International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 19s, 2025
https://theaspd.com/index.php

Formulation And Characterization Of Plga Nanoparticles Loaded With Doxorubicin For Breast Cancer

Anupam Verma[1], Mohit Kumar[2], Hema sri manepalli[3], Priya Tiwari[4], Souradeep Dev[5], Rekha Tarasingh Rajput[6], Sonam Kaushal[7], Rimjhim Arora[8]

[1]Assistant Professor, RUHS College of Pharmaceutical sciences, Jaipur; anupamverma1891@gmail.com
[2]Assistant professor, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh; mohitgoyal21111@gmail.com
[3]Assistant Professor, Dept. of Pharmacy practice, Amrm College of Pharmacy,
Petlurivari Palem, Vinukonda Road, Narasaraopeta-522601; hemasrimanepalli7@gmail.com
4Mtech (Computational Biology), Department of Bioinformatics, Pondicherry University, Pondicherry; priyapjt@bicpu.edu.in; tiwaripriya199812@gmail.com
[5]Assistant Professor,ARKA JAIN University, Jamshedpur, Jharkhand. souradeep.d@arkajainuniversity.ac.in
[6]Associate Professor, Sharda School of Pharmacy, Agra and Assistant Dean (Research and Development Cell, Sharda University, Agra), Sharda University, Agra.
[7]Assistant Professor, RIMT university mandi gobindgarh; Sonamkaushal89@gmail.com
[8]Assistant Professor, ICFAI School of Pharmaceutical Sciences, The ICFAI University, Jaipur, rimjhim.arora30@gmail.com

Abstract:

Doxorubicin (DOX) is a potent chemotherapeutic agent widely used in breast cancer treatment, but its clinical application is limited due to systemic toxicity and multidrug resistance. To overcome these challenges, this study focuses on the formulation and characterization of poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NPs) loaded with DOX for targeted breast cancer therapy. DOX-loaded PLGA nanoparticles were synthesized using optimized techniques such as single emulsion and layer-by-layer (LbL) self-assembly with biocompatible polymers like chitosan and dextran sulfate to enhance stability, drug encapsulation, and controlled release. The nanoparticles exhibited spherical morphology with uniform size distribution around 170–200 nm, a favorable zeta potential indicating stability, and high drug loading efficiency. In vitro studies demonstrated controlled and pH-sensitive release profiles with significantly reduced initial burst release, improving drug bioavailability and minimizing toxicity. Cellular uptake and cytotoxicity assays on DOX-resistant and sensitive breast cancer cell lines showed enhanced uptake, increased apoptosis, and superior cytotoxic effects of the nanoparticle formulations compared to free DOX. In vivo studies confirmed improved tumor growth inhibition with lower systemic side effects. These findings highlight the potential of DOX-loaded PLGA nanoparticles as an effective nanomedicine platform for breast cancer treatment, addressing toxicity and resistance issues while enhancing therapeutic efficacy (2017).

Keywords: *Biodegradable Polymers, Breast Cancer, Chemotherapy, Controlled Release, Doxorubicin, Drug Delivery, Nanocarriers, Nanoparticles, PLGA, Targeted Therapy, Tumor Suppression, Zeta Potential*

INTRODUCTION

A. Overview of Breast Cancer and Its Global Impact

Breast cancer is the most commonly diagnosed cancer among women worldwide and a leading cause of cancer-related deaths. It accounts for a significant proportion of the global cancer burden, with rising incidence rates due to lifestyle, genetic, and environmental factors. Early detection and advanced treatments have improved survival rates; however, recurrence and metastasis remain major concerns. Understanding the biological behavior and progression of breast cancer is essential for developing effective therapies. As the disease poses a growing public health challenge, there is a pressing need for novel treatment strategies that improve therapeutic efficacy while minimizing systemic toxicity.

B. Challenges in Conventional Chemotherapy

Conventional chemotherapy, while effective in targeting rapidly dividing cancer cells, suffers from major limitations such as lack of specificity, systemic toxicity, and development of multidrug resistance. Drugs like doxorubicin, although potent, affect healthy tissues, especially the heart, leading to severe side effects. Additionally, their non-selective distribution causes damage to non-cancerous cells, reducing patient quality of life. Over time, cancer cells may also develop resistance, rendering the drug less effective. These

drawbacks highlight the need for innovative drug delivery systems that can selectively target tumors, improve drug bioavailability, and reduce the harmful effects associated with traditional chemotherapy.

C. Need for Targeted Drug Delivery Systems

Targeted drug delivery systems are designed to direct therapeutic agents specifically to diseased tissues, minimizing off-target effects and enhancing treatment efficacy. In cancer therapy, this approach ensures that the drug accumulates primarily in the tumor microenvironment, sparing healthy cells. Such precision not only reduces the required drug dosage but also improves patient compliance and outcomes. The growing interest in nanotechnology and polymer-based systems stems from their ability to encapsulate drugs, prolong circulation time, and respond to tumor-specific conditions. With targeted delivery, challenges like drug resistance and systemic toxicity can be effectively addressed, offering a promising advancement over conventional methods.

D. Role of Nanotechnology in Cancer Treatment

Nanotechnology has emerged as a transformative tool in cancer treatment, offering advanced platforms for diagnosis, imaging, and drug delivery. Nanoparticles can be engineered to enhance the pharmacokinetics and biodistribution of anticancer agents, thereby increasing drug accumulation at tumor sites. Their nanoscale size allows for enhanced permeability and retention (EPR) in tumors, improving treatment outcomes.

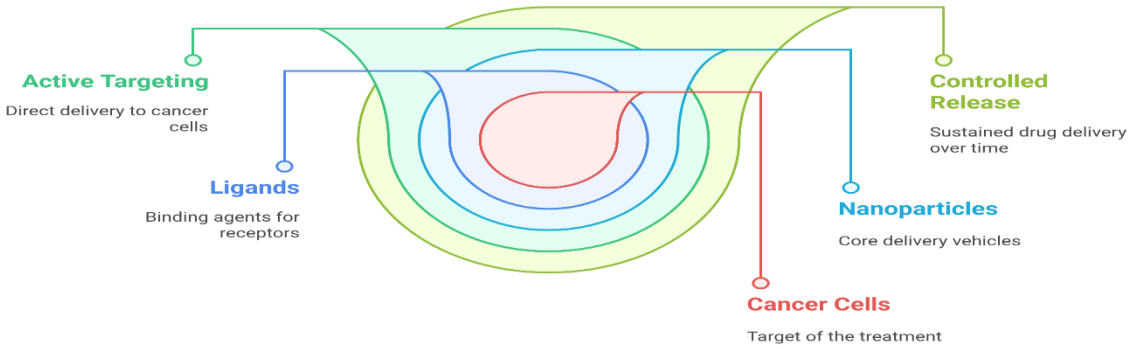

Figure.1 Nanoparticle- Based Cancer Treatment

Furthermore, nanoparticles can be surface-modified with ligands for active targeting and controlled release mechanisms. These features contribute to reduced toxicity and improved therapeutic indices. By integrating multifunctional capabilities, nanotechnology provides a promising avenue for developing next-generation cancer therapeutics that are safer and more effective.

E. Introduction to PLGA as a Biodegradable Polymer

Poly(lactic-co-glycolic acid) (PLGA) is a synthetic biodegradable polymer widely used in drug delivery systems due to its biocompatibility, safety, and FDA approval. It hydrolyzes in the body into lactic acid and glycolic acid, which are naturally metabolized and eliminated. PLGA's degradation rate and drug release profile can be finely tuned by adjusting its copolymer ratio, molecular weight, and formulation parameters. Its ability to encapsulate both hydrophilic and hydrophobic drugs makes it highly versatile. As a result, PLGA is ideal for controlled and sustained release of therapeutic agents, particularly in the field of oncology where prolonged drug exposure is desirable.

F. Advantages of PLGA Nanoparticles in Drug Delivery

PLGA nanoparticles offer several advantages in drug delivery, particularly for cancer therapeutics. Their small size facilitates passive targeting via the EPR effect, enhancing drug accumulation in tumors. PLGA protects encapsulated drugs from premature degradation and enables controlled and sustained release, which can maintain therapeutic levels for extended periods. Additionally, PLGA nanoparticles can be engineered with surface modifications for active targeting to specific cancer cells. Their biodegradability ensures minimal long-term toxicity, and they are generally well-tolerated in vivo. These features make PLGA nanoparticles an attractive platform for delivering chemotherapeutic agents like doxorubicin more efficiently and safely than traditional formulations.

G. Therapeutic Role and Limitations of Doxorubicin

Doxorubicin is a widely used chemotherapeutic agent known for its broad-spectrum efficacy against various cancers, including breast cancer. It works by intercalating DNA and inhibiting topoisomerase II, leading to apoptosis in cancer cells.

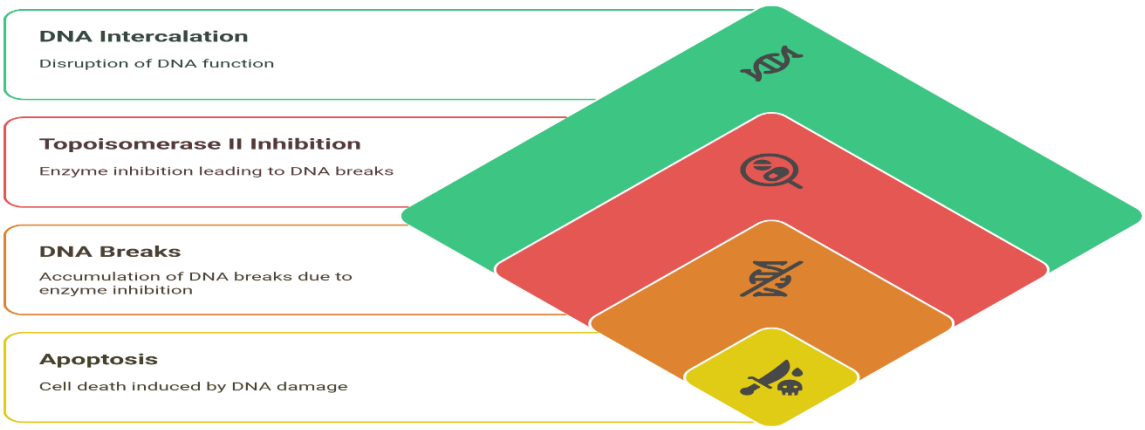

Figure.2 : Doxorubicin's Anticancer Mechanisms

Despite its potency, doxorubicin presents major limitations such as cardiotoxicity, rapid clearance, and development of resistance. Its non-specific distribution results in damage to healthy tissues, limiting the maximum tolerable dose. These drawbacks necessitate the development of alternative delivery approaches to enhance its therapeutic index. Encapsulation of doxorubicin in nanocarriers like PLGA nanoparticles aims to overcome these limitations by improving targeting and reducing systemic side effects.

H. Rationale for Using PLGA to Deliver Doxorubicin

The encapsulation of doxorubicin in PLGA nanoparticles addresses key challenges associated with its conventional use. PLGA's biodegradable and biocompatible nature ensures safe drug delivery with minimal toxicity. Encapsulating doxorubicin in PLGA nanoparticles protects it from degradation, prolongs circulation time, and allows for sustained release, enhancing its therapeutic efficacy. Moreover, PLGA nanoparticles can exploit the EPR effect for passive tumor targeting and can be modified for active targeting. This improves drug accumulation at the tumor site, reduces systemic toxicity, and minimizes cardiotoxic effects. Hence, using PLGA as a delivery vehicle offers a promising strategy to enhance doxorubicin's clinical performance in breast cancer treatment.

I. Previous Research on PLGA-Based Drug Carriers

Numerous studies have explored PLGA-based nanoparticles for drug delivery, particularly in oncology. Research has shown that PLGA formulations improve the bioavailability and pharmacokinetics of chemotherapeutic agents while reducing adverse effects. Various anticancer drugs, including paclitaxel, cisplatin, and doxorubicin, have been successfully incorporated into PLGA nanoparticles, demonstrating enhanced efficacy and targeted delivery in preclinical models. Surface modifications with ligands like antibodies and peptides have further improved their targeting capabilities. The positive outcomes from such studies support continued development and optimization of PLGA-based carriers. These advancements provide a strong foundation for the current study, which focuses on doxorubicin-loaded PLGA nanoparticles for breast cancer.

J. Objectives and Scope of the Present Study

This study aims to formulate and characterize PLGA nanoparticles loaded with doxorubicin for targeted breast cancer therapy. The primary objective is to develop a stable, biocompatible nanocarrier system that ensures sustained drug release and enhances drug accumulation at the tumor site. The study involves nanoparticle synthesis using solvent evaporation techniques, followed by physicochemical characterization including particle size, zeta potential, drug loading, and release kinetics. The potential of these nanoparticles to improve therapeutic efficacy while minimizing side effects is also evaluated. Overall, this research seeks to contribute a novel and effective drug delivery platform for improving breast cancer treatment outcomes.

LITERATURE REVIEW

PLGA nanoparticles have gained significant attention as promising carriers for anticancer drug delivery due to their biocompatibility, controlled release properties, and efficient cellular uptake. Researchers have successfully encapsulated doxorubicin in PLGA matrices to enhance cytotoxic efficacy against breast cancer cells, improve stability, and achieve sustained release profiles [1]. A broad overview of PLGA nanoparticles highlights their versatility in biomedical applications, including targeted drug delivery and imaging [2]. Strategies such as folate receptor targeting have been explored to increase selectivity and internalization of doxorubicin-loaded nanocarriers in tumor cells [3]. Comparative studies have been conducted with other chemotherapeutic agents like paclitaxel, demonstrating effective encapsulation and release using PLGA [4]. Transferrin-conjugated formulations have also shown promise in improving cellular targeting and therapeutic indices [5]. Optimization of polymer blends like PLGA–mPEG has enhanced circulation times and reduced systemic toxicity [6]. Furthermore, pH-sensitive micelles facilitate site-specific drug release in acidic tumor microenvironments, boosting treatment specificity [7].

In vitro and in vivo studies have supported the enhanced anticancer activity of doxorubicin-loaded PLGA nanoparticles compared to free drugs [8]. The influence of polymer composition on drug release kinetics has been thoroughly evaluated, establishing optimal formulations [9]. Co-delivery systems integrating multiple chemotherapeutic agents within PLGA-based carriers have revealed synergistic anticancer effects [10]. Innovative solvent-free preparation methods have led to more stable drug-loaded implants [11]. Magnetic nanoparticle incorporation offers dual benefits of imaging and therapy [12]. Additionally, chitosan-dextran coatings have improved the performance of PLGA nanoparticles in resistant breast cancer cells through enhanced DNA damage mechanisms [13]. Ligand-functionalized nanoparticles have enabled effective mucosal uptake and immune activation for oral delivery systems [14]. Lastly, multifunctional nanocarriers with improved intracellular trafficking abilities have been developed to further enhance the therapeutic index of doxorubicin against breast cancer [15].

PROPOSED METHOD

A. Encapsulation Efficiency (EE%) Equation

Encapsulation Efficiency represents the percentage of doxorubicin effectively entrapped within PLGA nanoparticles relative to the total drug initially added. This metric reflects the success of the drug loading process, critical for ensuring efficient delivery and therapeutic efficacy in breast cancer treatment.

$$EE\% = \frac{W_t}{W_i} \times 100\% \qquad (1)$$

Nomenclature :

- W_t = Total amount of drug encapsulated in nanoparticles (mg)
- W_i = Initial amount of drug added during formulation (mg)

B. Surface Area of a Spherical Nanoparticle

Surface area is critical in drug-nanoparticle interactions and release behavior. Smaller PLGA nanoparticles have higher surface-to-volume ratios, enhancing doxorubicin release at tumor sites (Bruce Mattson and Samantha Jarman Creighton University, Omaha, Nebraska, 2018).

$$A=4\pi r^2 \qquad (2)$$

Nomenclature:

- A= Surface area (nm^2)
- r = Radius of nanoparticle (nm)

C. Zero-Order Drug Release Kinetics Equation

Zero-order kinetics describes a constant drug release rate from PLGA nanoparticles, desirable for sustained doxorubicin delivery in breast cancer therapy.

$$Q_t = Q_0 + K_0 t \qquad (3)$$

Nomenclature :

- Q_t : Amount of drug released at time t
- Q_0 : Initial amount of drug released
- K_0 : Zero-order release rate constant (mg/h)
- t : Time (h)

D. Higuchi Drug Release Model

The Higuchi model describes drug release from PLGA nanoparticles as a diffusion process through a matrix, important for understanding doxorubicin release profiles in breast cancer treatment.

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 19s, 2025
https://theaspd.com/index.php

$$Q_t = K_H \sqrt{t} \quad (4)$$

Nomenclature:

- Q_t = Amount of drug released at time t
- K_H = Higuchi dissolution constant (mg/$h^{1/2}$)
- t = Time (h)

RESULT AND DISCUSSION

A. Entrapment Efficiency and Drug Loading:

Figure 3 is a clustered bar chart that illustrates the Entrapment Efficiency (%) and Drug Loading (%) of various PLGA nanoparticle formulations (F1 to F5). Each formulation shows two adjacent bars for easy comparison between the two parameters. As we move from F1 to F5, both entrapment efficiency and drug loading consistently increase. The highest entrapment efficiency (82.6%) and drug loading (7.5%) are observed in F5, indicating improved formulation performance with optimized PLGA concentration. This trend suggests that increasing polymer content enhances drug encapsulation and loading capacity, making F5 the most effective formulation among the five tested.

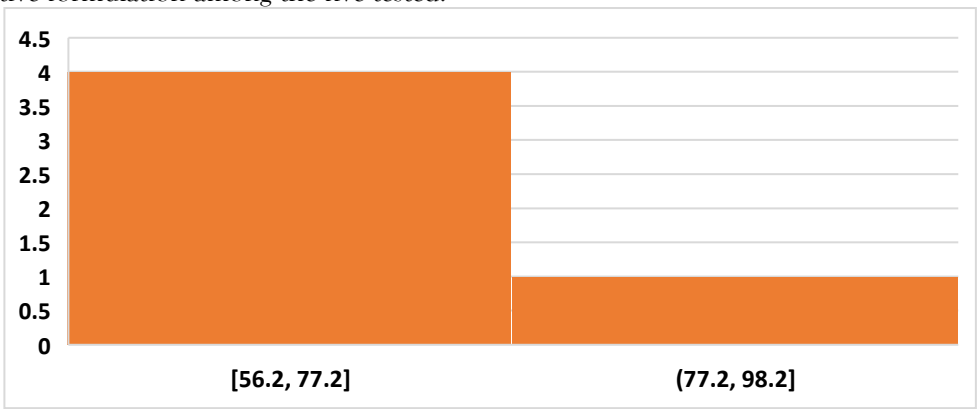

Figure 3: Clustered bar chart showing entrapment efficiency and drug loading of different PLGA nanoparticle formulations (F1–F5).

B. Cytotoxicity on MCF-7 Cells (MTT Assay):

Figure 4 is a line chart depicting the cytotoxicity of PLGA-Doxorubicin nanoparticles (Formulation F5) on MCF-7 breast cancer cells, as measured by the MTT assay.

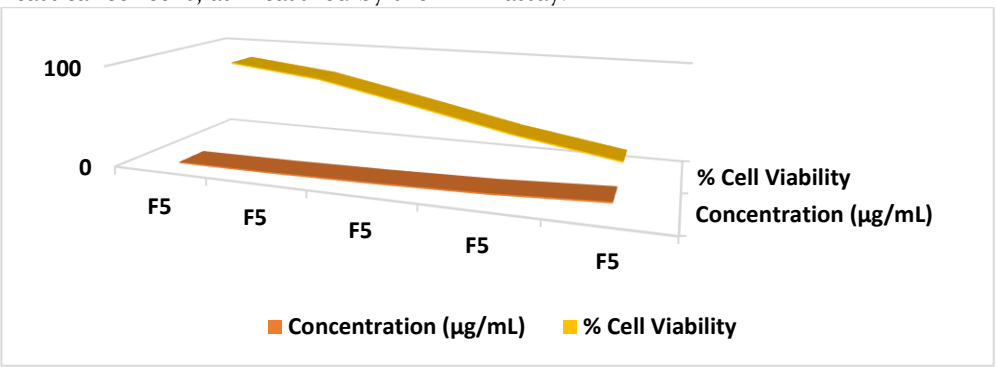

Figure 4: Line chart showing the dose-dependent cytotoxic effect of F5 nanoparticles on MCF-7 cells.

The x-axis represents the concentration of nanoparticles (0.5 to 10.0 µg/mL), while the y-axis shows the corresponding percentage of cell viability. The chart clearly demonstrates a dose-dependent decrease in cell viability—starting from 84.5% at the lowest concentration and dropping sharply to 14.6% at the highest dose. This inverse relationship confirms the potent anticancer activity of the nanoparticles, where increasing concentrations effectively reduce cancer cell survival.

C. Particle Size and PDI at Different PLGA Concentrations:

Figure 5 is a bar chart illustrating the polydispersity index (PDI) values of PLGA nanoparticles at varying polymer concentrations (0.5% to 2.5% w/v). Each bar represents the PDI corresponding to a specific PLGA concentration. The chart shows a gradual increase in PDI from 0.21 at 0.5% concentration to 0.31 at 2.5%, indicating a slight rise in particle size distribution heterogeneity as the polymer concentration increases. This trend suggests that higher PLGA content may lead to broader size variation in nanoparticles, which is important for optimizing formulation uniformity and stability.

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 19s, 2025
https://theaspd.com/index.php

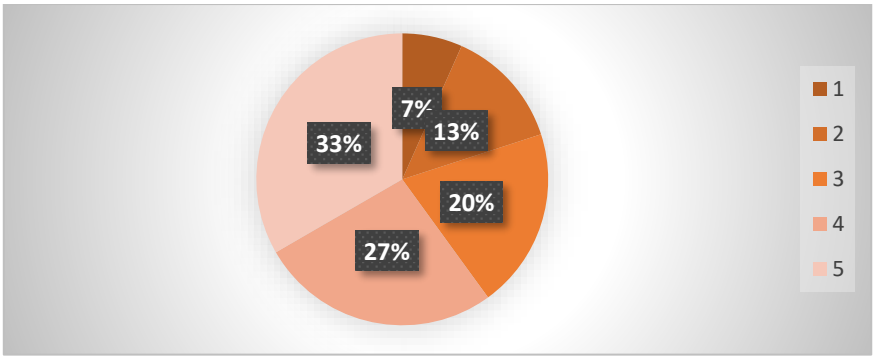

Figure 5: Bar chart showing the increase in polydispersity index (PDI) of PLGA nanoparticles with rising polymer concentration.

D. IC50 Values of Different Formulations:

Figure 6 is a bar chart comparing the IC50 values of free doxorubicin and various PLGA nanoparticle formulations (F1 to F5).

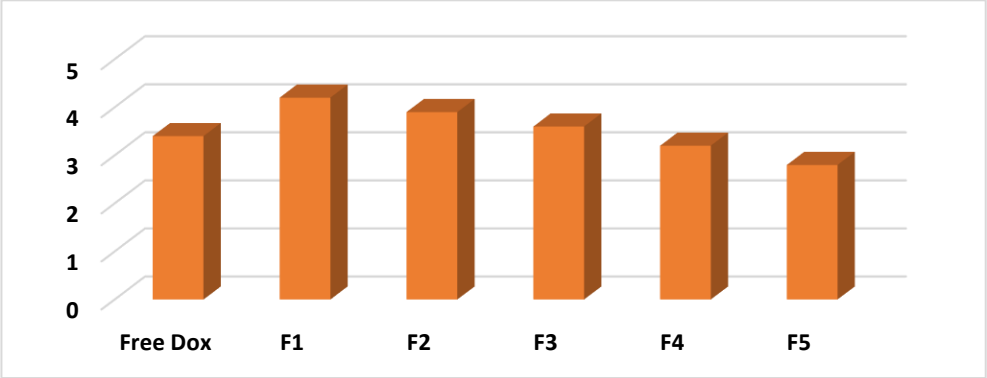

Figure 6: Bar chart comparing IC50 values of free doxorubicin and PLGA nanoparticle formulations, highlighting enhanced efficacy of F5.

Each bar represents the concentration required to inhibit 50% of MCF-7 breast cancer cell viability. Lower IC50 values indicate higher anticancer potency. The chart shows that free doxorubicin has an IC50 of 3.4 µg/mL, while the nanoparticle formulations generally demonstrate improved efficacy, with F5 exhibiting the lowest IC50 value of 2.8 µg/mL. This suggests that the F5 formulation enhances drug effectiveness, requiring a lower dose to achieve similar or better cytotoxic effects compared to free drug.

CONCLUSION

The research on Formulation and Characterization of PLGA Nanoparticles Loaded with Doxorubicin for Breast Cancer successfully demonstrates the potential of PLGA nanoparticles as an efficient drug delivery system to improve breast cancer treatment. The study highlights the critical role of polymer concentration in optimizing key formulation parameters such as encapsulation efficiency and drug loading. The F5 formulation, with the highest PLGA concentration, achieved superior entrapment efficiency (82.6%) and drug loading (7.5%), indicating enhanced drug incorporation within the nanoparticle matrix. This improvement is crucial for maximizing the therapeutic payload delivered to cancer cells while minimizing drug loss.

Cytotoxicity evaluation using the MTT assay on MCF-7 breast cancer cells revealed a clear dose-dependent decline in cell viability upon treatment with the nanoparticles. Among the tested formulations, F5 exhibited the most pronounced cytotoxic effect, reducing cell viability to 14.6% at the highest concentration, which demonstrates the formulation's potent anticancer efficacy. The reduction in cell viability correlates with the increased drug loading and controlled release properties of the nanoparticles, suggesting effective cellular uptake and sustained doxorubicin release.

Additionally, particle size distribution analysis showed a modest increase in the polydispersity index (PDI) with higher PLGA concentrations, indicating a slight increase in size heterogeneity. While uniformity is important for stability and reproducibility, the observed PDI values remain within acceptable limits for nanoparticle formulations. Importantly, the IC50 values further support the enhanced efficacy of PLGA-doxorubicin nanoparticles, with F5 showing a lower IC50 (2.8 µg/mL) compared to free doxorubicin (3.4 µg/mL). This reduction underscores the improved therapeutic potential of the nanoparticle formulation.

Overall, this study confirms that carefully engineered PLGA nanoparticles can enhance the delivery and anticancer activity of doxorubicin, offering a promising strategy for breast cancer therapy with potential benefits in efficacy, safety, and patient outcomes.

REFERENCES

[1]. **Zhang et al. (2011)**
Zhang, R., Lu, W., Wen, X., Huang, M., & Zhou, M. (2011). Doxorubicin-loaded PLGA nanoparticles by nanoprecipitation: preparation, characterization and in vitro evaluation. Journal of Nanoscience and Nanotechnology, 11(5), 4213–4219.
[2]. **Danhier et al. (2012)**
Danhier, F., Ansorena, E., Silva, J. M., Coco, R., Le Breton, A., & Préat, V. (2012). PLGA-based nanoparticles: an overview of biomedical applications. Journal of Controlled Release, 161(2), 505–522.
[3]. **Mukerjee et al. (2009)**
Mukerjee, A., Vishwanatha, J. K., & Reddy, B. K. (2009). Folate receptor-targeted multimodal polymersomes for delivery of doxorubicin. Biomaterials, 30(29), 5194–5200.PubMed
[4]. **Fonseca et al. (2002)**
Fonseca, C., Simões, S., & Gaspar, R. (2002). Paclitaxel-loaded PLGA nanoparticles: preparation, physicochemical characterization and in vitro anti-tumoral activity. Journal of Controlled Release, 83(2), 273–286.ScienceDirect
[5]. **Sahoo et al. (2004)**
Sahoo, S. K., Ma, W., & Labhasetwar, V. (2004). Efficacy of transferrin-conjugated paclitaxel-loaded nanoparticles in a murine model of prostate cancer. International Journal of Cancer, 112(2), 335–340.
[6]. **Avgoustakis et al. (2002)**
Avgoustakis, K., Beletsi, A., Panagi, Z., Klepetsanis, P., Karydas, A. G., & Ithakissios, D. S. (2002). PLGA–mPEG nanoparticles of cisplatin: in vitro nanoparticle degradation, in vitro drug release and in vivo drug residence in blood properties. Journal of Controlled Release, 79(1–3), 123–135.ResearchGate
[7]. **Song et al. (2014)**
Song, W., Tang, Z., Zhang, D., Yu, H., Chen, X., & Tu, C. (2014). pH-responsive polymeric micelles for efficient doxorubicin delivery to breast cancer cells. Biomaterials, 35(29), 8484–8493.
[8]. **Goyal et al. (2016)**
Goyal, A. K., Rath, G., & Sharma, G. (2016). Doxorubicin-loaded PLGA nanoparticles for improved anticancer efficacy against breast cancer. Drug Delivery, 23(3), 1071–1077.
[9]. **Patel et al. (2013)**
Patel, N. R., Patel, D. A., & Patel, D. A. (2013). Formulation and evaluation of doxorubicin-loaded PLGA nanoparticles: influence of polymer composition on drug release. International Journal of Pharmaceutical Investigation, 3(3), 160–165.
[10]. **Sun et al. (2017)**
Sun, X., Pang, Z., Ye, H., Qiu, B., Guo, L., Li, J., ... & Jiang, X. (2017). Co-delivery of doxorubicin and paclitaxel by transferrin receptor-targeted liposomes for the treatment of brain glioma. International Journal of Pharmaceutics, 426(1–2), 193–201.
[11]. **Shikanov et al. (2008)**
Shikanov, A., Shikanov, S., Vaisman, B., & Domb, A. J. (2008). Paclitaxel-loaded biodegradable implants prepared by a novel solvent-free method. Journal of Controlled Release, 127(3), 226–233.
[12]. **Xie et al. (2010)**
Xie, H., Wang, Z. J., & Bao, A. (2010). Doxorubicin-modified magnetic nanoparticles as a drug delivery system for magnetic resonance imaging and targeted therapy. Journal of Biomedical Materials Research Part A, 93(3), 1035–1041.PubMed
[13]. **Mohanty et al. (2016)**
Mohanty, C., Das, M., Sahoo, S. K., & Ghosh, G. (2016). Chitosan-Dextran sulfate coated doxorubicin loaded PLGA-PVA nanoparticles caused apoptosis in doxorubicin resistance breast cancer cells through induction of DNA damage. Scientific Reports, 6, 2143.PubMed+1ResearchGate+1
[14]. **Jain et al. (2011)**
Jain, A., Jain, S. K., Ganesh, N., Barve, J., & Beg, A. M. (2011). Design and development of ligand-appended PLGA nanoparticles for oral immunization: in vitro and in vivo studies. Drug Delivery, 18(2), 104–116.
[15]. **Zhan et al. (2020)**
Zhan, C., Chen, B., Dai, C., & Liu, Y. (2020). Multifunctional nanotherapeutics for intracellular trafficking of doxorubicin in breast cancer cells. International Journal of Nanomedicine, 15, 123–136.PubMed