International Journal of Engineering Research and Science & Technology

ISSN 2319-5991 www.ijerst.com
Vol. 22, No. 2(1), 2026

Biodegradable Polymer Nanocomposites for Controlled Drug Delivery with Self-Regulated pH-Responsive Mechanisms

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Abstract:

The objective of the current research is to investigate the possibilities of biodegradable polymer nanocomposites in controlled drug delivery, paying particular attention to pH-responsive mechanisms. The study examines how these nanocomposites react to the different pH levels that are encountered in biological systems, including a tumor or in the gastrointestinal system. This paper focuses on the manufacturing techniques of such nanocomposites such as emulsion polymerization and electrospinning methods that are crucial in the attainment of elevated drug loading performance and regulated discharge. The study focuses on creating drug delivery systems that have the ability to target specific sites, improve therapeutic outcomes, and minimize side effects, by the use of biodegradable natural and synthetic polymers. Moreover, the article outlines both existing issues, including, but not limited to, stability, mass production, and toxicity, and the further research directions to enhance the functionality and scalability of pH-responsive drug delivery systems. The results of the study make good contributions to the evolution of the high level drug delivery systems to be used in the fields of cancer therapy, gastrointestinal medication delivery and gene therapy. The identified study suggests to apply multifunctional nanocomposites to achieve better drug stability, bioavailability, and targeted release, and this is one of the major advances in the sphere of controlled drug delivery systems.

Keywords: Biodegradable polymers, nanocomposites, pH-responsive, drug delivery, cancer therapy, gene therapy.

Introduction

Drug delivery systems are some of the most important in the contemporary healthcare system as they provide a safe and effective means of delivering therapeutic agents to the intended point of action. The old way of delivery of drugs, using the oral form, in the form of tablets, capsules, injections and topical preparations, has been used extensively over the decades to treat multiple illnesses (Haider et al., 2024). Though such practices are easy and inexpensive, they do have a number of constraints that are likely to influence treatment outcomes. Poor bioavailability is one of the major problems in which a large part of the drug being administered is either degraded, metabolized or not uptaken by the body. As an illustration, several drugs taken orally are susceptible to hepatic first-pass metabolism in the liver which decreases the concentration of active drug that enters the systemic circulation (Afzal et al., 2022). The second consideration is another significant drawback of conventional drug delivery systems, i.e. site-specific targeting since the drugs do not target specific areas and affect normal and diseased tissues. Such universal distribution may cause critical side effects and toxicity especially in chemotherapy. Furthermore, the delivery system used in conventional methods tends to release drugs at high rates causing uncontrolled drug release and changes in drug concentration in the blood. Such variations can lead to either subtherapeutic levels or even toxic levels which limits the overall efficacy of treatment. Consequently, there is increased demands of superior drug delivery approaches in a manner of enhancing drug stability, effectiveness in targeting, and controlled and prolonged releases of therapeutic agents (Idrees et al., 2020).

Controlled drug delivery systems have been proposed to overcome limitations of conventional drug administration. These systems administer drugs at preset times and directly to targeted locations. Controlled

delivery enhances treatment by maintaining therapeutic drug concentration with minimal side effects. Key benefits include reduced dosing rates for better patient compliance and elimination of sudden drug concentration increases that could cause toxicity. Specific delivery schemes can target drugs to diseased zones, producing optimal therapeutic effects while minimizing harm to normal cells. These features make controlled delivery particularly important in cancer therapy, gene therapy, and antimicrobial treatment. Scientists are focusing on creating materials and technologies for precise drug delivery (Kuperkar et al., 2024). Nanotechnology has revolutionized drug delivery through nanoscale carriers that deliver therapeutic molecules precisely. Nanoparticles, nanocapsules, liposomes, dendrimers, and nanofibers possess high surface area, adjustable chemistry, and increased permeability. These properties allow nanocarriers to entrap drugs, prevent early degradation, and reach specific biological targets. Nanotechnology-based delivery systems improve drug solubility and stability, particularly for drugs with low water solubility. Surface modifications enable targeted delivery to diseased tissues or cells, such as nanoparticles utilizing the increased permeability-retention effect in tumors. Additionally, nanotechnology enables regulated drug release over time, driving extensive research to enhance therapeutic outcomes (Singh et al., 2019).

Biodegradable polymers have gained significant interest in biomedical research due to their capacity to break down to non-toxic products. When coupled with nanoscale materials, these polymers produce nanocomposites with enhanced mechanical, chemical and biological properties. Biodegradable polymer nanocomposites provide an ideal platform for drug delivery by ensuring therapeutic agents are encapsulated, safely delivered to targets, and released controllably. Common biodegradable polymers in drug delivery include natural polymers like chitosan, alginate, gelatin, hyaluronic acid, and synthetic polymers such as PLA, PGA, PLGA, and PCL. These polymers are widely used due to their biocompatibility, biodegradability, and ability to form flexible nanostructures. When combined with nanoparticles, polymer nanocomposites can improve drug load capacity, stability and release behavior, making them promising for advanced drug delivery systems. pH-responsive drug delivery systems have attracted attention due to their responsiveness to pH changes in biological conditions. The human body has varying pH levels across tissues and cellular compartments, from acidic stomach environment (pH 1-3) to neutral blood and tissues (pH 7.4). Tumor tissues and inflamed regions exhibit lower pH levels between 6.5 and 6.8, which pH-responsive systems target. These systems activate drug release through polymer swelling, degradation, or breaking of acid-sensitive bonds. By enabling targeted drug release in specific environments and reducing systemic toxicity, pH-responsive systems offer improved therapeutic efficacy. They are widely explored for cancer therapy, gastrointestinal drug delivery and targeted antimicrobial therapy (Nawaz et al., 2022).

3.6 Research Gap and Study Objectives

Even with the substantial progress in the use of nanotechnology drug delivery system, there are still numerous obstacles to the creation of effective and consistent pH-responsive biodegradable polymer nanocomposites. Most of the systems available have low stability thus resulting in the premature leakage of drugs before reaching their target site. Also, it is still challenging to be able to target and release accurately and under physiological conditions because of the biological environment variations. The second weakness is that the reaction to pH changes is slow or inadequate and thus it might decrease the efficiency of the drug delivery systems in the quickly varying pathological conditions. Moreover, mass production and reproducibility of these nanocomposites are other areas that need research.

Considering these limitations, the present study aims to explore the potential of biodegradable polymer nanocomposites for controlled drug delivery with self-regulated pH-responsive mechanisms. The main objectives of this study are:

1. To analyze the properties and advantages of biodegradable polymer nanocomposites in drug delivery applications.
2. To investigate the mechanisms of pH-responsive drug release in different biological environments.
3. To evaluate fabrication methods and design strategies for improving drug loading, stability, and release efficiency.

4. To identify current challenges and future research directions in the development of advanced smart drug delivery systems.

Through this investigation, the study seeks to provide insights into the development of efficient, safe, and targeted drug delivery platforms for improved therapeutic outcomes.

4. Biodegradable Polymers Used in Drug Delivery

The capability to degrade safely into the biological environment into non-toxic byproducts has made biodegradable polymers an essential part in the process of creating an advanced drug delivery system. The key strengths of these polymers include biocompatibility, degradation control, and the capacity of these polymers to deliver therapeutic agents efficiently. Biodegradable polymers are also used as drug delivery vehicles in drugs delivery applications to prevent rapid degradation of drugs, drug stabilizing, and control and targeted release. On the basis of their origin, biodegradable polymers applied in drug delivery can be categorised into natural polymers and synthetic polymers. Natural polymers are biologically sourced and are highly biocompatible, and, on the other hand, synthetic polymers are chemically modified to obtain accurate control on their physicochemical characteristics and degradation. Depending on the compatibility with drugs to use, the degradation rate, mechanical strength, and the type of therapy required, the right biodegradable polymers are to be selected.

Table 1: Types of polymers

Polymer Type	**Polymer**	**Repeating Unit / Chemical Formula**	**Source / Composition**	**Key Properties**	**Degradation Mechanism**	**Drug Delivery Applications**
Natural Polymer	Chitosan	$(C_6H_{11}NO_4)_n$	Derived from chitin in crustacean shells	Biocompatible, biodegradable, cationic polymer, mucoadhesive	Enzymatic degradation by lysozyme	Oral drug delivery, nasal delivery, gene delivery
	Alginate	$(C_6H_8O_6)_n$	Extracted from brown seaweed	Hydrophilic polysaccharide, gel-forming polymer	Ion exchange and hydrolysis	Protein delivery, hydrogel drug carriers
	Gelatin	Approximate repeating unit: $(C_{102}H_{151}N_{31}O_{39})_n$	Derived from collagen	Excellent film-forming ability, biodegradable	Enzymatic degradation	Microspheres, nanoparticles for controlled drug release
	Hyaluronic Acid	$(C_{14}H_{21}NO_{11})_n$	Glycosaminoglycan present in connective tissues	High water retention, receptor targeting ability	Enzymatic degradation by hyaluronidase	Targeted cancer drug delivery

Synthetic Polymer	Poly(lactic acid) (PLA)	$(C_3H_4O_2)_n$	Polyester synthesized from lactic acid	Biocompatible, good mechanical strength	Hydrolysis → lactic acid	Nanoparticles, controlled release systems
	Poly(glycolic acid) (PGA)	$(C_2H_2O_2)_n$	Synthetic aliphatic polyester	High crystallinity, fast degradation	Hydrolysis → glycolic acid	Short-term drug delivery carriers
	Poly(lactic-co-glycolic acid) (PLGA)	$(C_3H_4O_2)x(C_2H_2O_2)y$	Copolymer of PLA and PGA	Tunable degradation rate, FDA approved	Hydrolysis → lactic acid + glycolic acid	Vaccines, anticancer drug delivery
	Polycaprolactone (PCL)	$(C_6H_{10}O_2)_n$	Semi-crystalline polyester	Slow degradation, flexible polymer	Hydrolysis of ester bonds	Long-term sustained drug delivery

Natural and synthetic biodegradable polymers have their own benefits in the field of drug delivery as demonstrated in Table 1. The natural polymers usually have better biocompatibility, bioactivity and environmentally friendly processing and are used in other areas like tissue engineering, wound healing and targeted drug delivery. They however, can have limitations like variations in composition as well as comparatively lower mechanical strength. Conversely, synthetic biodegradable polymers offer more control of molecular structure, degree of degradation and drug release kinetics. The use of the polymers like PLGA and PLA has been researched so much because they have predictable degradation characteristics and have been approved by the regulatory bodies to be used in biomedicine. With the positive characteristics of these polymers in combination with nanomaterials, a system of polymer nanocomposite is able to be established that can increase the drug loading capacity, stability, and selective and stimuli-responsive release of drugs. The above innovations have played a vital role towards the design of the next-generation smart drug delivery systems.

Researchers use polymer functionalization, or chemical modification of the polymer to introduce desired functional groups or targeting ligands, to make the biodegradable polymers in drug delivery systems. Functionalization enhances drug loading potential, target efficiency and environmental responsiveness. Attaching hydrophilic or hydrophobic groups to alter the solubility and drug encapsulation properties of the polymer is one of them. Hydrophilic functional groups enhance the dispersion of polymer nanoparticles in biological fluids whereas hydrophobic ones are used to enhance the hydrophobic loading of drugs. The other approach is to have targeting ligands like antibodies, peptides, or small molecules attached to the polymer surface. These ligands facilitate specificity to find certain cell receptors and allow the delivery of drugs to diseased tissues and reduce the impact on healthy cells. The functionalization could also add stimuli-reactive elements so that the polymers could be triggered by environmental factors such as pH, temperature, or enzymatic action, or release drugs in acidic tumor conditions or intracellular locations. pH-sensitive functional groups could be added to allow the functionalization. These adjustments allow the smart delivery of drug system, which is able to discharge therapeutic agents on the basis of particular physiological environments. Functionalization of biodegradable polymer nanocomposites is important in improving the efficiency, selectivity, and responsiveness of nanocomposites to enhance their use in advanced drug delivery (Noreen et al., 2022).

5. Nanocomposite Materials for Drug Delivery

The nanocomposites materials have become a significant category of advanced materials in biomedical engineering and drug delivery systems. These materials are shaped by mixing polymer with nanoscale materials like nanoparticles, nanotubes or nanosheets. During incorporation into polymer matrices, the physicochemical and biological characteristics are highly enhanced. Nanocomposites provide a flexible platform for drug delivery to encapsulate drugs, stabilize them, and release therapeutic drugs in a targeted manner. Their nanoscale structure enables effective interaction with biological systems, making them useful in cancer therapy, antimicrobial treatment, and gene delivery. The development of polymer nanocomposites has gained importance due to their ability to address traditional drug delivery limitations. Nanocomposites are materials where at least one component has a size of 1-100 nanometers. In drug delivery, polymer nanocomposites are created by loading nanoparticles into a biodegradable polymer matrix. The polymer surrounds the therapeutic agent while nanoparticles add functionality to the system. The structure varies based on nanoparticle nature and synthesis method. Typically, nanoparticles are evenly dispersed throughout the polymer to create a homogenous structure, enhancing mechanical strength and bio-environment contact. Their large surface area improves drug molecule interactions and loading rates. Polymer nanocomposites can form various shapes like nanoparticles, nanofibers, hydrogels, nanocapsules and micelles (Iacob et al., 2021). Drugs can be physically entrapped in the polymer network or chemically attached to polymer chains. The structure prevents premature drug degradation and enables controlled release based on environmental factors. These nanocomposites comprise a biodegradable polymer matrix with functional nanoparticles that enhance structural, mechanical and therapeutic properties. They can incorporate various nanomaterials like metal nanoparticles, mesoporous silica, carbon nanotubes, graphene oxide and magnetic nanoparticles to improve drug delivery efficiency. Every kind of nanoparticle provides a particular property like antimicrobial activities, large surface area to adsorb drugs, and magnetic targeting, or mechanical strength. The schematic diagram of the structure of biodegradable polymer nanocomposites and the distribution of various nanoparticles in polymer matrix are shown in Figure 1.

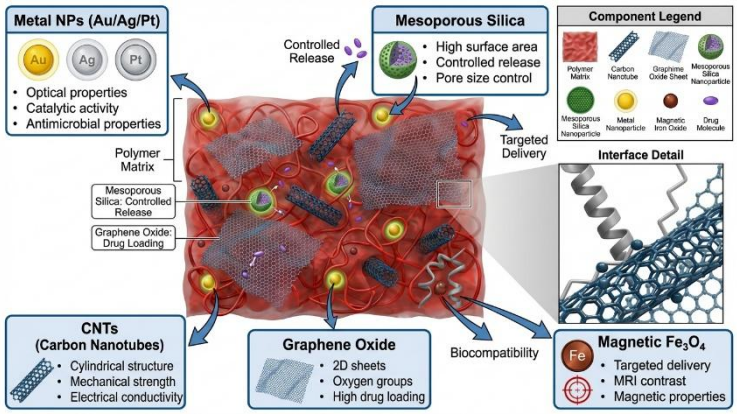

Figure 1. Structure of biodegradable polymer nanocomposites incorporating different nanoparticles for controlled drug delivery.\

The polymer matrix as illustrated in Figure 1, is the primary carrier system, which entraps the drug molecules and carries various forms of nanoparticles in its network structure. Mesoporous silica nanoparticles can be used to deliver therapeutic molecules because their porous structure allows them to release came drugs under control and because the high surface area and affinity of graphene oxide and carbon nanotubes increase drug load. Metal nanoparticles e.g. gold and silver add more functionalities like those of antimicrobial and catalytic properties. Magnetic nanoparticles like Fe 3 O 4 allow externally targeted delivery of drugs using magnetic fields thereby enhancing target-drug delivery. The concertation of these nanoparticles in a biodegradable polymer system creates multifunctional nanocomposits system that can deliver drugs in a controlled, targeted and effective way.

Drug delivery systems based on nanocomposites have major benefits over traditional carriers. The high loading capacity of nanoparticles is due to their high surface area and porous frameworks of nanocomposites that enable the inclusion of a high concentration of therapeutic agents in nanoparticles. This increases efficiency in deliveries and decreases the amount of carrier material required. The other advantage is an increase in the stability of drugs. Most of the drugs are vulnerable to the environment such as temperature, pH and enzymatic inactivation. Polymer

nanocomposites with encapsulation of drugs avoid early degradation and length shelf life, and the polymer matrix avoids early release of drugs into the targets. Nanocomposites carriers allow regulated release of drugs. With modifications of the composition of polymer matrix and nanoparticle, it is possible to create systems of gradual drug release so that therapeutic levels could be preserved, and doses could be reduced in frequency. In addition, the nanocomposits systems can be used to deliver drugs with a targeted delivery by changing the surfaces with ligands or antibodies or peptides specific to a target cell. This makes the drug more concentrated at the diseased sites and less exposure to healthy tissues which lowers the side effects. In general, nanocomposites have offered a dynamic system through which an improved and better therapeutic performance and low-toxicity drug delivery systems can be developed (Alshawwa et al., 2022).

6. Mechanism of pH-Responsive Drug Delivery

pH-responsive drug delivery systems are a significant type of stimuli-responsive nanocarrier that is developed to release therapeutic agents as a reaction to alterations in the local pH environment. Biological systems have tissues and cellular compartments that have different pH conditions, as such, pH-responsive polymers and nanocomposites are designed to take advantage of these differences to release drugs site-specifically enhancing therapeutic efficacy and reducing side effects. These systems are made up of biodegradable polymers or polymer nanocomposites which change structurally or chemically as it reacts to certain pH conditions. Among the alterations are swelling of polymer network, change in electrostatic interaction, cleavage of acid sensitive bonds, which are studied in the controlled drug release field in cancer therapy, gastrointestinal drug delivery and intracellular drug targeting whereby the pH variation induces drug release. There are microenvironments that have different levels of pH in the human body. Acidic properties of the stomach (pH 1-3) may destroy drugs before the target is reached. PH-responsive carriers shield drugs against the acidic stomach environment and liberate drugs in higher-pH environments in the intestines. The normal tissues and blood have a neutral pH of 7.4 which necessitates stability of the drug delivery systems. An increased metabolic activity causes the tumor microenvironment to be slightly acidic (pH 6.5-6.8) which is used as a release strategy by ph-responsive nanocomposites to release anticancer drugs. At the cells level, drug delivery systems get into the cells via endocytosis into endosomes (pH 5-6) where the acidic environment leads to the release of drugs. pH-responsive systems involve the polymers that possess functional groups that are changed through a structural or chemical mechanism (Lai et al., 2024). The most important processes are protonation and deprotonation, swelling of the polymer and breaking of acid labile bonds. Protons cause the amino groups of polymers to be protonated in an acidic place. Carboxyl-group polymers are deprotonated during alkaline conditions. Polymer swelling is the effect that arises when the pH varies leading to the absorption of water which forms pores through which the drug is released. Bonds that are acid-labile break in an acidic environment leading to the disintegration of the matrix. These systems may work independently or in combination with each other to enable the design of systems to meet special pH conditions. pH sensitive drug delivery systems are self-controlled drug delivery system that responds to the biological environment. In such systems, the drug is contained at pH 7.4 during circulation and releases when carriers get to an acidic, such as tumor tissue, environment (Chu et al., 2022). Self-regulated release not only minimizes toxicity but also minimizes the negative effects and also maintains the therapeutic levels. Such system may be combined with nanocomposites of silica, graphene oxide, or magnetic nanoparticles to achieve better control of the drug and pH-responsive drug delivery is a promising approach to designing smart therapeutic systems to treat diseases with abnormal pH environment.

7. Fabrication Methods of Polymer Nanocomposites

Polymer nanocomposites fabrication has a significant role in defining the structural, mechanical and functional characteristics of drug delivery system. Various critical attributes including drug loading efficiency, release kinetics, stability and size of the particle are affected by the methodology of synthesis. To achieve preparation of polymer-based nanocomposites using nanoparticles embedded in biodegradable polymer matrices, a variety of fabrication methods have been invented. The goals of these techniques include having a uniform dispersion of the nanoparticles, high encapsulation efficiencies and controlled drug release behavior (Sun et al., 2023). Some of the frequently employed methods of fabrication include emulsion polymerization, nanoprecipitation, electrospinning, and layer-by-layer assembly. The two methods have their own merits in terms of the type of properties and use of the nanocomposite drug delivery system.

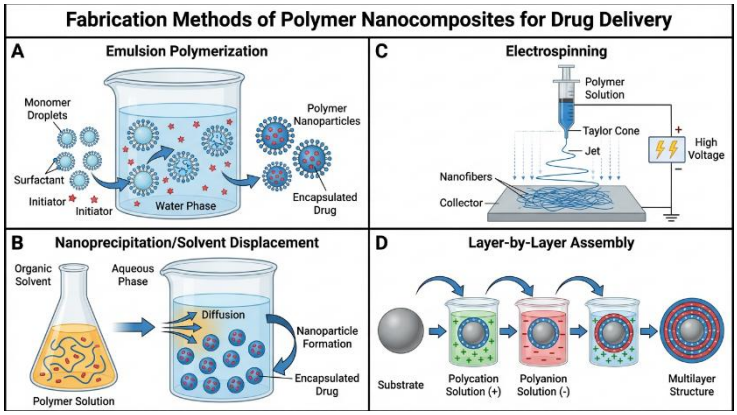

Figure 2. Fabrication strategies for polymer-based nanocomposites in biomedical drug delivery

Figure 2 shows the key fabrication methods that are usually used in the preparation of polymer nanocomposites that have applications in drug delivery systems. These methods allow therapeutic agents to be incorporated into polymer matrices and the size of the particles, morphology and drugs release properties to be controlled. In emulsion polymerization (Figure A), the monomers are polymerized in an aqueous medium that is composed of surfactants and initiators, where polymer nanoparticles are obtained, which can encapsulate drug molecules. The method of nanoprecipitation or solvent displacement (Figure B) incorporates the use of polymers in organic solvent and the addition of a solution to an aqueous phase resulting in the rapid diffusion of solvent and the creation of drug-saturated nanoparticles. Figure C discusses electrospinning which is used to create nanofibrous structures by using a high voltage on the polymer solution to form continuous nanofibers with a high surface area that will provide increased drug loading and controlled release. The operating principle of layer-by-layer assembly (Figure D) lies in the fact that oppositely charged polymers or nanoparticles can be deposed in multilayer nanostructures of desired thickness and composition. The techniques of fabrication mentioned enable researcher to create nanocomposite drug carriers that have a designed structural characteristics, enhanced stability and effective drug delivery functions.

8. Drug Loading and Controlled Release Mechanisms

The polymer nanocomposite of drug delivery system requires drug loading and controlled release to be crucial in design. Efficient drug loading is a method that makes sure that a sufficient quantity of therapeutic agent is loaded into the carrier system whereas controlled release mechanisms control the speed and period of drug release at the target site. The benefits of biodegradable polymer nanocomposites are that nanocomposite properties can be modified to regulate the drug encapsulation, stability, and release characteristics. Environmental stimulus triggered drug release in pH-responsive systems is possible, such as acidic tumor microenvironment. Its efficacy is determined by encapsulation mode, release mechanism, mechanisms that affect drug diffusion and degradation of the polymer. Drug encapsulation entails the therapeutic agent as either a physical encapsulation or chemical conjugation in polymer nanocomposites carriers. Physical encapsulation involves the introduction of drugs in the polymer matrix by non-covalent interactions, without compromising their biological activity. This is by methods such as nanoprecipitation or solvent evaporation, in which drugs are encased in the polymer structure. Drug release takes place by diffusion or decomposition of polymer (Chu et al., 2022). Covalent bonds are developed between the drug and the polymer in chemical loading by stimulus-sensitive linkers. Stability and minimized premature leakage is achieved through chemical conjugation but its modification must be done with care to retain therapeutic properties. The selection of the two methods is determined by the nature of the drug and its use. The release of the drugs by the polymer nanocomposites is governed by mathematical models. The Higuchi model is a release model that is released due to diffusion in the homogeneous matrices and is proportional to the square root of time. When the release is not strictly controlled by diffusion, the Korsmeyer Peppas model is used to examine it, with a release exponent to denote the type of mechanism. The first-order model of kinetics is used to explain release rates as a function of the rest of the drug concentration. These models aid in the comprehension of release mechanisms and design foreseeable systems. Releases in nanocomposits are affected by a number of factors. The degradation of polymer happens either by enzymatic reactions or hydrolysis. The size of the particle influences

the release rate where smaller particles diffuse rapidly and the pH environment influences releasing by changing the ionization degree of polymer functional groups (He et al., 2020). The release profiles are dependent on drug-polymer interactions, where the intensity of the interactions slows down the release. Scholars are able to rationalize these interactions to give the intended release properties in polymer nanocomposites.

9. Biomedical Applications

The pH-responsive biodegradable polymer nanocomposites that are biodegradable have attracted a lot of interest in biomedical research because of their capability to deliver drugs to their targets in a controlled and targeted manner. These superior nanocarriers offer the benefits of biodegradable polymers and functional nanoparticles to boost the therapeutic effect and reduced side effects. The fact that such systems can react to certain biological factors, including changes in pH, would allow them to release the drug with specificity to the required site of action. Consequently, there is an increasing interest in polymer nanocomposite-based drug delivery systems in numerous biomedical uses such as cancer therapy, gastrointestinal drug delivery, gene therapy as well as antimicrobial treatment. These multifunctional properties can be used to enhance drug stability, bioavailability and decrease toxicity and so they are very promising in the next generation of therapeutic approaches. One of the most significant uses of pH-responsive polymer nanocomposites drug delivery systems is in cancer therapy. The traditional chemotherapy has had its shortcomings such as inability to deliver drugs specifically, side effects, and poor therapeutic efficacy (Li et al., 2022). The traditionally used anticancer drugs have the potential of treating both cancerous and normal cells, leading to systemic toxicity. pH-responsive nanocomposite carriers allow targeting tumor cells with the anticancer drugs. The pH of tumor tissues (6.5-6.8) is lower than that of normal tissues (neutral pH). Polymer nanocomposites that are pH-sensitive groups can be stable under normal conditions but upon entering acidic conditions in tumors, the structure is altered, releasing drugs at the sites of tumors. To target and increase drug loading, nanoparticles such as gold, graphene oxide or magnetic particles may be added. Targeting ligands functionalize surface of the nanocomposites and enhance recognition of cancer cells by the pH-responsive polymer nanocomposites thereby enhancing the effectiveness of chemotherapy without side effects (Christodoulou et al., 2025).

A pH-responsive nanocomposite drug delivery system has a major biomedical application in gastrointestinal drug delivery. The GIT has marked changes in pH of which the stomach is highly acidic (pH 1-3) and the intestine is neutral to slightly alkaline (pH 6-75). Acid is known to degrade most drugs, particularly proteins, peptides and antibiotics; therefore pH-responsive polymer nanocomposites can be utilized as a method to protect the drug, whereby the polymer nanocomposites are not subjected to acidic environments, but rather to an increased pH in the intestine, thus dissolving (Desai et al., 2023). It is a guarantee of maximum absorption sites and optimal bioavailability and efficacies of the drug. These systems can be employed in oral delivery of drugs such as insulin, probiotics and anti-inflammatory agents in gastrointestinal diseases. Gene therapy, the treatment of genetic mutation diseases by the introduction of genetic material, experiences such problems as enzyme degradation and low cellular absorbance. Polymer nanocomposites are also good vectors of DNA and RNA as they preserve nucleic acids and help in cellular absorption. pH-responsive nanocomposites release genetic material in cells following endocytosis whereby the pH-sensitive polymers release DNA or RNA into the cytoplasm to enhance gene transfection, nanoparticles enhance the delivery efficiency of the DNA or RNA. Antimicrobial therapy also uses polymer nanocomposite systems to overcome the conventional logic of antibiotic resistance resistance to drugs. pH-responsive nanocomposites have the capability of releasing antibiotics as needed by environmental factors such as pH, focusing drugs in the sites of infection to treat chronic diseases and help heal wounds. These biodegradable systems have offered an efficient system of controlled delivery of therapeutic agents (Kruk & Winnicka, 2022).

10. Challenges and Limitations

Although advancements have been made in the development of biodegradable polymer nano-composites to be used in processing pH-responsive drug delivery systems, the application of such systems has been restricted by a number of challenges. Toxicity and biocompatibility are one of the major issues. Biodegradable polymers are usually non-toxic, although the use of nanoparticles such as metal nanoparticles or carbon nanotubes can be toxic. Not all nanomaterials can be cleared, thus causing chronic effects whose long-term effects are not clearly known.

Before use in clinical trials, the toxicity and biodistribution of nanoparticles should be carefully assessed. The other difficulty is mass production of nanocomposite drug carriers. Does not easily scale to industrial manufacturing Laboratory fabrication techniques Laboratory fabrication techniques are not necessarily scalable to industrial manufacturing. It continues to be difficult to achieve high reproducibility of particle size and efficiency in drug loading on large scale, and the cost of production can be a limitation to commercial use. Another limitation is regulatory approval. Agencies need thorough considerations to be made to make sure safety and efficacy. Since carriers in nanotechnology may involve complicated materials, the process of regulation may be time-consuming. The standardized principles of the assessment of nanomedicine products are under development, which may slow down the translation into clinics. Nanocomposite systems are also problematic in terms of their stability. Drug carriers should not be damaged during storing and administration. Stability may be compromised by factors such as temperature and pH that may cause premature leaking of drugs or aggregation of nanoparticles. In order to overcome these problems, interdisciplinary studies are necessary to come up with safer, more stable and scalable nanocomposites in drug delivery (Geszke-Moritz & Moritz, 2024; Li et al., 2022).

11. Future Perspectives

The potential of biodegradable polymer nanocomposites in drug delivery is very bright and more advanced and intelligent therapeutic systems are being researched on. The application of artificial intelligence (AI) in designing drug delivery is one of the new directions. Machine learning algorithms and AI have the potential to examine vast amounts of data pertaining to drug properties, polymer characteristics and bio-data to optimize the design of nanocarrier. The technologies can aid in forecasting drug loading effectiveness, release dynamics, and targeting functionality, therefore, hastening the creation of more effective drug delivery frameworks. The other significant line of research is the creation of the multi-stimuli responsive drug delivery systems. Although some of the existing systems can react to one stimulus, like pH, the next generation of nanocomposites will be able to react to several stimuli, such as temperature, redox, enzymes, or light. Such multi-responsive systems are capable of offering better control over the release of drugs which enhance treatment effectiveness of multi-complex biological environments. There is also a prospect of future drug delivery technologies having a significant impact due to the development of smart nanomedicine platforms. Smart nanocarriers have the ability to build-in diagnostic and therapeutic properties in a unified system that allows real time monitoring of the treatment responses. These systems are also known as theranostic platforms and they integrate drug delivery with imaging methods to add disease diagnoses and treatment at the same time. Moreover, the creation of individualized drug delivery systems is achieving more and more popularity. Personalized medicine tries to customize the treatment plans by taking into account the internal patient factors like the genetic profile, the progress of the disease and metabolic reactions. Polymer nanocomposites could be developed to be patient-specific in drug delivery to enhance treatment, and minimize side effects at the same time. All in all, it is anticipated that the future of drug delivery system will be in the form of more efficient, safer and patient specific drug delivery systems due to further advances in nanotechnology, materials science and biomedical engineering.

Conclusion:

Finally, the potential of biodegradable polymer nanocomposites to the controlled and pH-responsive drug delivery systems is significantly pointed out in this study. These systems are targeted to deliver drugs with high precision, stability, and minimal side effects because of the advantageous features of biodegradable natural and synthetic polymers, and are suitable in the field of cancer therapy, gastrointestinal drug delivery, and gene therapy. The researchers highlight the significance of pH-responsive systems, which can be utilized to release a drug in a controlled manner in a particular biological environment, e.g. a tumor or acidic region of the GI tract. Despite the significant advances, stability, mass production and toxicity remain some of the challenges that prevent the widespread use of these nanocomposites in clinical applications. The areas of future investigation include raising the reproducibility of the fabrication techniques, scaling fabrication production and increasing the biocompatibility of the nanocomposites. Artificial intelligence (AI) integration into the development of drug delivery systems has also demonstrated a potential promising future of streamlining the design and effectiveness of the systems. With the current progress in nanotechnology, materials science, and biomedical engineering, biodegradable polymer nanocomposites will serve a significant role in the dynamic creation of personalized, safer, and more effective drug delivery systems.

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