmonary toxicity; lymphedema	(Prat A, *et al.,* 2015)
Chemotherapy	Cytotoxic effects on dividing cells	Broad efficacy across subtypes	Myelosuppression, resistance, systemic side effects	(Perou CM, *et al.,* 2000 & McCart Reed AE, *et al.,* 2021)
Endocrine Therapy	Blocks or reduces estrogen signaling	Targeted and less toxic	Only effective in ER/PR+ tumors; endocrine resistance	(Cserni G. 2020)

Clinical Uses In Er+ Breast Cancer And Chemoprevention

Initially approved for the prevention and treatment of postmenopausal osteoporosis, raloxifene demonstrated secondary benefits in reducing the risk of invasive breast cancer, particularly in ER-positive subtypes. (Menta A, *et al.,* 2018) It has since been recognized for its role in breast cancer chemoprevention among high-risk postmenopausal women. Raloxifene is especially useful in patients who are intolerant to tamoxifen, offering a comparable risk-reduction profile with a lower incidence of endometrial cancer and thromboembolic events. (McDonald S, *et al.,* 2004)

Limitations: Solubility, Bioavailability, And Target Restriction

Although clinically advantageous, raloxifene has many pharmacokinetic disadvantages. Due to its low aqueous solubility, its first-pass hepatic clearance is remarkable, which restricts oral measurable availability and systemic exposure as well as efficacy. (Mann RM, *et al.,* 2019) Since raloxifene is a SERM, it is also limited to the ER-positive tumors and cannot target receptor-negative or triple-negative cancers, which lack the target within the molecule that would be targeted by the pharmaceutical. (Nielsen S, *et al.,* 2023)

Rationale For Nanocarrier-Based Reformulation

To address these shortcomings, investigators have tested the potential of encapsulating raloxifene in nanostructured lipid carriers (NLCs) as a drug delivery system that will increase solubility, protect drugs against metabolism, and induce tumor specificity. (Kerlikowske K, *et al.,* 1998) NLCs can help achieve sustained release and enhance tissue penetration and provide a reliable re-formulation approach to enhance bioavailability and increase the use of raloxifene in the context of combination therapies to overcome its limitations of use in only hormone-sensitive tumors.

Curcumin: A Phytochemical With Anticancer Promise

Biological Properties: Antioxidant, Anti-Inflammatory, Antiproliferative

Curcumin, a phenolic compound collected in Curcuma longa (turmeric) rhizomes, is increasingly gaining attention in scientific communities due to its complex biologic action, among which are the anticancer, antimicrobial, antioxidant and anti-inflammatory trends. (Radovic N, *et al.,* 2019) Curcumin has been used to coordinate cancer hallmarks, which entail cell proliferation, programmed cell death, proliferation rate, angiogenesis, and metastasis, but not normal cells, in therapeutic oncology. (Pediconi F, *et al.,* 2018)

Molecular Targets In Breast Cancer Cells

Curcumin has multiple molecular actions in exerting antiproliferative effects especially in breast cancer. It plays an inhibitory role by inhibiting nuclear factor kappa B (NF-kB) activation, reduction in the expression level of cyclin D1, inhibiting matrix metalloproteinases (MMPs)

and altering the epidermal growth factor receptor signaling (EGFR). These signaling pathways lead to the arrest of tumor cells in their cell cycle, induction of apoptosis, prevention of invasion and metastasis. In addition, curcumin has also been reported to make breast cancer sensitive to appreciating agents, which leads to its prospects as an adjuvant therapy. (Gradishar WJ, *et al.,* 2022)

Bioavailability Constraints And Instability

Nevertheless, curcumin has a high bioactivity in vitro; however, its clinical translation has not been realized because of poor gastrointestinal absorption, low water solubility, rapid metabolism, and clearance. (Kerr AJ, *et al.,* 2022 & Shien T, *et al.,* 2020) The pharmacokinetic disadvantages lead to subtherapeutic plasma levels post oral administration thus severely restricting it's in vivo anticancer efficacy. In addition, the curcumin is poorly soluble chemically in neutral or alkaline conditions, thereby making less absorbable in the body. (Wang L, *et al.,* 2016 & Lostumbo L, *et al.,* 2004)

Need For Drug Delivery Enhancement

Current studies on drug delivery attempt to counter the therapeutic downfalls of curcumin by testing platforms based on nanotechnology to enhance curcumin solvency, curb degradation, and allow selective and slow release. The nanostructured lipid carrier (NLC) platform, specifically, has such potential because there is a prospect of encapsulating hydrophobic drugs in lipid matrices without ruining the structural integrity of curcumin. (Wang X, *et al.,* 2018 & Tang L, *et al.,* 2018) Curcumin-containing NLC formulations are one of the cornerstone developments in taking curcumin to clinical use in treatment of breast-cancer.

Nanostructured Lipid Carriers (NLCs): A Modern Drug Delivery Approach

Composition And Design Principles Of Nlcs

Nano-structured lipid carriers (NLCs) represent the second generation of a nano-delivery system based on the second-generation lipid nano-delivery system, described as solid- liquid matrices and formed by dispersing a blend of lipids in an aqueous medium stabilized using emulsifying surfactants. The benefits of this hybrid matrix structure model are a high encapsulation level, high physical stress, and tunable and controlled drug release. (Kirby AM. 2018 & Bartelink H, *et al.,* 2007) NLCs delay the crystallization process and create structural imperfections by including liquid lipid regions within a solid lipid structure, and are able to encapsulate greater quantities of therapeutic materials than regular solid lipid nanoparticles (SLNs). (Overgaard M, *et al.,* 2022)

Advantages Over Conventional Nanocarriers (E.g., SLNs, Liposomes)

In comparison to other traditional-based nanoparticles such as SLNs and liposomes, NLCs have better drug-entrapment ability, improved structural stability, prolonged shelf life, and outstanding in vivo characteristics. The problem that has been frequently encountered with SLNs includes the issue of low drug loading because of their hard crystalline nature and threat of expulsion of drugs during storage. (Whelan TJ, *et al.,* 2015) Although liposomes are quite successful in encapsulating hydrophilic agents, they can be affected by the stability and scalability restraints. On the contrary, NLCs enhance the bioavailability of drugs with a poor water-solubility profile, shields labile drug agents against enzymatic degradation processes, and enhancing sustained release of the therapeutic agent at the tumor location. (Davis-Turak J, *et al.,* 2017 & Rana MRR, *et al.,* 2024)

Dual-Drug Encapsulation: Synergistic Delivery Of Raloxifene And Curcumin

It is hypothesized that the physicochemical malleability of NLCs promotes the ability to co-deliver several other therapeutic agents, like raloxifene and curcumin. The ability of these two drugs to synergistically act against cancer can be achieved with this dual encapsulation method, as both drugs could be released into tumor tissues at the same time, where they can be effectively used together to treating cancer cells. (Al-Hilli Z, *et al.,* 2021 & Maniruzzaman M, *et al.,* 2025 & Sun YS, *et al.,* 2017) Co-delivery will improve the drug ratios at the tumor and also delinked the drug levels in the system and might increase efficacy and minimize resistance.

Preclinical Evidence of NLC Efficacy In Breast Cancer Models

The raloxifene and curcumin loaded NLCs showed better cytotoxicity and selective delivery in cancer cells lines and animal models due to raloxifene and curcumin as per the preclinical research. (Maniruzzaman, M., *et al.,* 2025 & Debien V, *et al.,* 2023) These conjugations resulted in strong intracellular levels, a leveled circulation time and increased tumor uptake. Notably, NLC-based delivery has high systemic toxicity when compared to free drugs, a point that is likely to advance its translational potential. These findings promote the prospect of NLCs as a sophisticated system of personalized and combinational cancer care in future. (Jaman MS, *et al.,* 2018 & Husinka L, *et al.,* 2020 & Ye F, *et al.,* 2023)

Toward Personalized And Targeted Breast Cancer Therapy

Breast cancer is highly heterogeneous, which constitutes a major obstacle to the success of therapy, especially when it comes to some aggressive subtypes, including triple-negative breast cancer (TNBC) and HER2-positive ones. (Dieci MV, *et al.,* 2019 & Jaman MS. 2025) One of the most serious issues in the prospective treatment regimens is the drug resistance, both innate and acquired one. Cancer cells also find ways to escape the cytotoxic effects of chemotherapies and endocrine-based therapy by overexpressing the efflux pumps, altering drug target

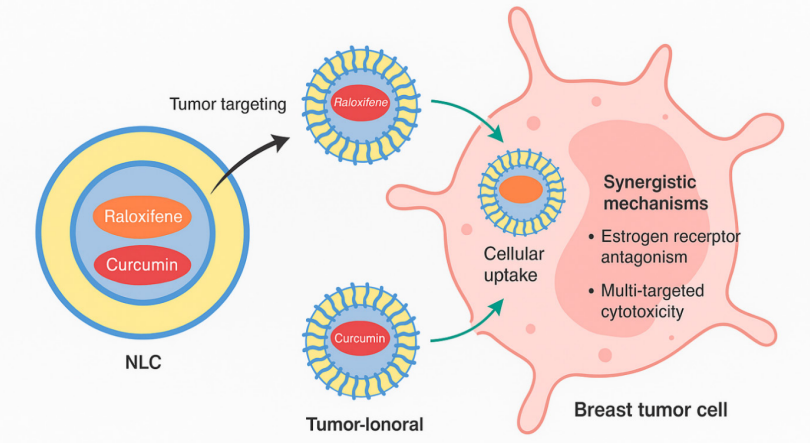

Figure 1: Schematic Representation of NLC-Mediated Co-delivery of Raloxifene and Curcumin to Breast Tumor Cells

sites, or producing survival signaling (e.g., PI3K/AKT/mTOR). (Maniruzzaman M, *et al.,* 2025 & Wu YT, *et al.,* 2018) At the same time, off-target toxicity reduces the maximum tolerable concentration of chemotherapeutic agents that may conditionally interrupt the efficacy of treatment and even the quality of life of patients. (Jaman MS, *et al.,* 2024 & Korde LA, *et al.,* 2021 & Alam S, *et al.,* 2017) To overcome these shortfalls, nanostructured lipid carriers (NLCs) are a revolutionary solution providing specificity and a decrease in systemic toxicity of the drug. NLCs design using lipid enables them to flock to tumor tissues through the enhanced permeability and retention (EPR) effect, hence reducing NLC accumulation in healthy cells. (Song D, *et al.,* 2024 & Sobuj DR, *et al.,* 2025) This targeted release, apart from raising the local concentration of the therapy agents like raloxifene and curcumin, it can also lead to controlled and sustained drug release with minimal and infrequent side effects. Furthermore, NLCs facilitate the combination therapy, which helps to deliver more than one drug using the same platform. This approach can enable synergistic activity at the tumor level, which will aid in evading resistance measures and expand therapeutic window. The rationale of co-encapsulating both raloxifene and curcumin in NLCs lies in the provision of two modes of action, which inhibit cell signaling through estrogen receptors and cancerous signaling cascades. (Andre F, *et al.,* 2022) NLCs possess a great potential to be included in the precision oncology model in the future. Through optimized individualization of drug combination and dosing schedules to the tumors themselves, NLC-based systems could promote personalized therapy paradigm. Preclinical accomplishments propose a well-marked way to clinical improvement, but more studies regarding the feasibility of expanding the capability of a particular infection are necessary. (Jaman MS, *et al.,* 2026)

Future Perspectives

In spite of efforts made on diagnostic and therapeutic strategies, breast cancer has been a challenging disease in terms of increased incidence, resistance to treatments, as well as the severe toxicity of conventional methods of treatment. Surgery, radiotherapy, chemotherapy, and endocrine agents are conventional treatments, but especially in pathologically aggressive forms like TNBC, their survival contribution dictates the need to find alternatives, better, more effective, and non-toxic. (Abasher, M. M., *et al.,* 2023) In that regard raloxifene and curcumin have come up as potential agents to treat hormone responsive and more widespread breast cancer therapy. Raloxifene delivers selective estrogen receptor modulation; curcumin has proven to have a multi-faceted anticancer action along both inflammatory and proliferative routes. Their combination does provide the likelihood of a synergistic effect especially made to surpass the pharmacokinetic challenges of poor solvency and low bioavailability. Nanostructured lipid carriers (NLCs) provide an attractive means of addressing these issues in delivery as it would lead to improvements in drug stability as well as tumor specific targeting, and would facilitate controlled and dual-drug delivery. The synergetic co-delivery of raloxifene and curcumin not only enables them to reveal their full therapeutic potential. There is also a decreased systemic toxicity. As the NLC-based strategies become integrated into clinical workflows, particularly as part of the personalized and precision oncology, their overall transformative potential should be discussed. (Shinnwai, A. E. 2024) Further preclinical confirmation and clinical trials should be done with proper design to provide safety, scalability, and long-term advantages. The utilization of this platform has the potential to improve the quality of care in breast cancer treatment to a vast extent.

CONCLUSION

In summary, the synergistic co-delivery of raloxifene and curcumin via nanostructured lipid carriers represents a mechanistically sophisticated strategy capable of overcoming traditional pharmacokinetic barriers while simultaneously amplifying multi-pathway anticancer efficacy. By integrating selective estrogen receptor modulation with broad-spectrum anti-inflammatory and antiproliferative signaling interference, this dual-drug nanoplatform holds the potential to attenuate tumor

progression with reduced systemic toxicity, particularly in aggressive subtypes such as TNBC. As NLC-based therapeutics continue to advance toward clinical translation, rigorously designed preclinical and clinical studies will be essential to validate their safety, scalability, and long-term therapeutic benefit within the evolving framework of precision oncology.

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