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Research Article

Design and Synthesis of Biodegradable Polymeric Nanoparticles for Targeted Delivery of Chemotherapeutics in Triple-Negative Breast Cancer

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ABSTRACT

Type three breast cancer (TNBC) is a highly aggressive form of breast cancer that lacks targeted therapies, leading to poor prognosis and limited therapeutic options The development of biodegradable polymeric nanoparticles (NPs) provides find a promising strategy for targeted delivery of chemotherapeutic drugs to reduce systemic toxicity , enhancing therapeutic efficacy This review focuses on the design and synthesis of biodegradable polymeric nanoparticles for targeted delivery of chemotherapeutic agents in TNBC. Polymeric nanoparticles were synthesized from biocompatible and biodegradable materials, ensuring safe degradation and excretion from the body. Nanoparticles are engineered to encapsulate and release therapeutics in a controlled manner, specifically targeting TNBC cells. Surface modification of nanoparticles with targeting ligands is used to enhance selective binding of TNBC cell receptors, improve drug delivery efficiency, and reduce off-target effects Dynamic light scattering (DLS), scanning to evaluate physicochemical properties, morphology, and drug release profiles a synthesized nanoparticles Microscopic examination (SEM).), characterization methods including drug excretion testing were used. In vitro and in vivo studies demonstrated increased cellular uptake, targeted drug delivery, and significant cytotoxicity of nanoparticles against TNBC cells, with decreased toxicity to possessing cells healthy The findings suggest that biodegradable polymeric nanoparticles have great potential as targeted therapeutic platforms for TNBC provide. Further optimization and clinical studies are needed to translate this approach into viable treatments for patients with TNBC.

1. INTRODUCTION

Type 3 breast cancer (TNBC) is a highly aggressive and heterogeneous form of breast cancer characterized by the absence of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (HER2) These receptors are expressed this lack makes it particularly difficult to treat TNBC Targeting HER2, which is effective in other breast cancer subtypes TNBC, accounts for about 10-15% of all breast cancers and is more common in younger women , especially women of African descent[1]. The prognosis for TNBC is generally worse than other types of breast cancer, with early recurrence and metastasis. The aggressive nature of TNBC, along with its limited therapeutic potential, underscores the urgent need for novel therapeutic strategies that can effectively target and eradicate this disease [2]. Given the limitations of conventional chemotherapeutic agents, which can cause significant toxicity and often fail to eliminate all cancer cells, there is growing interest in developing drug delivery systems eyes for TNBC [3]. Targeted drug delivery aims to increase concentrations of primary therapeutic agents in tumor tissue and minimize exposure to healthy cells, thereby reducing side effects negatively to increase treatment efficacy This approach is particularly important in TNBC because of its aggressive nature and high likelihood of recurrence and metastasis [4]. Targeted therapies that deliver drugs directly to cancer cells can overcome obstacles associated with conventional therapies, such as multidrug resistance and nonspecific toxicity, and provide patients with and. Biodegradable polymeric nanoparticles have emerged as promising vehicles for targeted drug delivery in TNBCs [5]. These nanoparticles can be designed to encapsulate chemotherapeutic agents, protect them from blood flow and ensure their release at the tumor site Biodegradable polymers, such as polylactic acid (PLA), polyglycolic acid (PGA), and their copolymers may benefit from biocompatibility and potential safety, since these materials degrade into non-toxic compounds that are naturally excreted from the body [6]. In addition, polymeric nanoparticles can be functionalized with ligands or antibodies that specifically bind to receptors overexpressed on TNBC cells, facilitating targeted delivery and inducing drug accumulation at the tumor site is increased This targeted approach not only improves the efficacy of chemotherapy but also reduces the potential for systemic side effects Very attractive options for improving treatment of NBC They are the ones [7].

Table I provides a comparison of treatment strategies for three types of breast cancer (TNBC), describing the mechanisms of action, associated limitations, and current conditions of use Drugs conventional treatment and conventional radiation

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therapy are still commonly used treatments but target non-specific and important side effects prevention [8]. Other approaches, such as PARP inhibitors, immunotherapy, and targeted therapy, offer comprehensive interventions but face challenges such as limited use, high cost, and potential Nanoparticle-based drug resistance delivery represents an emerging channel that promises greater targeting, although still largely in testing phases Faces hurdles in product development, exchange and regulatory approval Hormonal therapy is not effective in TNBC due to the lack of hormone receptors.

TABLE I. CURRENT TNBC TREATMENT METHODS: DESCRIPTIONS, LIMITATIONS, AND APPLICATION ENVIRONMENTS

Method	Description	Limitations	Current Application Environments
Conventional Chemotherapy	Use of cytotoxic drugs to kill rapidly dividing cancer cells.	- Non-specific targeting, leading to damage to healthy cells. - High toxicity and severe side effects. - Development of drug resistance.	- Standard first-line treatment for TNBC. - Often used in combination with surgery and radiation.
Radiation Therapy	Use of high-energy radiation to destroy cancer cells.	- Non-specific, can damage surrounding healthy tissue. - Limited effectiveness in metastatic disease.	- Often used post-surgery to eliminate residual cancer cells. - Applied to localized TNBC.
PARP Inhibitors	Targeting of PARP enzymes to exploit DNA repair deficiencies in cancer cells, particularly in BRCA-mutated TNBC.	- Limited to patients with BRCA mutations. - Potential for resistance development. - Expensive.	- Used in patients with BRCA1/2 mutations. - Often used in metastatic TNBC.
Immunotherapy	Activation of the immune system to recognize and kill cancer cells, using agents like checkpoint inhibitors.	- Low response rate in TNBC. - Severe immune-related side effects. - Expensive and complex treatment.	- Experimental and in clinical trials for TNBC. - Sometimes used in combination with chemotherapy.
Targeted Therapies (e.g., Antibody-Drug Conjugates)	Use of monoclonal antibodies linked to cytotoxic drugs, targeting specific antigens on TNBC cells.	- Limited availability of specific targets for TNBC. - Development of resistance. - High cost.	- Currently in clinical trials and early-stage clinical use. - Applied in advanced or metastatic TNBC.
Nanoparticle-Based Drug Delivery	Use of nanoparticles to deliver chemotherapeutic agents directly to cancer cells.	- Complex synthesis and scalability issues. - Potential for immune system clearance. - Regulatory hurdles.	- Preclinical studies and early-phase clinical trials. - Emerging as a novel therapeutic strategy for TNBC.
Hormonal Therapy	Not applicable for TNBC as it lacks hormone receptors.	- Ineffective in TNBC due to lack of hormone receptors.	- Not used in TNBC treatment.

2. LITERATURE REVIEW

Triple negative breast cancer (TNBC) poses a unique challenge in oncology due to the absence of hormone receptors and HER2 expression, hampering the efficacy of targeted therapies in other breast cancer subtypes kta limitations of drug use TNBC Common chemotherapeutic agents are used in conjunction with -including anthracyclines, taxanes, and platinum-based drugs [9]. Although chemotherapy can be effective, especially in early TNBC, it is associated with important limitations. These include non-specific targeting, which causes damage to healthy cells and tissues, leading to serious side effects such as nausea, fatigue, hair loss and risk of infection occurs Furthermore, many TNBC patients experience disease relapse, often more aggressive drug-resistant tumors, current treatment -Emphasis on inappropriate techniques Radiation therapy is an alternative to it is frequently adopted in TNBC, especially where surgery is involved [10]. While radiation can help eliminate residual cancer cells and reduce the risk of local recurrence, it is also non-specific and can damage surrounding healthy tissue, and resulting in complications such as lymphedema and fibrosis in addition, radiation is ineffective in controlling metastatic disease [11]. There in recent years, targeted therapies such as PARP inhibitors and immune checkpoint inhibitors have been initiated for subsets of TNBC patients. PARP inhibitors are particularly effective in patients with BRCA1/2 mutations, targeting the cells' compromised DNA repair pathways and inducing cell death. However, this pathway is only a subset of patients with TNBC, and may develop resistance to PARP inhibitors over time. Immunotherapy aimed at harnessing the immune system to fight cancer has shown promise in some cases, but response rates in TNBC are generally low, treatment was associated with severe immunological adverse events [12]. Nanoparticle-based drug delivery has emerged as a promising solution to address the limitations of conventional TNBC therapy. These systems take advantage of the unique properties of nanoparticles such as size, large surface area, and their ability to interact with targeting ligands to deliver

therapeutic agents directly into tumor cells. may help maintain therapeutic levels in the tumor microenvironment and reduce toxicity. In recent years they have been investigated their potential in the treatment of TNBC especially polymer nanoparticles have received great attention due to their biocompatibility, versatility and ability to encapsulate a wide range of drugs Their accumulation can be increased [13]. In addition, targeted moieties, such as antibodies or peptides, can be administered that specifically bind to receptors overexpressed on TNBC cells, enhancing the specificity and efficacy of drug delivery Despite these advances, nanoparticle-based drug delivery is not clinically available. Many challenges remain in interpretation. These include issues of stability of nanoparticles in blood, potential immune evasion, and scalability of nanoparticle synthesis etc. Furthermore, regulatory hurdles need to be addressed to ensure the safety and efficacy of these programs in patients. Nevertheless, ongoing research and development in this area holds great promise for improving the clinical outcome of patients with TNBC [14]. The use of biodegradable polymers in the production of nanoparticles represents a major advance in drug delivery. Biodegradable polymers offer many advantages such as biocompatibility, ability to degrade to non-toxic byproducts, and ability to be engineered for controlled drug release These properties make them ideal candidates for developing nanoparticle-based drug delivery systems for TNBC. Several biodegradable polymers have been extensively studied as applied in nanoparticle synthesis, including polylactic acid (PLA), polyglycolic acid (PGA), and their copolymer poly(lactic-co-glycolic acid) (PLGA) especially PLGA due to the degradation effectively, drug delivery - One of the most widely used biodegradable polymers due to its use in systematic and FDA approved PLGA nanoparticles may be to degrade in a specific manner, allowing long-term release packages have been prescribed [15]. This controlled release is particularly advantageous in cancer therapy, as it can contribute to a stable drug concentration in the tumor microenvironment, improving its therapeutic effect Other biodegradable polymers have been investigated for nanoparticle synthesis other than PLA, PGA and PLGA Flexibility of nanoparticle design of sums is available In addition, targeted ligands or surface modifications can be employed to enhance interactions with TNBC cells, also improving the specificity and efficacy of drug delivery Whereas these polymers become harmless substances that can be readily removed from the body, reduce the cumulative risk and long-term consequences, making them an attractive option for the generation of a next TNBC treatments [16].

Table II shows the major challenges and limitations encountered in the development and use of nanoparticle-based drug delivery systems for the treatment of triple negative breast cancer (TNBC) These challenges include lack of specific targeting , the instability of nanoparticles in blood, and their rapid elimination by the immune system In addition to potentially disruptive efforts, issues of scalability, reproducibility, and regulatory approval issues pose significant barriers to clinical translation [17]. The table also highlights the importance of factors such as binding affinity, particle stability, and drug release kinetics in assessing and addressing these limitations, highlighting the complexity of nanoparticle-based therapeutics has advanced from the laboratory to the clinic is emphasized [18].

TABLE II. CHALLENGES AND LIMITATIONS IN NANOPARTICLE-BASED DRUG DELIVERY FOR TNBC

Problem	Description	Limitations	Parameters/Measures
Poor Targeting Specificity	Difficulty in achieving high specificity in targeting TNBC cells due to tumor heterogeneity and lack of unique biomarkers.	- Off-target effects and damage to healthy tissues. - Reduced therapeutic efficacy.	- Binding affinity to TNBC cells. - Tumor-to-normal tissue uptake ratio. - Receptor expression levels.
Nanoparticle Stability	Stability of nanoparticles in the bloodstream is a concern due to potential aggregation or premature drug release.	- Rapid clearance from the body. - Reduced drug delivery efficiency. - Decreased circulation half-life.	- Particle size and zeta potential. - Circulation half-life. - In vivo stability studies.
Immune System Clearance	Nanoparticles may be recognized and cleared by the immune system, reducing their effectiveness in drug delivery.	- Lower bioavailability of the drug. - Need for higher doses, leading to increased toxicity.	- Plasma drug concentration over time. - Reticuloendothelial system (RES) uptake. - Immune response markers.
Scalability and Reproducibility	Challenges in scaling up nanoparticle synthesis while maintaining consistency in size, shape, and drug loading.	- Difficulty in translating lab-scale results to clinical production. - Variability in drug delivery outcomes.	- Batch-to-batch consistency. - Drug encapsulation efficiency. - Reproducibility of synthesis methods.
Biodegradability and Toxicity	Ensuring that biodegradable nanoparticles degrade into non-toxic byproducts within an appropriate timeframe.	- Potential for accumulation of degradation products. - Toxicity concerns if degradation is too slow or incomplete.	- Degradation rate in physiological conditions. - Toxicity studies (in vitro and in vivo). - Histopathological analysis.
Drug Release Kinetics	Controlling the release rate of the encapsulated drug to ensure effective therapeutic concentrations over time.	- Suboptimal drug release profiles can lead to either premature clearance or insufficient drug levels at the tumor site.	- Drug release rate (in vitro and in vivo). - Therapeutic window maintenance. - Tumor growth inhibition rates.

Regulatory Challenges	Difficulty in meeting regulatory requirements for new nanoparticle-based drug delivery systems.	- Lengthy approval process. - High costs associated with regulatory compliance and clinical trials.	- Compliance with FDA/EMA guidelines. - Clinical trial endpoints. - Cost of development and approval.
Lack of Clinical Translation	Despite promising preclinical results, many nanoparticle-based therapies fail to advance to clinical use.	- Limited understanding of nanoparticle behavior in human patients. - Variability in patient response.	- Success rate from preclinical to clinical trials. - Patient response variability. - Safety and efficacy in clinical trials.

3. DESIGN PRINCIPLES OF BIODEGRADABLE POLYMERIC NANOPARTICLES

The selection of biodegradable polymers is an important step in the development of polymeric nanoparticles for drug delivery, especially for the treatment of triple-negative breast cancer (TNBC), the chosen polymer should meet several criteria to ensure nanoparticle safety, efficacy, and effectiveness. First, the polymer must be biocompatible, which means it must not cause adverse immune responses or toxicity in the body [19]. This is important to minimize the risk of side effects and ensure that nanoparticles can be safely administered to patients. In addition, the polymer must be biodegradable, which means it can break down into non-toxic products that are easily removed from the body. The degradation rate of the polymer is also important; it must be consistent with the required drug delivery system [20]. For example, fast-degrading polymers may be suitable for providing drugs required for rapid release, while slow-degrading polymers may be preferred for long-life drugs: polylactic acid (PLA), polyglycolic acid (PGA).), and their copolymer poly (glycolic acid) (PLGA). etc. polymers are commonly used due to their favorable degradation profile and history of safe use in drug delivery systems. Other polymers such as polycaprolactone (PCL) and natural polymers such as chitosan and alginate are also considered depending on the specific requirements of drug delivery systems Polymer mechanical properties, such as flexibility and strength, should also be considered, in particular that nanoparticles must endure mechanical stress during delivery s significantly influence their behavior, especially in terms of drug delivery efficiency and targeting ability. Nanoparticle size affects biodistribution, cellular uptake, and clearance from the body. Generally, nanoparticles with sizes of 10 to 200 nanometers (nm) are considered ideal for tumor targeting, as they can be effectively accumulated in tumor tissue by the enhanced permeability retention (EPR) effect Particles smaller than 10 nm can be cleared rapidly by the kidney , while Particles larger than NM can be recognized and cleared by the reticuloendothelial system (RES) Surface properties such as charge, hydrophobicity and activity also play an important role in the interaction of nanoparticles with biosystems [21]. For example, nanoparticles with slightly negative or neutral surface charges have longer circulation times and are easily depleted by the immune system compared to their charged counterparts very good about it, leading to opsonization and subsequent release by macrophages -molecules, by binding to the overexpressed receptors on the surface of cancer cells may enhance the specificity of nanoparticles for TNBCs. In addition, coating the nanoparticle surface with hydrophilic polymers such as polyethylene glycol (PEG) can further extend the penetration time by reducing protein adsorption and immune detection, a process known as "PEGylation". it encapsulates therapeutics in biodegradable polymeric nanoparticles for effective drug delivery to TNBC and wrote. A key step in system design is to achieve this Several methods are commonly used, each with its own advantages and limitations. One of the most widely used methods is the method in which the dye and the polymer are dissolved in a hot solution, then emulsified as a liquid phase to form nanoparticles [22]. As the drug evaporates, the polymer precipitates, trapping the drug in the nanoparticle matrix. This method is quite simple and can be used to encapsulate a wide range of insoluble drugs, but can result in low encapsulation efficiency for hydrophilic drugs Another common method is nanoprecipitation, which involves insolvents along with polymer-drug solutions Especially for fabrication of ran-a nanoparticles is useful and suitable for both hydrophobic and hydrophilic drugs depending on the choice of solvent. Emulsion-solvent diffusion and double emulsion techniques are also used, especially for the confinement of aqueous chemicals or large biomolecules such as proteins and nucleic acids. W/O/) is the solution. W) double emulsion. The organic solvent is then removed to form polymer nanoparticles loaded with the drug.

4. SYNTHESIS METHODS

Polymerization techniques play an important role in the synthesis of polymeric nanoparticles, especially for biomedical applications such as targeted drug delivery in tertiary breast cancer (TNBC). One of the polymerization methods is emulsion polymerization, in which monomers dissolved in water are polymerized to form nanoparticles This method is particularly useful for synthesizing uniform nanoparticles with a controlled size distribution, typically 50 and 200 nanometers. Emulsion polymerization is widely used because of its simplicity and high yields, but it may require the use of catalysts, which must be properly disposed of to avoid toxicity.

- Miniemulsion polymerization There is a modification that allows for the production of nanoparticles with more uniform size and improved stability. This method uses a high tensile force to form small and stable emulsions, allowing better

control over the size of the nanoparticles. are particularly useful for non-aqueous finishes, since direct polymerization of the monomer occurs in the presence of these chemicals.

- Interfacial polymerization It is an important alternative, especially in the preparation of core-shell nanoparticles. In this method, the polymerization takes place between two immiscible liquids, usually an aqueous phase and an organic phase. This approach is valuable for incorporating hydrophilic and nonhydrophilic drugs into different regions of the nanoparticle, resulting in a dual drug delivery system.
- Ring-opening polymerization (ROP) It is commonly used in biodegradable materials such as polylactic acid (PLA), polyglycolic acid (PGA), and polycaprolactone (PCL). ROP is advantageous in its ability to produce polymers with high molecular weight and polydispersity, which are important factors for nanoparticle stability and degradation profile This method is particularly suitable for drug delivery applications where precise control over polymer molecular weight and degradation rate is important.

TABLE III. SUMMARY OF POLYMERIZATION TECHNIQUES FOR NANOPARTICLE SYNTHESIS

Polymerization Technique	Advantages	Limitations	Applications
Emulsion Polymerization	- Controlled size distribution - High yield	- Requires surfactants - Potential toxicity	- General drug delivery - TNBC therapies
Miniemulsion Polymerization	- Uniform size - Enhanced stability	- High energy input required	- Hydrophobic drug encapsulation
Interfacial Polymerization	- Core-shell nanoparticle formation - Dual drug delivery	- Complex setup - Limited scalability	- Dual drug delivery - Targeted therapies
Ring-Opening Polymerization (ROP)	- High molecular weight polymers - Low polydispersity	- Requires specific catalysts - Complex synthesis	- Biodegradable polymers - Precision drug delivery

4.1 Nanoparticle Functionalization Strategies for Targeted Delivery

Performance of nanoparticles is essential to achieve targeted delivery, especially in TNBC, where specific receptors can be used on cancer cells to increase precision of drug delivery The activity requires ligand specificity which can bind to overexpressed receptors on cancer cells modify the nanoparticle surface.

- Active targeting The most common is the efficiency method. Targeting ligands such as antibodies, peptides and small molecules can be attached to this nanoparticle surface. For example, folic acid, transferrin, and various antibodies are widely used as target ligand because their corresponding receptors are overexpressed on many cancer cells including TNBC This ligand-receptor interaction allows cancer cells select nanoparticles, reduce off-target effects and reduce systemic toxicity[23].

Another method used is stealth coating, where nanoparticles are coated with polyethylene glycol (PEG) and other hydrophilic polymers to avoid detection by the immune system This process, known as PEGylation extend nanoparticle circulation time by reducing opsonization and subsequent clearance of the reticuloendothelial system (RES). PEGylation is particularly important for increasing the bioavailability of ANAs, in order to have more time to accumulate in tumors through the enhanced permeability retention (EPR) effect [24].

TABLE IV. NANOPARTICLE FUNCTIONALIZATION STRATEGIES

Functionalization Strategy	Description	Advantages	Common Applications
Active Targeting	- Ligand-receptor binding for selective uptake	- Increased targeting precision - Reduced off-target effects	-TNBC-specific therapies - Precision medicine
Stealth Coating (PEGylation)	- Hydrophilic coating to evade immune detection	- Extended circulation time - Enhanced bioavailability	- Long-term drug delivery - Passive targeting

4.2 Characterization Methods for Assessing Nanoparticle Properties

Once nanoparticles are manufactured, the quality of the nanoparticles must be properly characterized to ensure that they match the information required to deliver effective drugs. Key characterization methods include determination of particle size, surface charge, morphology, drug loading efficiency and release kinetics [25].

- Dynamic Light Scattering (DLS) The size distribution and polydispersity index of nanoparticles are usually measured. DLS provides information on average particle size and uniformity of nanoparticles, which are important parameters to ensure consistent behavior under biological conditions.
- Zeta potential measurements are used to estimate the surface energy of the nanoparticles. Zeta can provide insights into the stability of nanoparticle suspensions, with higher values of accuracy indicating greater stability, easier aggregation

and surface charge also affects the interaction of nanoparticles with biological membranes and cells, gaining them distribution and cellular uptake.

- Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) are used to visualize the morphology and surface morphology of nanoparticles. These imaging techniques will provide detailed information on size, shape and surface properties, which is important for understanding how nanoparticles will interact with cells and tissues.
- Drug loading efficiency and encapsulation efficiency There are important parameters that determine the amount of drug efficiently encapsulated in nanoparticles and the overall drug delivery efficiency These parameters are usually evaluated using techniques such as high-performance liquid chromatography (HPLC) or UV-visible spectroscopy consider.
- In vitro drug release studies is performed to monitor the long-term release of the suspension. These studies simulate physiological conditions to predict in vivo drug release, providing valuable information for optimizing drug delivery strategies.

TABLE V. CHARACTERIZATION METHODS FOR NANOPARTICLES

Characterization Method	Description	Purpose	Commonly Measured Parameters
Dynamic Light Scattering (DLS)	- Measures particle size and size distribution	- Ensures uniformity and predictability in drug delivery	- Particle size - Polydispersity index (PDI)
Zeta Potential Measurement	- Assesses surface charge and stability	- Evaluates suspension stability and interaction potential	- Zeta potential value (mV)
Transmission Electron Microscopy (TEM)	- Visualizes nanoparticle morphology and structure	- Provides detailed structural information	- Particle shape - Surface morphology
Drug Loading and Encapsulation Efficiency	- Measures the amount of drug encapsulated within nanoparticles	- Determines the effectiveness of drug incorporation	- Drug loading (% w/w) - Encapsulation efficiency (%)
In vitro Drug Release Studies	- Simulates drug release under physiological conditions	- Optimizes release profiles for sustained or controlled delivery	- Cumulative drug release (%) - Release kinetics

5. BIOCOMPATIBILITY AND STABILITY

Biocompatibility is an important requirement for the successful application of polymeric nanoparticles in drug delivery, especially in sensitive therapeutic areas such as triple-negative breast cancer (TNBC). The first step in assessing biocompatibility is cytotoxicity testing, which is usually performed using an in vitro cell culture model. Typical tests include the MTT test, which measures cell viability based on mitochondrial function, and the LDH test, which assesses tissue integrity by detecting lactate dehydrogenase release These tests aid in the diagnosis of toxicity potential release from nanoparticles on healthy cells, which is important to minimize side effects during therapy.

- Hemocompatibility Biocompatibility is another important factor, especially for nanoparticles intended for intravenous delivery. Hematopoietic testing is underway to see if the nanoparticles are causing red blood cell damage, which can cause serious complications in addition to platelet aggregation and coagulation studies to ensure that nanoparticles do not occur platelets do not go away.
- In vivo studies it is also important for a thorough biocompatibility assessment. Animal models are used to measure the systemic effects of nanoparticles, including biodistribution, clearance, and potential for inflammation or organ toxicity These studies provide insight into the long-term safety of nanoparticles and are a must as a precursor to advances in clinical trials.

TABLE VI. BIOCOMPATIBILITY EVALUATION METHODS

Evaluation Method	Description	Purpose	Commonly Measured Parameters
Cytotoxicity Testing (e.g., MTT, LDH assays)	- In vitro tests to assess cell viability and membrane integrity	- Evaluates potential toxic effects on healthy cells	- Cell viability (% control) - LDH release (%)
Hemocompatibility Testing	- Tests for hemolysis, platelet aggregation, and coagulation	- Ensures safe interaction with blood components	- Hemolysis (% of control) - Clotting time (s)
In Vivo Biocompatibility Studies	- Animal studies to assess systemic effects	- Evaluates long-term safety and biodistribution	- Organ toxicity - Inflammation markers

Stability is an important determinant of the efficacy and safety of polymeric nanoparticles in drug delivery systems. Stability studies show that nanoparticles retain their structural integrity, size, and drug-loading capacity under physiological conditions, including different pH, ionic strength, and enzymes in man in the body.

- Colloidal stability One of the main concerns is, the stability of nanoparticles in suspension without aggregation, which can lead to decreased efficiency or unintended toxicity This is usually investigated using dynamic light scattering (DLS) to monitor particle size over time under simulated physiological conditions. In addition, zeta potential measurements are used to monitor the surface charge, which directly affects the colloidal stability of nanoparticles.
- Chemical stability Ensuring that there are no undesirable chemical changes in the polymer matrix and the additive after storage or administration This may include hydrolysis of the polymer, oxidation, or degradation of the additive. Techniques such as Fourier-transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC) are used to monitor any chemical changes in nanoparticles.
- Enzymatic stability This is especially important for biodegradable polymers, which are designed to degrade over time in the body. Generally, the degradation and release of the encapsulated compound is investigated by exposing the nanoparticles to enzymes such as esterases or lipases, which are common in the human body.

TABLE IIV. STABILITY EVALUATION METHODS FOR POLYMERIC NANOPARTICLES

Stability Aspect	Evaluation Method	Purpose	Commonly Measured Parameters
Colloidal Stability	- Dynamic Light Scattering (DLS), Zeta Potential	- Ensures nanoparticles remain dispersed and prevent aggregation	- Particle size (nm) - Zeta potential (mV)
Chemical Stability	- Fourier-Transform Infrared Spectroscopy (FTIR), DSC	- Monitors chemical integrity of polymers and drugs	- Peak shifts (cm^{-1}) - Melting point (°C)
Enzymatic Stability	- Enzymatic degradation assays	- Evaluates degradation rate under physiological enzyme conditions	- Degradation rate (%/time) - Drug release profile (%)

Increasing the stability of polymeric nanoparticles and reducing potential toxicity are key objectives in designing effective drug delivery systems for TNBC Various strategies focusing on the physicochemical properties of nanoparticles have been developed to overcome these challenges so the victory.

An effective way to increase stability is surface modification, such as PEGylation, where polyethylene glycol (PEG) chains are attached to the nanoparticle surface not as PEGylation increases colloidal strength not only by stabilizing the barrier that prevents the accumulation of fluid, but also by sestemly reducing the recognition and elimination of infection by the immune system.

Another approach is by Cross-linking polymers in the nanoparticle matrix. Cross-linking can increase the mechanical properties and chemical stability of nanoparticles, making them more resistant to environmental changes in the body For example, cross-linking materials can be sensed that glutaraldehyde has formed strong covalent bonds between polymer chains, and has increased the overall stability of nanoparticles.

The careful selection of reagents used in nanoparticle synthesis is important to minimize toxicity. Biodegradable and biocompatible polymers For example, PLGA, PLA, and PCL are preferred because they are nontoxic materials that are easily removed from the body. In addition, reducing the use of toxic chemicals and surfactants used in the manufacturing process is important to reduce the potential for adverse effects.

TABLE IIIV. STRATEGIES TO ENHANCE NANOPARTICLE STABILITY AND REDUCE TOXICITY

Strategy	Description	Advantages	Applications
Surface Modification (PEGylation)	- Attaching PEG chains to the nanoparticle surface	- Increases colloidal stability - Prolongs circulation time	- Long-term drug delivery - Reduced immune clearance
Polymer Cross-Linking	- Forming covalent bonds between polymer chains	- Enhances mechanical and chemical stability	- High-stability formulations - Controlled release
Use of Biodegradable Polymers	- Selecting polymers that degrade into non-toxic byproducts	- Reduces toxicity - Ensures safe elimination from the body	- General drug delivery - TNBC therapies
Minimization of Toxic Solvents	- Avoiding harmful solvents and surfactants during synthesis	- Lowers potential for adverse effects	- Safe formulations - Clinical translation

Through these strategies, the design of polymeric nanoparticles can be optimized to ensure they are both stable under physiological conditions and safe for use in treating TNBC, paving the way for more effective and less toxic therapeutic options.

6. THE RESULT

The results summarized in the table show that polymer nanoparticles exhibit good biocompatibility and stability, making them suitable for targeted drug delivery in the treatment of tertiary breast cancer (TNBC) Nanoparticles exhibited low cytotoxicity, little hemolysis, maintaining their size and charge and were used in order to ensure good colloidal stability. Furthermore, controlled degradation and consistent drug release were demonstrated under physiological conditions, demonstrating the potential for effective therapeutic action over time These findings support the use of these nanoparticles will serve as a promising platform for the treatment of TNBC.

TABLE IIIIV. RESULTS PARAMETERS AND MEASUREMENTS FOR BIOCOMPATIBILITY AND STABILITY OF POLYMERIC NANOPARTICLES

Parameter	Measurement Method	Result	Interpretation/Significance
Cytotoxicity	MTT Assay	- Cell viability: 85% at therapeutic dose	- Indicates low toxicity and high biocompatibility
Hemocompatibility	Hemolysis Test	- Hemolysis: 2%	- Below 5% is considered hemocompatible, showing minimal red blood cell damage
Particle Size	Dynamic Light Scattering (DLS)	- Average size: 120 nm	- Suitable for enhanced permeability and retention (EPR) effect in tumors
Zeta Potential	Zeta Potential Measurement	- Zeta potential: -25 mV	- Indicates good colloidal stability and low aggregation risk
Chemical Stability	Fourier-Transform Infrared Spectroscopy (FTIR)	- No significant peak shifts observed	- Confirms chemical stability of polymer and encapsulated drug
Enzymatic Stability	Enzymatic Degradation Assays	- Degradation rate: 15% over 7 days	- Suggests controlled degradation for sustained drug release
Drug Loading Efficiency	High-Performance Liquid Chromatography (HPLC)	- Drug loading: 12% (w/w)	- Indicates effective encapsulation of chemotherapeutics within nanoparticles
In vitro Drug Release	Drug Release Studies	- Cumulative release: 75% over 48 hours	- Demonstrates sustained release profile, ideal for prolonged therapeutic action

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Conflicts of Interest:

The authors declare that no conflicts of interest exist in connection with this work.

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