ISSN: 0976-7126
Kumar & Dubey, 16(8):10-20, 2025

International Journal of Pharmacy & Life Sciences
Open Access to Researcher

PLGA-Based Dual Drug Delivery and Targeted Nanoparticle Systems for Enhanced Breast Cancer Therapy

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Article info

Received: 08/04/2025

Revised: 11/06/2025

Accepted: 15/06/2025

www.ijplsjournal.com

Abstract

A major source of concern is the growing global concern regarding cancer, a disease that has attracted the attention of scientists in recent decades. Breast cancer is the most common type of cancer that affects women worldwide and is caused by cells in the breast. Breast cancer accounted for 25% of all cancer diagnoses in 2012. The process of metastasis begins with the invasion of adjacent organs and continues with the dissemination of lymph nodes, invasion of blood vessels, and the spread of cancer to other parts of the body. Hormone therapy, radiation therapy, chemotherapy, poly-chemotherapy, and surgical removal of cancerous tissue are the current options for treating breast cancer.PLGA-based nanoparticles have the potential to enhance treatment efficacy. In comparison to other polymers, nanoparticles derived from PLGA are well-suited for clinical trials.

This is because PLGA has been approved for use in a variety of drug delivery systems by both the FDA and the EMA. Biomedical research into drug delivery with PLGA or polymers derived from PLGA has many promising avenues for maximizing therapeutic (antitumor) efficacy while minimizing adverse effects.

Keywords: PGLA, Cancer, Nanoparticle

Introduction

Cancer is one of the most terrible diseases that people can get because it can spread to almost any part of the body through uncontrolled cell growth and metastasis. In 2012, the World Health Organization reported that 14.1 million people worldwide were diagnosed with cancer. 7.4 million men and 6.7 million women made up the population. By the end of 2035, this number is expected to reach an astonishing 24 million. A major source of concern is the growing global concern regarding cancer, a disease that has attracted the attention of scientists in recent decades. Breast cancer is the most common type of cancer that affects women worldwide and is caused by cells in the breast. Breast cancer accounted for 25% of all cancer diagnoses in 2012. The process of metastasis begins with the invasion of adjacent organs and continues with the dissemination of lymph nodes, invasion of blood vessels, and the spread of cancer to other parts of the body. Hormone therapy, radiation therapy, chemotherapy, poly-chemotherapy, and surgical removal of cancerous tissue are the current options for treating breast cancer.

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When breast cancer patients are treated systemically, they often get anti-cancer drugs such

as anthracyclines, gemcitabine, alkylating agents, capecitabine, 5-fluorouracil, eribulin, taxane, and vinorelbine. Paclitaxel, or PAX, a chemotherapy drug, was first isolated from the Pacific Ocean in 1971 and is typically prescribed to breast cancer patients. The chemical's low bioavailability is a significant limitation due to its low water solubility. To address this issue of hydrophobia, the Food and Drug Administration (FDA) and the World Health Organization (WHO) approved Taxol®, a paclitaxel formulation that had been introduced in 1993. This formulation includes cremophore-EL®, a toxic organic solvent that helped eliminate the problem of paclitaxel's hydrophobic interaction. Abraxane®, a new paclitaxel formulation, received approval from the FDA and the European Medicines Agency in 2005 and 2008, respectively, for the treatment of breast cancer. Abraxane®, a formulation based on nanotechnology, contains albumin-conjugated paclitaxel. Among the many advantages that nano-delivery systems offer over conventional methods of drug administration are the reduction of potentially harmful excipient side effects, the enhancement of solubility, and the improvement of controlled medication release. In this section, we discussed the dangers of

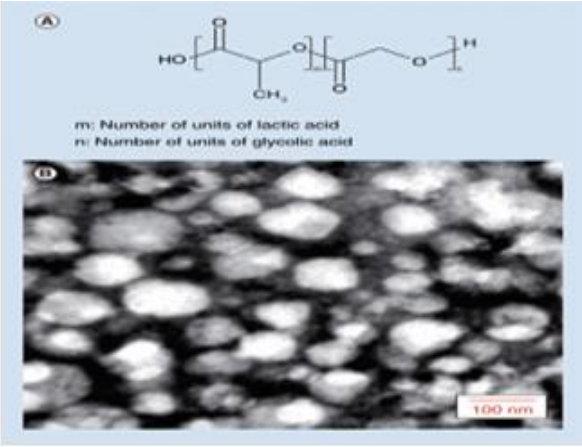

Figure 1.1Poly (Lactic-Coglycolic Acid) (PLGA) and PLGA Nanoparticles (NPs): A Chemical Examination

Properties of PLGA

The random ring opening copolymerization of two monomers—lactic acid and glycolic acid—creates the copolymer poly (lactic-co-glycolic acid). These monomers are cyclic dimers made up of one, four, and five diones. This copolymer is frequently produced with the help of a variety of catalysts, such as aluminum isopropoxide, tin (II) alkoxides, and tin (II) 2-ethylhexanoate. Through ester linkages between glycolic or lactic acid monomeric units, polylactic acid (PLGA) produces aliphatic, linear, and amorphous polyesters. Typically, the monomer ratio is used to distinguish between various PLGA forms. Consider PLGA 50:50 as an illustration of a copolymer, in which lactic acid and glycolic acid make up 50% of the total. In contrast to conventional devices, PLGA is biocompatible, has a long history of biomedical use, is simple to inject into the bloodstream, and has been shown to be beneficial for prolonged drug release (up to days, weeks, or months). PLGA is a desirable biodegradable polymer for use in nanomedicine research because it hydrolyzes in the body and breaks down into its component biodegradable metabolites, lactic acid and glycolic acid. Through the Krebs cycle, these monomers follow a straightforward metabolic pathway for solubilization into CO2 and water. This lessens the likelihood of harm to the entire system. The FDA and the European Medicines Agency (EMA) have approved a number of PLGA-based human drug delivery systems.

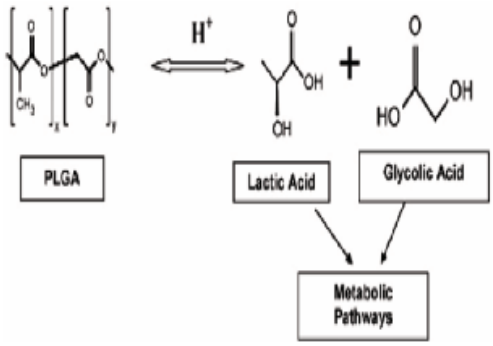

Figure 1.2Processing PLGA by hydrolysis

Because of this, the ability of nanoparticle surface charges to bind to and be absorbed by cells is critically important. The ability of nanoparticles with a cationic surface charge to interact with cells improves, which in turn accelerates and extends the rate of internalization. The negative charges of PLGA nanoparticles can be transformed into neutral or positive charges by

surface modification, such as chitosan coating or PEGylation of the polymer.

Methodology

Single- or double-emulsion-solvent evaporation method

During the evaporation process that results in the production of PLGA NPs, the most common combination of solvent and a single or double emulsion is used. Oil-in-water (o/w) emulsification occurs in a single-emulsion process, whereas water-in-oil-in-water (w/o/w) emulsification occurs in a double-emulsion process. The w/o/w method is the most effective for encapsulating water-soluble drugs like vaccines, peptides, and proteins. Steroids, on the other hand, work best when encapsulated using the o/w method. Solid/oil/water (s/o/w) approaches utilizing PLGA-based microspheres have occasionally been used for larger water-soluble peptides like insulin. Organic solvents like dichloromethane, chloroform, and ethyl acetate can be used in the o/w method to dissolve polymers. A surfactant or emulsifying agent like gelatin, poly(vinyl alcohol), polysorbate-80, poloxamer-188, etc. is used to create an oil-in-water (O/W) emulsion after the drug has been dissolved or dispersed into the prepared polymer solution. You have a few options for removing the organic solvent from a stable emulsion: keep stirring the mixture, raise the temperature, or apply pressure. Both of these methods make use of techniques like high-speed homogenization and sonication. For larger-scale pilot production, alternatives based on low-energy emulsification are required, despite the effectiveness of these methods on a smaller scale. The stir rate, dispersion agent type and quantity, temperature, and organic and water phase viscosities can all be changed to change the size. Emulsions of oil and water, in which water acts as a nonsolvent, reduce the complexity of the washing phase, eliminate recycling, and simplify and improve process economics by preventing agglomeration. On the other hand, other emulsions can be used. Limiting homogenization to liposoluble medications is impractical due to its high energy requirements.

Emulsification solvent diffusion(ESD) method

At room temperature, the solvent and water need to be thoroughly mixed before the Quintanar-Guerrero et al. method can be used. If this is done, both liquids will initially be in thermodynamic equilibrium. The organic solvent containing the polymer and medication is emulsified in an aqueous surfactant solution by employing a high-speed homogenizer, typically with PVA added as a stabilizing component. The next step is to add water to the o/w emulsion system while continuously stirring. The solvent then diffuses out of the inner phase as a result of this phase change. A nano-precipitated polymer and colloidal nanoparticles are the final results. The final approaches to solvent elimination are evaporation and vacuum steam distillation. The straightforwardness, small size distribution, high consistency from batch to batch, simplicity, and high encapsulation efficiency (up to 70%) of this method are just a few of its many advantages. The need to extract a lot of water from the suspension is one disadvantage. Because pharmaceuticals that are water-soluble leak into the saturated-aqueous outer phase, emulsification reduces the effectiveness of encapsulation.

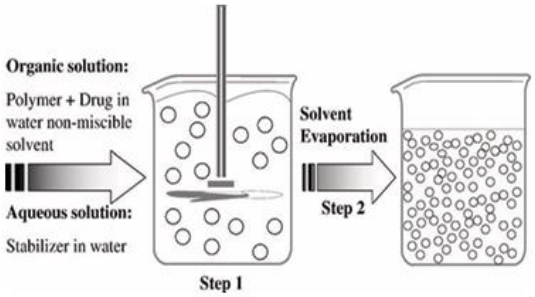

Figure 1.3. Emulsification-Evaporation Technique: A Schematic

Emulsification reverse salting-out method

An aqueous solution containing the salting-out agent and a colloidal stabilizer is combined with a water-miscible solvent, such as acetone, in the emulsification reverse salting-out method. Some examples of these solutions include magnesium chloride, calcium chloride, or polyvinyl pyrrolidone. After that, the mixture is vigorously mechanically agitated. When an oil-in-water emulsion is subjected to a high concentration of water, the acetone diffuses further into the water phase, resulting in the formation of nanoparticles. The dilution forces the polymer solvent out of the emulsion droplets, which results in a sudden drop in the salt concentration in the continuous phase. Cross-flow filtration is used to get rid of the

solvent and salting out agent. The emulsification diffusion method uses salts to avoid harsh purification phases, despite being merely a modification of the salting-out method. The primary benefit of salting out is that it lessens the stress experienced by protein encapsulants. Salting out may be suitable for heat-sensitive chemicals because it does not require raising the temperature. The primary limitations are that they can only be used with lipophilic medications and require extensive nanoparticle cleaning procedures.

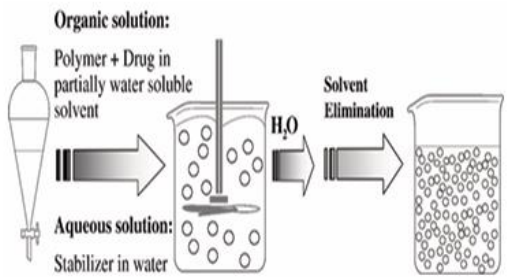

Figure 1.4. The ESD Method Presented in a Graphical Format

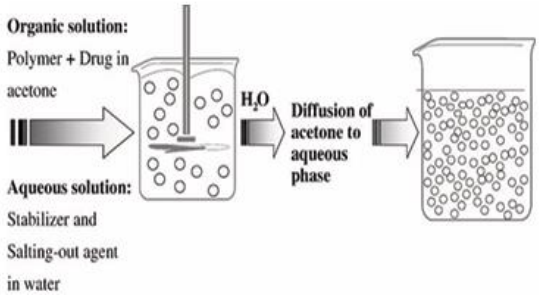

Figure 1.5. A Salting-out Technique Schematic

Nanoprecipitation method

The nanoprecipitation process, also known as the solvent displacement technique, consists of only one stage. The three fundamental components of nanoprecipitation are a polymer-based system, a polymer-derived solvent, and a polymer-based nonsolvent. Both hydrophobic and hydrophilic medications have demonstrated the potential of this strategy, although the latter are typically utilized more frequently. Using a polar, water-miscible solvent like ethanol, acetone, methanol, or acetonitrile, medications and polymers can be dissolved. Drop by drop, the solution is delicately added to the surfactant-containing aqueous solution. The instantaneous formation of nanoparticles is caused by the solvent's rapid diffusion. The solvent will be removed in the final step by applying a lower pressure.

Aim of study

to create and test dual drug delivery and targeted nanoparticle systems based on PLGA for enhanced breast cancer therapy with minimal side effects and increased therapeutic efficacy.

Objectives

- Create PLGA nanoparticles that can both contain drugs and release them in a controlled manner.
- Make Drug Loading and Release Profiles more effective for therapeutic purposes.
- Make use of specific ligands for breast cancer cells to improve the efficiency of targeting.
- Conduct in vitro studies on breast cancer cell lines to evaluate cytotoxicity and cellular uptake.
- Test the effectiveness of drug delivery and tumor-targeting in animal models for in vivo therapeutic efficacy.

Breast Cancer Classification: Based Molecular Subtype

A superior method for consistently diagnosing and classifying breast cancer is to evaluate biological indicators that are primarily responsible for the disease. Human epidermal growth factor receptors-2 (HER2+/HER2) and hormone receptors that regulate estrogen and progesterone levels may be high in these individuals. The four most typical types of intrinsic molecules are depicted in Figure 2.4:

Luminal-Asubtype

This type of breast cancer lacks the cell-growth markers HER2 (HER2-) and Ki-67. Despite this, it has receptors for estrogen (ER+) and progesterone (PR+). The Luminal-A subtype is linked to the best possible outcome and accounts for 74% of breast cancer cases in women. These carcinomas grow at a slower rate and are less aggressive than other molecular breast cancer subtypes.

Luminal-B subtype

It is thought to be breast cancer when the Ki-67 protein level is high and the ER, PR, and HER2 proteins are expressed positively. The more dangerous Luminal-B subtype, which affects 10% of women diagnosed, accounts for approximately 10% of breast cancer cases.

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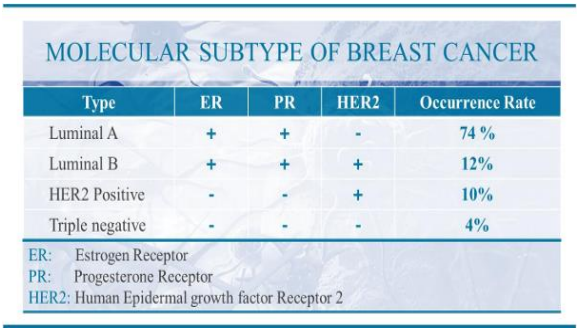

MOLECULAR SUBTYPE OF BREAST CANCER

Type	ER	PR	HER2	Occurrence Rate
Luminal A	+	+	-	74 %
Luminal B	+	+	+	12%
HER2 Positive	-	-	+	10%
Triple negative	-	-	-	4%

ER: Estrogen Receptor
PR: Progesterone Receptor
HER2: Human Epidermal growth factor Receptor 2

Figure2.4Molecular subtypes of breast cancer: a comprehensive overview

Triple negative subtype

Twelve percent of all breast cancers in women are basal-like or triple negative. A patient is said to be a triple negative if they test negative for both HER2 and hormone receptors (ER- and PR-). Black women are more likely to get this disease than white women or people who have the BRCA-1 gene mutation. Since there is currently no specific targeted therapy for this type of breast cancer, its short-term prognosis is worse than for others.

HER2-enriched subtype

A subtype of breast cancer known as HER2-enriched develops in about 4% of cases when hormone receptors are negative but HER2 is present. Compared to other types of breast cancer, these cancers are more aggressive and have a greater tendency to spread quickly. Regardless, advances in targeted pharmaceutical approaches have made it more difficult to treat HER2 subtype breast cancer.

Other Rare Breast Cancers

Tubular carcinomain Breast

When breast cancer is invasive, it spreads into surrounding tissues and goes beyond the milk duct. The majority of tubular carcinomas appear to be tubes and are only about one centimeter in diameter. Because they are less aggressive, treatments for cancer have a better chance of working with these carcinomas. According to reports, women in their early 50s are the most likely to be diagnosed with tubular carcinoma.

Medullary carcinoma in Breast

It is extremely uncommon for invasive ductal carcinoma subtypes to affect more than 3-5% of breast cancer patients. Because of this tumor's similarity to the medulla in the brain, I named it medullary breast cancer. Even though the risk is still higher for all women, women with the BRCA-1 mutation have a higher risk of developing breast cancer in their late 40s and early 50s. Because it develops slowly and only spreads to lymph nodes, this type of breast cancer is easier to treat than others.

Mucinous carcinoma in Breast

Colloid carcinoma is another name for this extremely uncommon form of invasive ductal carcinoma. Mucinous carcinoma typically affects women in their late 60s and early 70s, particularly after menopause, but it can occur at any age. This breast cancer can be treated because it is benign and has not spread.

Papillary carcinoma in Breast

This rare form of invasive carcinoma affects less than 1 to 2 percent of breast cancer patients. The abnormal cells may rapidly multiply, exhibit a distinct border, and have tiny, finger-like projections. This cancer strikes women of a certain age more frequently.

Cribriform carcinoma in Breast

A rare and unusual form of breast cancer is caused when cancerous cells invade the connective tissue (stroma) of the breast. When the nest's cells appear normal, it may be difficult to see the nest-like structure that forms between the lobules and the breast duct.

Paget's Disease of the Nipple

In this rare form of breast cancer, a group of abnormal cells clusters around or inside the nipple. This malignancy, which begins in the ductal region of the nipple and spreads to the surface and areolar region of the breast, is characterized by itchiness and inflammation.

Phyllodes tumors in Breast

This subtype accounts for statistically less than one percent of all breast cancer cases. The Greek word for "structure like a leaf" is "phyllodes." This is an excellent analogy for the process by which tumor cells divide and multiply. This type of breast cancer is well-known for its rapid progression, despite the fact that it rarely spreads to other parts of the body (metastasizes).

Male breast cancer

Pandemics of male breast cancer are extremely uncommon. For the purpose of research, only a small number of cases have been gathered and made available. An elevated estrogen level and a strong hereditary tendency in the BRCA-1 and

BRCA-2 genes are the primary causes of this type of cancer.

Chemotherapy: Main Stay For Breast Cancer Treatment

Chemotherapy, also known as chemotherapy, is a treatment for cancer that involves injecting or ingesting chemicals that kill tumors. The treatment with chemotherapeutic drugs aims to stop cancer cells from growing and spreading. Chemotherapy can be administered orally or intravenously. Neoadjuvant chemotherapy may be administered to a patient prior to surgery. This procedure is frequently performed to shrink the tumor in order to make breast cancer surgery simpler and less invasive. Doctors can monitor how tumors respond to anti-cancer medications with neoadjuvant chemotherapy, which may help them modify treatment plans or suggest additional chemotherapies.

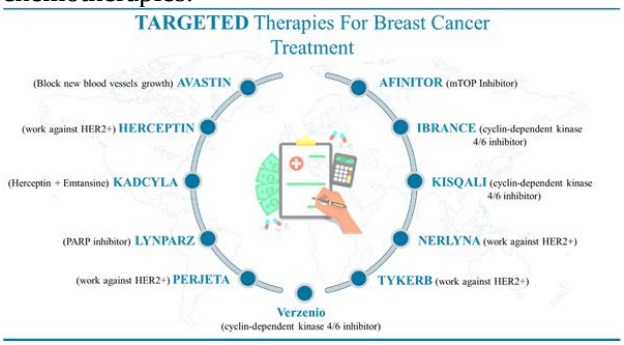

Figure 2.9. Breast cancer treatment options include several targeted therapeutic agents.

The course of treatment that a patient receives following breast cancer surgery is referred to as adjuvant chemotherapy. Most of the time, this method is used to get rid of any remaining cancer cells. When cancer cells in the tail cells multiply uncontrollably, it may lead to the development of additional breast tumors or other body tumors. Adjuvant chemotherapy reduces the likelihood of breast cancer returning.

Chemotherapyformoraggressive andadvanced Breast Cancer

Despite the fact that the cells of advanced breast cancer originated in the breast, they have already spread to other organs. Patients with this kind of cancer typically receive a variety of cytotoxic medications, either individually or in combination. Figure 2.10 depicts breast cancer chemotherapy.

Figure 2.10The many chemotherapeutic agents used to combat breast cancer.

Chemotherapy Combination

In an effort to halt the growth of tumors, numerous chemotherapeutic medications are now being prescribed to patients. These medications are chosen for the specific mechanism by which they kill cells. With continued use, the possibility of patients developing resistance to a single therapeutic medication increase. As a result, it may be difficult to obtain even a single chemotherapeutic agent, necessitating higher dosages, more potential adverse effects, and even the accidental killing of healthy cells. Chemotherapeutic combinations of two or more substances have recently been used more frequently due to the issues with conventional single-agent treatments. A breast cancer combination treatment plan includes chemotherapy, hormone therapy, radiation, and immunotherapy. Low-dose combinations of several drugs can be used to lessen the severity of chemotherapy side effects. The possibility of a synergistic effect is made even greater by the fact

that distinct drugs exert their effects in distinct ways.

Advantagesofcombinationalstrategiesincancer therapy

A novel approach that takes into account the limitations of specific chemotherapy drugs has the potential to improve chemotherapy's therapeutic efficacy. Our second conclusion is that if we employ a combination approach, anti-cancer medications may have fewer adverse effects, which may enhance therapy. It is common knowledge that combination therapy can help overcome the drawbacks of single-drug treatments.

- It can control a variety of signaling pathways.
- It has the potential to both lessen the negative effects of chemotherapy and increase its overall efficacy.
- It may circumvent the process of medication resistance when treating cancer.

A few of the advantages of combination therapy, a cancer treatment strategy that has gained popularity in recent years, are listed below.

1. Using a combined therapy allows us to first take advantage of synergy's primary benefit. When taken together, medication synergy performs better than individual treatments. Because of these advantages, the focus of drug research efforts has shifted dramatically toward investigating novel combination medications. Chemotherapeutic drugs can be analyzed using combination index isobolograms to maximize their effectiveness against cancer while minimizing their side effects on healthy cells. Caspase-3 and caspase-9 are both activated by celecoxib, which has a synergistic effect on cholangiocarcinoma. It is a cyclooxygenase-2 inhibitor based on emodin. Gemcitabine/paclitaxel and a mTOR inhibitor (RAD001) performed just as well against cells from non-Hodgkin lymphoma.
2. The primary factor that contributes to the failure of chemotherapeutic drug therapy is the capacity of cancer cells to develop resistance to a particular treatment. The multi drug efflux pump is a well-known mechanism that, over time, helps cancer cells develop multidrug resistance (MDR). The main drug efflux pumps that are overexpressed in human cancer are multidrug resistance protein-1 (MRP-1), membrane P-glycoprotein (P-gp), and breast cancer resistance protein (BCRP). These proteins are mainly responsible for the removal of chemotherapy medicines from the tumor area. Consider the possibility that P-gp inhibitors and other modulator inhibitors could collaborate to block the MDR proteins that cancer cells overexpress to combat the MDR effect. A new study found that naked mouse brains treated with third-generation P-gp inhibitors like tariquidar and elacridar contained significantly more paclitaxel. Because they reduced P-gp expression, elacridar and tariquidar were harmful to the blood-brain barrier.
3. When gemcitabine and carboplatin were given to people with metastatic ovarian cancer simultaneously, a very high degree of anticancer activity was found. In another instance, it was demonstrated that when Zosuqidarco was administered to patients with myeloid leukemia, it increased the anti-cancer effects of doxorubicina and cytarabine. Paclitaxel and curcumin were found to have a greater cytotoxic effect on Helicoells when administered concurrently, according to a subsequent study. This combination not only increased the effectiveness of fighting cancer by lowering the dose of paclitaxel, but it also made it less likely for patients to experience its side effects.

Commonly Employed Combination Therapy For Cancer Treatment

Radiotherapy along with chemotherapy

In the fight against breast cancer, this strategy has shown the most promise up to this point. When compared to radiation alone, breast cancer patients receiving treatment have a better chance of surviving. In the early 1970s, the combination of 5-fluorouracil and mitomycin-C had significant cytotoxic effects on patients with rectal cancer

receiving radiation treatment. Radiation therapy and the chemotherapeutic drug topotecan have been shown to be effective in treating glioblastoma multiforme and increasing patient survival rates in clinical studies. Similarly, in Phase II clinical trials for prostate cancer, tumor cells were more responsive to the vaccine after radiation therapy and a targeted vaccination that specifically targeted antigens.

Quantificationofdrug encapsulationanddrug loading

By dissolving the lyophilized NPs in acetonitrile, we were able to accomplish our objective of determining the drug's quantity in the NPs. After rapidly vorticing the mixture, it was placed in a shaking incubator at 37°C for three hours to extract the acetonitrile. To figure out how much medicine was in the final solution, Thermo-Scientific-Evolution-201) used ultraviolet (UV) absorption at a specific wavelength of 229 nm. We were able to determine the drug loading and encapsulation efficiency using the following formulas:

$$\text{Encapsulation Efficiency (\%)} = \frac{\text{Mass of encapsulated drug}}{\text{Mass of initial drug}} \times 100 \quad (1)$$

$$\text{Drug loading (\%)} = \frac{\text{Mass of encapsulated drug}}{\text{Mass of polymer used for encapsulation}} \times 100 \quad (2)$$

In-vitro drug release study

With a molecular weight threshold of 8,000 to 14,000, the dialysis bag was used to examine the in-vitro drug release from NPs. The bag received PAX-loaded NPs (20 mg/2 ml) one day after the dialysis membrane was pre-activated in PBS. In order to maintain pH 7.4 and 6.8, the dialysis bag was immersed in 20 mL of PBS containing 0.1% (v/v) Tween80, a non-ionic surfactant, at 37°C and 100 rpm. One milliliter of new medium was added to each set quantity of release medium to keep the sink running smoothly. The PAX concentration was then determined with an ultraviolet spectrophotometer operating at 229 nm. Results expressed as a percentage of cumulative medication release were obtained from three experiments.

Cellline and culture

AMITY University in Noida, India, provided the HEK-293 cell line, while the MCF 7 and MDA MB 231 cell lines were obtained from the NCCS in Pune, India. A mixture of growth medium (DMEM for MCF-7 and L-15 for MDAMB-231), 10% FBS, and one percent antibiotics (100 U/ml penicillin and 100 g/ml streptomycin) was used to seed the cells in a tissue culture flask. A humidified atmospheric incubator supplemented with 5% CO2 was used to keep the cells at 37°C throughout the incubation.

In-vitrocytotoxicitystudies

The standard MTT assay was used to test the NPs' in vitro toxicity to cells. The human breast cancer cell lines HEK293 and MCF7 and MDAMB231 were used to synthesize the NPs. To summarize, before the experiment, the cells were seeded onto a 96-well tissue culture plate at a density of 1 ten to the well and left for 24 hours. Using nutrient-rich particles, cells were cultivated for 0, 6, 12, 24, and 48 hours. Each well was re-incubated for four hours after adding 25 l of MTT solution (5 mg/ml). Dimethyl sulfoxide (DMSO) was used to dissolve the living-cell-produced formazanthus. Two reference wavelengths—570 and 630 nm—were used to quantify optical densities using a microplate reader (model-680, Bio-Rad). We were able to calculate the survival rate as a percentage of cells using the formula below:

$$\text{Cell viability (\%)} = \frac{\text{OD (Test well)}}{\text{OD (reference well)}} \times 100 \quad (3)$$

By repeating each test three times, we were able to verify every one of the findings.

Photoluminescencespectrophotometric analysisforcellularuptake

Before the experiment, I placed the cells in a 12-well plate with 2 105 cells per well for 24 hours to ensure that they absorbed the produced NPs. After three hours of incubation, the cells were treated with Rhd-PCL-NPs and SA-Rhd-PCL-NPs (10 mg/ml) before being washed with PBS. For cell extraction, 500 l of DMSO was used following trypsinization for collection. To further dilute the supernatant after it was collected, 2 milliliters of PBS were added. A Perkin Elmer LS55 fluorescence photoluminescence spectrophotometer, which makes use of Xe lamp excitation sources with wavelengths between 200 and 900 nm, was used to analyze the samples. The intensity of the encoded graphs indicates the NPs' uptake by cells.

Fluorescentmicroscopic analysisofcellular uptake

Torhodamine-loaded NPs were applied to HEK293, MCF7, and MDAMB231 cells to

demonstrate their selectivity against cancer cells. Using the appropriate cell growth medium, cells were plated into a 12-well tissue culture plate to achieve 70% confluence. Prior to the experiment, the cells were exposed to PCL-Rhd-NPs and SA-PCL-Rhd-NPs for up to three hours after the cell growth medium was removed. The cells were fixed for 15 minutes in a solution containing 4% paraformaldehyde after being rinsed with PBS. They were then washed twice with PBS after this. Each well was coated with 5 mL of DAPI (1 g/mL) to expose the cultivated cells' nuclei. The Nikon-ECLIPSE-Ti-U fluorescent microscope was used to take pictures of the relevant cells, and the inference was made by calculating the fluorescence intensity with the Image-J application.

Conclusion

The US Food and Drug Administration (FDA) has approved PLGA as a polymer for drug delivery for a number of reasons, including its biodegradability, drug biocompatibility, manufacturing simplicity, suitable biodegradation kinetics, and mechanical properties. Using PLGA-based nanoparticles to deliver medications has many advantages. They might prevent drugs from breaking down and make them more stable. Through endothelial fenestrations or overexpressed receptors, nanoparticles can also cross the blood-brain barrier and enter inflammatory or malignant organs. Because of this, targeted delivery of proteins, peptides, nucleic acids, or medicinal compounds to certain organs is now feasible. By continuously releasing the therapeutic substance from stable sources, PLGA-based nanoparticles have the potential to enhance treatment efficacy. In comparison to other polymers, nanoparticles derived from PLGA are well-suited for clinical trials. This is because PLGA has been approved for use in a variety of drug delivery systems by both the FDA and the EMA. Biomedical research into drug delivery with PLGA or polymers derived from PLGA has many promising avenues for maximizing therapeutic (antitumor) efficacy while minimizing adverse effects.

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Cite this article as:
Kumar J. and Dubey V. (2025). PLGA-Based Dual Drug Delivery and Targeted Nanoparticle Systems for Enhanced Breast Cancer Therapy. *Int. J. of Pharm. & Life Sci.*, 16(8):10-20.

Source of Support: Nil
Conflict of Interest: Not declared
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