



DEVELOPMENT OF PH-RESPONSIVE POLYMERIC NANOPARTICLES FOR TARGETED DOXORUBICIN DELIVERY IN BREAST CANCER: ADVANCES, DESIGN STRATEGIES, AND FUTURE PERSPECTIVES

Deepika Gupta ^{1,*}, Sourabh Jain ², Rohit ³, Shelly ⁴, Nivesh P. Singh Gurjar ⁵ and Ravindra B. Malabadi ^{6,7}

¹ Faculty of Pharmacy, Oriental University, Indore- 453555, Madhya Pradesh State, India.

² Analytical-R&D, Kusum Healthcare Pvt.Ltd. Chopanki, Bhiwadi, Alwar- 301019, Rajasthan State, India.

³ Department of Pharmaceutical science, Maharishi dayanand university, rohtak- 124001, Haryana State, India.

⁴ Centre for medical biotechnology, Maharishi dayanand university, rohtak- 124001, Haryana State, India.

⁵ Sage Institute of Research and Technology, Sage University Bhopal - 462022, Madhya Pradesh State, India

⁶ Miller Blvd, NW, Edmonton, Alberta, Canada.

⁷ Scientist and Consultant (Independent) in Biotechnology, Belagavi-590003, Karnataka State, India.

* Corresponding Author

Open Access Research Journal of Biology and Pharmacy, 2026, 18(01), 006–016

Publication history: Received on 02September 2026; revised on 11 October 2026; accepted on 13 October 2026

Article DOI: <https://doi.org/10.53022/oarjbp.2026.18.1.0051>

Copyright © 2026 Author(s) retain the copyright of this article. This article is published under the terms of the Creative Commons Attribution License 4.0

ABSTRACT

Breast cancer remains a major cause of cancer-related mortality among women worldwide. Although doxorubicin is widely used in chemotherapy, its clinical application is limited by cardiotoxicity, systemic toxicity, and non-specific drug distribution. pH-responsive polymeric nanoparticles offer a promising approach for targeted drug delivery by releasing doxorubicin in the acidic tumor microenvironment while maintaining stability under physiological conditions. Biodegradable polymers, including PLGA, PEG, chitosan, and poly(β -amino esters), have been investigated for developing these nanocarriers. Preclinical studies indicate improved intracellular drug delivery, enhanced antitumor activity, and potential reductions in systemic toxicity. This review highlights recent advances in the design, development, and therapeutic applications of pH-responsive polymeric nanoparticles for doxorubicin delivery in breast cancer, along with challenges in safety, clinical translation, and regulatory approval. These systems hold considerable potential for improving targeted cancer therapy.

Keywords: Ph-Responsive Nanoparticles, Polymeric Nanocarriers, Doxorubicin Delivery, Breast Cancer, Targeted Drug Delivery, Nanomedicine, Drug Resistance

1 INTRODUCTION

Breast cancer is the most frequently diagnosed cancer among women worldwide and represents a major global health burden[1-94-99].According to the **World Health Organization**, breast cancer accounts for a substantial proportion of cancer incidence and mortality among women globally[1, 94-99]. Despite significant improvements in early diagnosis and therapeutic strategies, chemotherapy remains a fundamental component of breast cancer treatment[1, 94-99]. Anthracycline antibiotics such as **Doxorubicin** are widely used due to their potent anticancer activity [1].

Doxorubicin exerts its cytotoxic effects through multiple mechanisms including DNA intercalation, inhibition of **Topoisomerase II**, and generation of reactive oxygen species. However, its clinical use is limited by severe adverse effects such as cardiotoxicity and systemic toxicity. These limitations have stimulated the development of advanced drug delivery systems to improve therapeutic outcomes. [2]

Nanotechnology has revolutionized drug delivery by enabling the development of nanoscale carriers capable of targeted and controlled drug release. Polymeric nanoparticles are among the most promising nanocarriers due to their biodegradability, biocompatibility, and ability to encapsulate various therapeutic agents. Stimuli-responsive nanoparticles have gained significant attention because they can release drugs in response to environmental triggers such as pH, temperature, enzymes, or redox conditions [3]. Among these stimuli, pH-responsive systems are particularly attractive for cancer therapy because tumor tissues exhibit an acidic microenvironment compared with normal tissues. Tumor extracellular pH typically ranges from **6.5–6.8**, whereas endosomal and lysosomal compartments have even lower pH values. This pH gradient can be exploited to trigger drug release specifically at tumor sites, thereby enhancing therapeutic efficacy and minimizing systemic toxicity[4].

2 TUMOR MICROENVIRONMENT AND PH GRADIENT

The tumor microenvironment (TME) plays a crucial role in cancer progression, metastasis, and drug delivery. It consists of cancer cells, stromal cells, immune cells, extracellular matrix components, and various signaling molecules that interact dynamically to influence tumor development. One of the most important characteristics of the TME is its altered metabolic profile, which significantly affects the local chemical environment [5].

Cancer cells typically exhibit metabolic reprogramming known as the **Warburg effect**, in which glucose is preferentially metabolized through glycolysis even in the presence of oxygen. This metabolic shift leads to increased production of lactate and hydrogen ions, resulting in acidification of the extracellular tumor environment. The accumulation of acidic metabolites contributes to tumor progression, invasion, and resistance to therapy [6].

In normal physiological tissues, the extracellular pH is tightly regulated at approximately **7.4**. In contrast, tumor tissues often display acidic extracellular pH values ranging between **6.5 and 7.2** due to enhanced glycolysis, insufficient blood perfusion, and inadequate lymphatic drainage. This difference between normal and tumor tissue pH creates a measurable pH gradient that can be exploited for targeted drug delivery strategies[7].

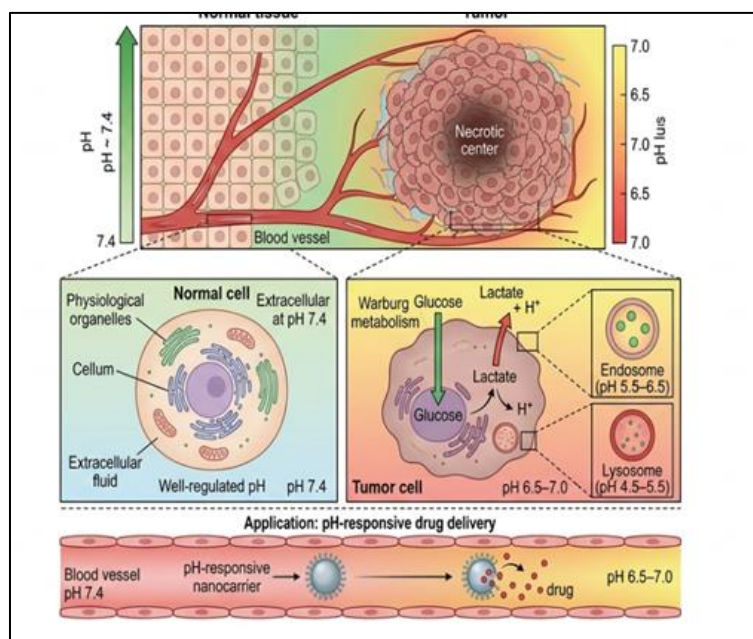


Figure 1: Tumor Microenvironment pH Gradient

Moreover, intracellular organelles such as endosomes and lysosomes possess even more acidic environments. Endosomes typically exhibit pH values between **5.5 and 6.5**, while lysosomes maintain pH values ranging from **4.5 to 5.5**. These acidic compartments play an essential role in the intracellular trafficking and degradation of nanoparticles after cellular uptake [8].

The existence of these pH gradients provides a valuable opportunity for designing **stimuli-responsive drug delivery systems**, particularly pH-sensitive nanoparticles. Such systems remain stable under physiological conditions but undergo structural changes or degradation in acidic environments, enabling selective drug release within tumor tissues. This strategy enhances therapeutic efficacy while minimizing systemic toxicity and adverse effects [9].

3 DOXORUBICIN IN BREAST CANCER THERAPY

Doxorubicin is one of the most widely used chemotherapeutic agents in the treatment of breast cancer. It belongs to the anthracycline class of antibiotics and has demonstrated significant antitumor activity against a broad range of malignancies. Due to its high cytotoxic potential, doxorubicin is commonly used either alone or in combination with other chemotherapeutic drugs for the management of breast cancer. However, its therapeutic application is limited by several dose-dependent toxicities and systemic side effects [10].

3.1 Mechanism of Action

Doxorubicin exerts its anticancer effects through multiple mechanisms:

- **DNA intercalation:** Doxorubicin intercalates between adjacent DNA base pairs, disrupting DNA replication and transcription processes [11].
- **Topoisomerase II inhibition:** The drug stabilizes the DNA-topoisomerase II complex and prevents the religation of DNA strands, resulting in DNA double-strand breaks and cell death [12].
- **Reactive oxygen species generation:** Doxorubicin undergoes redox cycling that produces reactive oxygen species (ROS), which damage cellular membranes, proteins, and nucleic acids [13].
- **Apoptosis induction:** The accumulation of DNA damage and oxidative stress ultimately activates apoptotic pathways leading to programmed cell death in cancer cells [14].

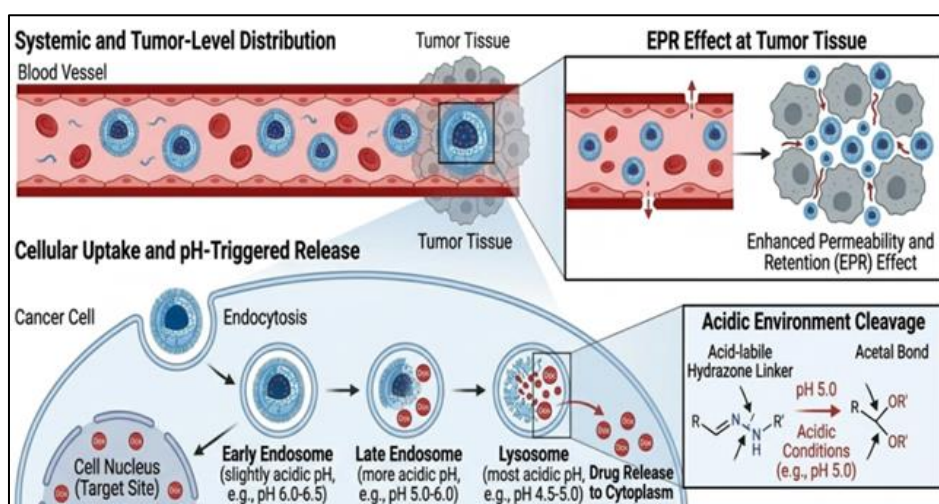


Figure 2: Mechanism of pH-Triggered Drug Release

3.2 Limitations of Doxorubicin Therapy

Despite its strong anticancer activity, doxorubicin therapy is associated with several significant limitations:

- **Cardiotoxicity:** One of the most serious adverse effects of doxorubicin is cumulative dose-dependent cardiotoxicity, which can lead to cardiomyopathy and congestive heart failure [15].
- **Myelosuppression:** Doxorubicin can suppress bone marrow activity, resulting in reduced production of blood cells and increased susceptibility to infections [16].
- **Drug resistance:** Cancer cells may develop resistance through mechanisms such as overexpression of efflux transporters, including **P-glycoprotein**, reducing intracellular drug accumulation [17].
- **Non-specific biodistribution:** Conventional doxorubicin lacks tumor specificity, leading to drug accumulation in healthy tissues and causing systemic toxicity [18].

These limitations emphasize the urgent need for **targeted and controlled drug delivery systems**, such as nanoparticle-based carriers, which can enhance drug accumulation in tumor tissues while minimizing adverse effects in normal organs [19].

4 POLYMERIC NANOPARTICLES IN DRUG DELIVERY

Polymeric nanoparticles are nanoscale drug carriers typically ranging from **10–200 nm** in diameter. These nanoparticles are generally composed of biodegradable and biocompatible polymers that can encapsulate therapeutic agents within their core or attach them to polymer chains through physical adsorption or chemical conjugation [20].

Several biodegradable polymers such as **Poly(lactic-co-glycolic acid)**, **Polyethylene glycol**, and **Chitosan** are widely used in the formulation of polymeric nanoparticles for drug delivery applications. These polymers provide excellent biocompatibility, controlled degradation, and the ability to modify surface properties for targeted therapy [21].

Polymeric nanoparticles (PNPs) are the most common among various polymer-based nanocarriers. During the past few decades, the significance of PNPs has increased exponentially in oncology. PNPs represent a large diversity in both structure and physiochemical properties. The main reason for its versatility is the huge variety of monomers that may be used to build up the polymer architectures [21]. Nanotechnology-based drug delivery systems have emerged as promising approaches to improve the performance of poorly water-soluble drugs [22]. Nanoparticles provide increased surface area, enhanced dissolution rate, improved permeation, sustained release behavior, and better therapeutic efficacy [23]. Nanoemulsions are thermodynamically or kinetically stable colloidal dispersions consisting of oil, water, surfactant, and co-surfactant, with droplet sizes generally ranging from 20 to 200 nm. Due to their extremely small droplet size and large interfacial surface area, nanoemulsions provide excellent solubilization and delivery of poorly water-soluble drugs [24].

The nanoliposomes can also be formulated to contain a variety of other active ingredients, such as stabilizers, preservatives, and other excipients. The nanoliposomes can be formulated to have a size range of approximately 20–200 nanometers and can also be designed to have different surface properties to further improve their stability, solubility, and bioavailability [25]. Micro-balloons also known as hollow microsphere are those system that tends to be one the most suitable approach for gastric retention micro balloons drug delivery system can be explained as it is containing empty particles of spherical shape without core identically having a size than 200 micrometers [26]. Synthesis of ecofriendly silver nanoparticles is of great importance in the field of nanotechnology. Nanotechnology is applied in every aspect of life—medicine, food, or the environment—and nanomaterials are available in different forms, such as powder, particles, clusters, tubes or films, and sizes [27].

5 PH-RESPONSIVE POLYMERIC NANOPARTICLES

pH-responsive polymeric nanoparticles are smart drug delivery systems specifically designed to release therapeutic agents in response to acidic environments. These nanocarriers exploit the pH gradient between normal tissues and tumor tissues to achieve site-specific drug delivery. Because tumor microenvironments and intracellular compartments such as endosomes and lysosomes are more acidic than normal physiological conditions, pH-responsive systems can selectively trigger drug release at the tumor site, thereby improving therapeutic efficacy and reducing systemic toxicity [28].

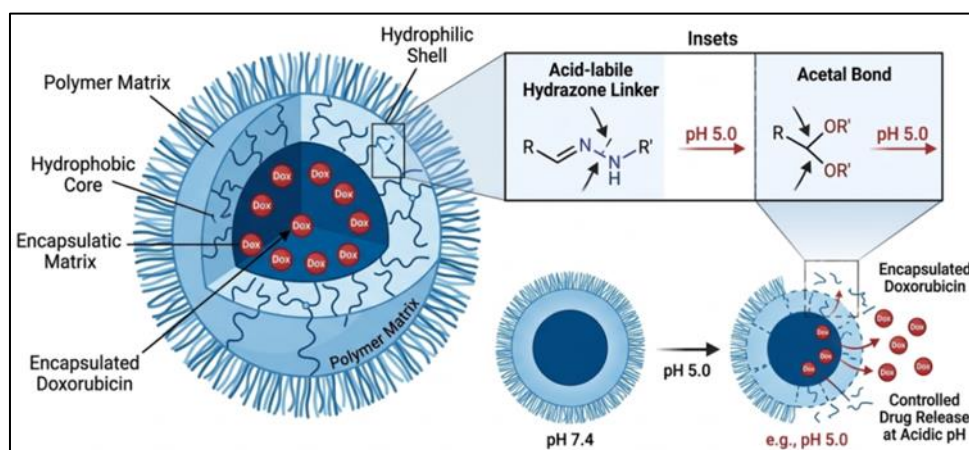


Figure 3: Structure of pH-Responsive Polymeric Nanoparticle

In these systems, drugs are often conjugated to polymers or encapsulated in nanoparticles using acid-sensitive chemical linkages that undergo cleavage under acidic conditions. Several types of pH-labile linkers have been widely investigated for designing stimuli-responsive nanocarriers [29].

These linkers remain relatively stable at physiological pH (~7.4) but undergo rapid hydrolysis in acidic environments typically found in tumor tissues or intracellular vesicles. As a result, the cleavage of these bonds triggers the release of the encapsulated drug specifically at the target site [30].

Among these strategies, hydrazone linkages have been extensively studied for the delivery of **Doxorubicin**. Hydrazone bonds are particularly attractive because they are stable under neutral conditions but are readily cleaved in mildly acidic environments. This property enables selective drug release within tumor tissues or endosomal compartments after nanoparticle internalization [31].

Recent studies have demonstrated that polymeric micelles containing doxorubicin conjugated through hydrazone linkers exhibit significantly enhanced drug release under acidic conditions (pH $\approx$ 5.5) compared with physiological pH (7.4). This pH-dependent release behavior improves intracellular drug availability and enhances anticancer activity against tumor cells while minimizing toxicity to normal tissues [32].

Overall, pH-responsive polymeric nanoparticles represent a promising strategy for targeted cancer therapy, particularly for improving the therapeutic performance of conventional chemotherapeutic agents [33].

Table 1: Polymers Used in pH-Responsive Systems

Polymer	Characteristics
Poly(lactic-co-glycolic acid) (PLGA)	Biodegradable, biocompatible, and approved by the U.S. Food and Drug Administration for drug delivery applications
Polyethylene glycol (PEG)	Improves nanoparticle stability, prolongs circulation time, and reduces immune recognition
Chitosan	Natural polymer with excellent biocompatibility, biodegradability, and mucoadhesive properties
Polycaprolactone	Hydrophobic biodegradable polymer with slow degradation rate suitable for sustained drug release
Poly(β -amino esters)	Synthetic polymer exhibiting intrinsic pH-responsive behavior due to protonation under acidic conditions

6 DESIGN STRATEGIES FOR PH-RESPONSIVE NANOPARTICLES

The design of pH-responsive nanoparticles involves incorporating acid-sensitive components into nanocarriers to enable selective drug release in acidic tumor environments. Various formulation strategies have been developed to enhance the stability, targeting ability, and therapeutic efficacy of these nanocarriers in cancer therapy [34].

6.1 Polymer-Drug Conjugates

In polymer-drug conjugates, chemotherapeutic agents such as **Doxorubicin** are chemically attached to polymer backbones through acid-labile linkages. These linkers remain stable in the bloodstream at physiological pH (~7.4) but undergo hydrolysis in acidic conditions found in tumor tissues or intracellular organelles. As a result, the drug is selectively released at the target site, improving therapeutic efficiency while minimizing systemic toxicity [35].

Commonly used biodegradable polymers for these conjugates include **Poly(lactic-co-glycolic acid)**, **Polyethylene glycol**, and **Chitosan**, which provide excellent biocompatibility and controlled degradation properties [36].

6.2 Polymeric Micelles

Polymeric micelles are nanosized structures formed through the self-assembly of amphiphilic block copolymers in aqueous environments. These micelles typically consist of two main structural components:

- **Hydrophobic core:** This region serves as the reservoir for loading hydrophobic anticancer drugs such as doxorubicin.
- **Hydrophilic shell:** The outer layer stabilizes the micelle in biological fluids and prolongs circulation time by reducing recognition by the immune system [37].

Polymeric micelles can be engineered to incorporate pH-sensitive bonds or polymers that destabilize under acidic conditions, thereby triggering drug release specifically within tumor tissues or intracellular compartments [38].

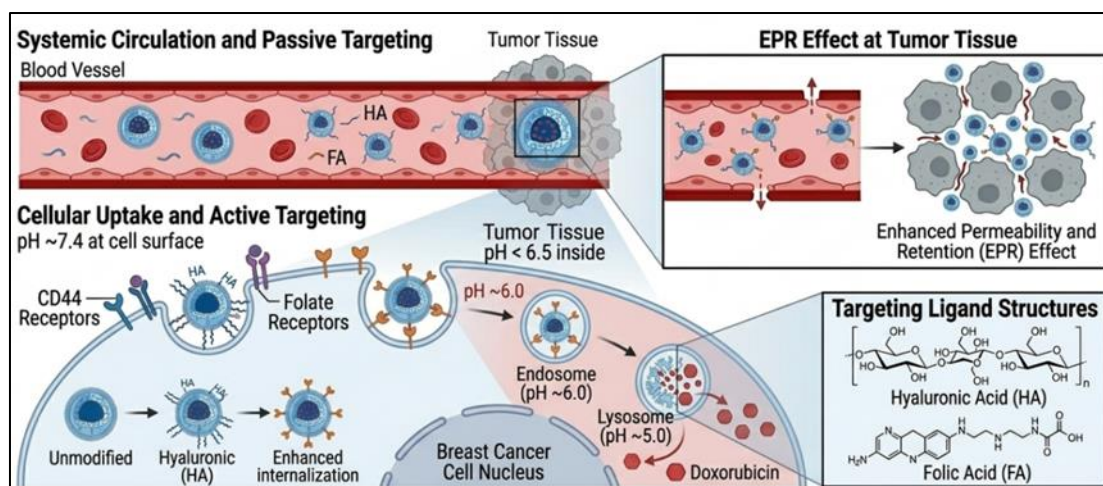


Figure 4: Targeted Delivery of Doxorubicin Using pH-Responsive Nanoparticles

6.3 Dual-Responsive Nanoparticles

Dual-responsive nanoparticles are advanced drug delivery systems designed to respond to more than one stimulus simultaneously, such as **pH and redox conditions**, pH and temperature, or pH and enzymatic activity. These systems provide improved control over drug release and enhance therapeutic efficiency by responding to multiple features of the tumor microenvironment [39].

For example, nanoparticles based on **Poly(β -amino ester)** have been developed as pH- and redox-responsive carriers for breast cancer therapy[40]. Overall, these design strategies significantly contribute to the development of advanced pH-responsive nanocarriers capable of improving the delivery and therapeutic performance of anticancer drugs [41].

7 POLYMERS USED IN PH-RESPONSIVE SYSTEMS

Various biodegradable and biocompatible polymers are widely used in the development of pH-responsive nanoparticles for anticancer drug delivery. These polymers provide structural stability, controlled degradation, and the ability to incorporate pH-sensitive functional groups that enable drug release in acidic tumor environments. The selection of appropriate polymers plays a critical role in determining nanoparticle stability, drug loading capacity, and release kinetics [42].

These polymers enable the fabrication of nanoparticles with **controlled drug release properties**, improved drug stability, and enhanced targeting capability for cancer therapy. By incorporating pH-sensitive linkages or functional groups within these polymers, researchers can design nanocarriers that selectively release drugs in the acidic tumor microenvironment, thereby improving therapeutic efficiency and reducing systemic toxicity [43].

In particular, polymeric systems combining **PEGylation** with biodegradable polymers such as PLGA have demonstrated enhanced pharmacokinetic properties and improved tumor accumulation due to prolonged circulation and reduced clearance by the reticuloendothelial system. These advances have significantly contributed to the development of more efficient nanocarriers for targeted chemotherapy [44].

8 TARGETING STRATEGIES IN BREAST CANCER NANOTHERAPY

Targeted drug delivery has become a key strategy in improving the therapeutic efficacy of nanomedicine for breast cancer treatment. Nanoparticle-based drug delivery systems can be engineered to selectively accumulate in tumor tissues through **passive targeting** or **active targeting** mechanisms, thereby enhancing drug concentration at the tumor site while reducing systemic toxicity [45].

8.1 Passive Targeting

Passive targeting primarily occurs through the **Enhanced Permeability and Retention effect**. Tumor tissues possess abnormal and highly permeable blood vessels with large endothelial gaps, allowing nanoparticles to penetrate and accumulate within the tumor interstitial space. [46].

8.2 Active Targeting

Active targeting involves the surface modification of nanoparticles with specific ligands that recognize and bind to receptors overexpressed on cancer cells. This ligand–receptor interaction facilitates selective uptake of nanoparticles by tumor cells, improving intracellular drug delivery and therapeutic outcomes [47].

Among these, hyaluronic acid has received significant attention due to its strong affinity for **CD44 receptor**, which is frequently overexpressed in many breast cancer cells [48].

By combining both passive and active targeting strategies, nanoparticle-based drug delivery systems can significantly enhance drug accumulation in tumors, improve therapeutic efficacy, and reduce off-target toxicity associated with conventional chemotherapy [49].

9 PRECLINICAL STUDIES

Numerous preclinical investigations have demonstrated that pH-responsive nanoparticle systems can significantly enhance the therapeutic efficacy of anticancer drugs in breast cancer treatment. These nanocarriers improve drug stability, increase tumor accumulation, and enable controlled drug release in acidic tumor environments. Such features help overcome many limitations associated with conventional chemotherapy [50].

10 CHALLENGES IN CLINICAL TRANSLATION

Although pH-responsive nanoparticle-based drug delivery systems have shown promising outcomes in preclinical studies, several challenges remain in translating these nanomedicine platforms into clinical practice. The complexity of nanoparticle formulation, safety considerations, and regulatory requirements often limit their large-scale development and commercialization [51].

Several major challenges associated with the clinical translation of nanoparticle-based drug delivery systems include:

- **Large-scale manufacturing:** Producing nanoparticles with consistent size, drug loading efficiency, and reproducibility at an industrial scale remains a significant challenge. Variations during production can affect the quality and therapeutic performance of nanomedicines [52].
- **Stability issues:** Nanoparticles may undergo aggregation, premature drug leakage, or chemical degradation during storage and transportation, which can compromise their effectiveness and shelf life [53].
- **Immunogenicity:** Some nanoparticle formulations may trigger immune responses or rapid clearance by the mononuclear phagocyte system, reducing their circulation time and therapeutic efficiency. Surface modification with polymers such as **Polyethylene glycol** is often used to improve biocompatibility and reduce immune recognition [54].
- **Regulatory hurdles:** Regulatory approval of nanomedicines requires extensive safety, toxicity, and pharmacokinetic studies. The absence of standardized regulatory guidelines for nanoparticle-based drug delivery systems can delay clinical approval processes [55].
- **Limited clinical trials:** Despite extensive preclinical research, only a limited number of nanoparticle-based therapies have successfully progressed to clinical trials or regulatory approval. This gap highlights the need for further clinical investigations to establish the safety and efficacy of nanomedicine-based therapies [56].

11 FUTURE PERSPECTIVES

The field of nanomedicine continues to evolve rapidly, offering promising opportunities for improving breast cancer therapy. Advances in nanotechnology, materials science, and molecular biology are expected to enhance the design and performance of pH-responsive nanoparticle systems. Future research is likely to focus on developing more efficient, multifunctional nanocarriers capable of achieving precise tumor targeting and controlled drug release [57].

Several important future research directions have been identified for improving nanoparticle-based drug delivery systems:

- **Multifunctional nanoparticles:** The development of multifunctional nanocarriers that combine diagnostic and therapeutic functions (theranostics) may enable simultaneous imaging and treatment of tumors, improving treatment monitoring and therapeutic outcomes [58].

- **AI-assisted nanomedicine design:** The application of **Artificial Intelligence** and machine learning techniques in nanomedicine may accelerate the design of optimized nanoparticle formulations by predicting drug–polymer interactions, toxicity profiles, and pharmacokinetic behavior [59].
- **Combination therapy:** Nanoparticle systems capable of delivering multiple therapeutic agents, such as chemotherapeutic drugs, gene therapy molecules, or immunomodulators, may enhance treatment effectiveness and overcome drug resistance in breast cancer [60].
- **Personalized drug delivery:** Advances in **Precision Medicine** may enable the development of individualized nanoparticle formulations tailored to a patient's genetic and molecular tumor profile, leading to improved treatment outcomes [61].
- **Clinical translation of nanocarriers:** Continued efforts are needed to bridge the gap between laboratory research and clinical application by conducting large-scale clinical trials and developing standardized regulatory frameworks for nanomedicine products [62].

12 TARGETED DELIVERY OF DOXORUBICIN (DOX)

The development of pH-responsive polymeric nanoparticles (PNPs) for targeted delivery of doxorubicin (DOX) represents a significant advancement in breast cancer therapy, addressing the major limitations associated with conventional chemotherapy. The acidic nature of the tumor microenvironment (TME), typically ranging from pH 6.5 to 6.8 compared to the physiological pH of 7.4, provides a unique trigger for site-specific drug release. Exploiting this pH gradient, smart polymeric systems have been engineered to remain stable in systemic circulation while undergoing structural transformations—such as swelling, degradation, or bond cleavage—under acidic conditions, thereby enabling controlled and targeted drug release.

Experimental studies have consistently shown that pH-responsive PNPs significantly enhance intracellular delivery of DOX, improve cytotoxic efficacy against breast cancer cells, and reduce off-target toxicity. These systems also exhibit the ability to overcome multidrug resistance mechanisms, such as drug efflux pumps, by facilitating endosomal escape and sustained intracellular drug release. Furthermore, optimization of particle size (typically 50–200 nm) supports passive targeting via the enhanced permeability and retention (EPR) effect, leading to increased accumulation in tumor tissues [64–65].

13 CONCLUSION

pH-responsive polymeric nanoparticles represent a promising platform for the targeted delivery of **Doxorubicin** in breast cancer therapy. By exploiting the acidic **tumor microenvironment**, these smart nanocarriers enable controlled drug release and improved tumor targeting compared with conventional chemotherapy. Such systems enhance drug accumulation at the tumor site while reducing exposure to healthy tissues, thereby improving therapeutic outcomes. Advances in polymer chemistry and nanotechnology have facilitated the development of multifunctional nanoparticles capable of incorporating features such as controlled drug release, surface modification for active targeting, and improved pharmacokinetic properties. Biodegradable polymers such as **Poly(lactic-co-glycolic acid)**, **Polyethylene glycol**, and **Chitosan** have played an important role in designing nanocarriers with enhanced stability and biocompatibility. These innovations contribute to improved therapeutic efficacy while minimizing systemic toxicity associated with conventional drug formulations.

Furthermore, the incorporation of advanced targeting strategies, including both passive targeting via the **Enhanced Permeability and Retention effect** and active targeting through ligand–receptor interactions, has significantly improved the specificity of nanoparticle-based drug delivery systems for breast cancer treatment. These strategies enhance the intracellular uptake of anticancer drugs and increase their therapeutic efficiency.

Overall, pH-responsive polymeric nanoparticles offer a highly promising approach for improving breast cancer therapy. With further technological advancements and successful clinical translation, nanomedicine-based drug delivery systems may play a pivotal role in the future of targeted cancer treatment.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Acknowledgments

I would like to thank Dr. Ravindra B. Malabadifor guidance and support.

Disclosure of conflict of interest

No conflict of interest to bed is closed.

REFERENCES

- [1] Bray F, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide. *CA Cancer J Clin.* 2021.
- [2] Minotti G, et al. Anthracyclines: molecular advances and pharmacologic developments in antitumor activity and cardiotoxicity. *Pharmacol Rev.* 2004.
- [3] Kumari A, Yadav SK, Yadav SC. Biodegradable polymeric nanoparticles based drug delivery systems. *Colloids Surf B Biointerfaces.* 2010.
- [4] Bae YH, Park K. Targeted drug delivery to tumors: myths, reality and possibility. *J Control Release.* 2011.
- [5] Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *Cell.* 2011;144(5):646–674.
- [6] Vander Heiden MG, Cantley LC, Thompson CB. Understanding the Warburg effect: the metabolic requirements of cell proliferation. *Science.* 2009;324(5930):1029–1033.
- [7] Gillies RJ, Raghunand N, Garcia-Martin ML, Gatenby RA. pH imaging in tumors: methods and applications. *IEEE Eng Med Biol Mag.* 2004;23(5):57–64.
- [8] Huotari J, Helenius A. Endosome maturation. *EMBO J.* 2011;30(17):3481–3500.
- [9] Bae YH, Park K. Targeted drug delivery to tumors: myths, reality and possibility. *J Control Release.* 2011;153(3):198–205.
- [10] Hortobagyi GN. Anthracyclines in the treatment of cancer. *Drugs.* 1997;54(Suppl 4):1–7.
- [11] Tacar O, Sriamornsak P, Dass CR. Doxorubicin: an update on anticancer molecular action and toxicity. *J Pharm Pharmacol.* 2013;65(2):157–170.
- [12] Pommier Y, Leo E, Zhang H, Marchand C. DNA topoisomerases and their poisoning by anticancer drugs. *Chem Biol.* 2010;17(5):421–433.
- [13] Minotti G, et al. Anthracyclines: molecular advances and pharmacologic developments. *Pharmacol Rev.* 2004;56(2):185–229.
- [14] Kumari A, Yadav SK, Yadav SC. Biodegradable polymeric nanoparticles based drug delivery systems. *Colloids Surf B Biointerfaces.* 2010;75(1):1–18.
- [15] Danhier F, et al. PLGA-based nanoparticles: an overview of biomedical applications. *J Control Release.* 2012;161(2):505–522.
- [16] Soppimath KS, et al. Biodegradable polymeric nanoparticles as drug delivery devices. *J Control Release.* 2001;70:1–20.
- [17] Brigger I, Dubernet C, Couvreur P. Nanoparticles in cancer therapy and diagnosis. *Adv Drug Deliv Rev.* 2002;54:631–651.
- [18] Peer D, et al. Nanocarriers as an emerging platform for cancer therapy. *Nat Nanotechnol.* 2007;2:751–760.
- [19] Torchilin VP. Multifunctional nanocarriers. *Nat Rev Drug Discov.* 2014;13:813–827.
- [20] Bae Y, Fukushima S, Harada A, Kataoka K. Design of environment-sensitive supramolecular assemblies for intracellular drug delivery. *Angew Chem Int Ed.* 2003;42:4640–4643.
- [21] Torchilin VP. Multifunctional nanocarriers for cancer therapy. *Nat Rev Drug Discov.* 2014;13:813–827.
- [22] Lee ES, Gao Z, Bae YH. Recent progress in tumor pH targeting nanotechnology. *J Control Release.* 2008;132:164–170.
- [23] Duncan R. Polymer–drug conjugates as anticancer nanomedicines. *Nat Rev Cancer.* 2006;6:688–701.
- [24] Danhier F, et al. PLGA-based nanoparticles: an overview of biomedical applications. *J Control Release.* 2012;161:505–522.
- [25] Torchilin VP. Structure and design of polymeric micelles for drug delivery. *Adv Drug Deliv Rev.* 2006;58:1532–1555.

- [26] Bae YH, Park K. Targeted drug delivery to tumors: myths, reality and possibility. *J Control Release*. 2011;153:198–205.
- [27] Mura S, Nicolas J, Couvreur P. Stimuli-responsive nanocarriers for drug delivery. *Nat Mater*. 2013;12:991–1003.
- [28] Shen Y, et al. Dual pH/redox-responsive nanoparticles for cancer drug delivery. *Biomaterials*. 2011;32:861–870.
- [29] Mura S, Nicolas J, Couvreur P. Stimuli-responsive nanocarriers for drug delivery. *Nat Mater*. 2013;12:991–1003.
- [30] Danhier F, et al. PLGA-based nanoparticles: an overview of biomedical applications. *J Control Release*. 2012;161:505–522.
- [31] Torchilin VP. Multifunctional nanocarriers. *Nat Rev Drug Discov*. 2014;13:813–827.
- [32] Maeda H, et al. Tumor vascular permeability and the EPR effect in macromolecular therapeutics. *J Control Release*. 2000;65:271–284.
- [33] Peer D, et al. Nanocarriers as an emerging platform for cancer therapy. *Nat Nanotechnol*. 2007;2:751–760.
- [34] Misra S, et al. Hyaluronan–CD44 interactions as potential targets for cancer therapy. *FEBS J*. 2011;278:1429–1443.
- [35] Bernkop-Schnürch A, Dünnhaupt S. Chitosan-based drug delivery systems. *Eur J Pharm Biopharm*. 2012;81:463–469.
- [36] Kievit FM, Zhang M. Surface engineering of iron oxide nanoparticles for targeted cancer therapy. *Acc Chem Res*. 2011;44:853–862.
- [37] **Gupta D**, Shrivastava AS, Malviya RK. Formulation design and evaluation of nasal toxicity study: Lamotrigine-encapsulated intranasal nanoliposome formulation for Huntington's disease (HD). *Latin American Journal of Pharmacy*. 2023;42(1).
- [38] Chaurasiya UK, **Gupta D**, Vengurlekar S, Jain SK. A review: Polymer-based nanoparticles as oral anticancer drug delivery systems. *International Journal for Research Trends and Innovation*. 2025;10(10).
- [39] Ameen Att E, **Gupta D**, Vengurlekar S, Jain SK. Formulation and evaluation of pulsatile drug delivery system of bronchodilator. *Int J Med Pharm Sci*. 2026;2(2):34–42. doi: [10.5281/zenodo.18495823](https://doi.org/10.5281/zenodo.18495823).
- [40] **Gupta D**. Generative AI & virtual screening: Reimagining drug design. *International Journal of Research and Analytical Reviews*. 2025;12(3):843–858.
- [41] Tupe A, **Gupta D**, Vengurlekar S, Jain SK. Intranasal mucoadhesive nanoemulsion of donepezil for brain targeting in Alzheimer's disease: A review. *International Journal of Novel Trends in Innovation (IJNTI)*. 2026;4(6).
- [42] Bondre S, **Gupta D**. Biological evaluation of novel Schiff base metal complexes: A review. *Int J Sci R Tech*. 2026;3(2):197–207. doi: [10.5281/zenodo.18661728](https://doi.org/10.5281/zenodo.18661728).
- [43] Mane PU, Manoj C, Pathan AA, **Gupta D**. Advanced analytical techniques for heavy metal detection: Principles, applications, and recent developments. *International Journal of Versatile Research and Analysis (IJVRA)*. 2026;4(9).
- [44] **Gupta D**, Shrivastava S, Malviya RK. Nanoliposome: An overview of types, preparation, evaluation and application. *International Journal of Pharmacy & Life Sciences*. 2022;12(11):17–26.
- [45] **Gupta D**, Shrivastava T, Vishwakarma D, Sharma A, Yadav J, Malabadi RB. *Acanthus ilicifolius* L.: ethnobotany, phytochemistry, pharmacology and synthesis of silver nanoparticles (AgNPs). *Magna Scientia Advanced Biology and Pharmacy*. 2026;19(01):31-52. <https://doi.org/10.30574/msabp.2026.19.1.0074>.
- [46] Pathan, A. A. , **Gupta, D.** & Malabadi, R. B., & (2026). Paper based enzymatic biosensor for rapid on-site detection of organophosphate. *International Journal of Science and Research Archive*, 20(3), 660–671. <https://doi.org/10.30574/ijsra.2026.20.3.1775>.
- [47] Singh Gurjar NP, Sharma SK, **Gupta D**, Vengurlekar S. Gastroretentivemicroballoons for oral drug delivery: formulation strategies, mechanistic insights, evaluation, clinical translation, and future perspectives. *J Front Multidiscip Res*. 2026;7(2):155–162. <https://doi.org/10.54660/JFMR.2026.7.2.155-162>.
- [48] Bhat VG, Masti SP, Narasagounder SS, Kurabetta LK, Gunaki MN, Hunashyal AA, Chougale RB, **Malabadi RB**. Antimicrobial silver nanoparticle-doped poly(vinyl alcohol)/guar gum/gum ghatti nanocomposites: A multifaceted step towards sustainable packaging. **Sustainable Food Technology**. The Royal Society of Chemistry. 2026;DOI: 10.1039/d5fb00825e.
- [49] **Malabadi RB**, Saini I, Chalannavar RK. Role of Nanoparticles in Plant Tissue Culture. *Magna Scientia Advanced Biology and Pharmacy*. 2026; 17:2:52-68.

- [50] Kolkar KP, **Malabadi RB**, Nethravathi TL, Chalannavar RK. Application of Nanotechnology, Artificial Intelligence (AI) and use of Yeast extract in Plant Tissue Culture: An Updated Review. International Journal of Science and Research Archive. 2025; 17(02); 230-247.
- [51] Kolkar KP, **Malabadi RB**, Sadiya MR, Chalannavar RK. Updates on some medicinal and ornamental plants-*Ayurvedic* medicines. World Journal of Advanced Research and Reviews. 2024; 23(01): 111-147.
- [52] **MalabadiRB**,Kolkar KP, Meti NT, ChalannavarRK.Vaccinedevelopment for coronavirus (SARS-CoV-2) disease (Covid-19); **Lipid nanoparticles**.**International Journal of Research and Scientific Innovations. 2021; 8(3): 189-195 (DOI: [dx.doi.org/10.51244/IJRSI.2021.8312](https://doi.org/10.51244/IJRSI.2021.8312)).**
- [53] Nityasree BR, Chalannavar RK, Kouser S, Divakar MS, Gani RS, SowmyashreeK, **Malabadi RB**. Bioinspired synthesis of zinc oxide nanoparticles by using leaf extract of *Solanum lycopersicum* L. for larvicidal activity of *Aedes aegypti* L. **Advances in Natural Sciences: Nanoscience and Nanotechnology. 2021;12(1):1-8.** (<https://doi.org/10.1088/2043-6262/abeaae>).
- [54] Khan SR, Ganguly A,**MalabadiRB**, Sunwoo HH, Parashar A, Teixeira da Silva JA, Mavanur RS. Targeting strategies and **nanocarriers** in **vaccines** and therapeutics. **Research in Biotechnology. 2011; 2(6):08-20.**
- [55] **Malabadi RB**, Chalannavar RK, Meti NT, Mulgund GS, Nataraja K, Vijayakumar S. Synthesis of antimicrobial **silver nanoparticles** by callus cultures and *in vitro* derived plants of *Catharanthus roseus*. **Research in Pharmacy. 2012; 2(6):18- 31.**
- [56] **Malabadi RB**, Meti NT, Mulgund GS, Nataraja K, Vijayakumar S. Synthesis of **silver nanoparticles** from *in vitro* derived plants and calluscultures of *Costus speciosus* (Koen.): Assessment of antibacterial activity. **Research in Plant Biology. 2012; 2(4): 32-42.**
- [57] **MalabadiRB**,Mulgund GS, Meti NT, Nataraja K, Vijayakumar S. Antibacterial activity of **silver nanoparticles** synthesized from whole plant extracts of *Clitoriaternatea*. **Research in Pharmacy. 2012; 2(4):11-21**
- [58] **MalabadiRB**,Lokare-Naik S, Meti NT, Mulgund GS, Nataraja K, Vijayakumar S. Synthesis of **silver nanoparticles** from *in vitro* derived plants and callus cultures of *Clitoriaternatea*; Evaluation of antimicrobial activity. **Research in Biotechnology. 2012; 3(5): 26-38.**
- [59] **MalabadiRB**, Meti NT, Chalannavar RK. Applications of nanotechnology in vaccine development for coronavirus (SARS-CoV-2) disease (Covid-19). **International Journal of Research and Scientific Innovations. 2021; 8(2): 191-198.**
- [60] Kolkar KP, **Malabadi RB**, Sadiya MR, Chalannavar RK. Updates on some medicinal and ornamental plants-*Ayurvedic* medicines. World Journal of Advanced Research and Reviews. 2024; 23(01): 111-147.
- [61] Malabadi RB, Sadiya MR,KolkarKP,Mammodova SS, Chalannavar RK, Baijnath H, Lavanya L, Munhoz ANR.Triple Negative Breast Cancer (TNBC): Signalling pathways-Role of plant-based inhibitors. Open Access Research Journal of Biology and Pharmacy.2024; 10(02): 028-071.
- [62] **Malabadi RB**, Kolkar KP, **Sadiya MR**, Veena Sharada B, Mammodova SS, Chalannavar RK, Baijnath H, Nalini S, Nandini S, Munhoz ANR.Triple Negative Breast Cancer (TNBC): *Cannabis sativa*-Role of Phytocannabinoids. World Journal of Biology, Pharmacy and Health Sciences. 2024; 17(03): 140-179.
- [63] **Malabadi RB**, **Sadiya MR**, Kolkar KP, Chalannavar RK, Baijnath H.*Tinospora cordifolia* (Amruthballi): Medicinal plant with Anticancer activity. Magna Scientia Advanced Biology and Pharmacy. 2024; 11(02): 001-019.
- [64] **Malabadi RB**, **Sadiya MR**, Kolkar KP, Mammadova SS, Chalannavar RK, Baijnath H. Role of Plant derived-medicine for controlling Cancer. International Journal of Science and Research Archive. 2024;11(01): 2502-2539.
- [65] **Malabadi RB**, **Sadiya MR**, **Prathima TC**, Kolkar KP, Mammadova SS, Chalannavar RK. *Cannabis sativa*: Cervical cancer treatment- Role of phytocannabinoids-A story of concern. World Journal of Biology, Pharmacy and Health Sciences. 2024; 17(02): 253-296.