Indian Journal of Novel Drug Delivery

IJNDD

An Official Publication of Karnataka Education and Scientific Society

Review Article

Smart Polymers for Smart Medicine: Unravelling the Role of Polymers in Drug Delivery

PANKAJ MHATRE, KEDAR BAVASKAR*, RUTUJA SAWANT, ASHISH JAIN

Department of Pharmaceutics, Shri. D.D. Vispute College of Pharmacy and Research Centre, Panvel- 410 206, Maharashtra, India

ARTICLE DETAILS

Article history:
Received on 29 January 2024
Modified on 17 February 2024
Accepted on 20 February 2024

Keywords:
Polymers,
Controlled Drug Release,
Pharmaceutical Excipient,
Drug Delivery.

ABSTRACT

Over the last few decades, after much research, several interesting characteristics and potential uses for polymers have been discovered. The current review focuses on the role of polymers in the pharmaceutical dosage forms such as in tablets, controlled release dosage forms, polymeric nanoparticles, tissue engineering, gene delivery, ocular drug delivery and many other novel drug delivery systems. In various dosage forms and drug delivery systems, the use of polymer results in drug release that is sustained, extended, modified, controlled, and targeted. An overview of pharmaceutical polymers, covering their properties, classification, drug release mechanism, and applications in drug delivery systems, is presented in this article. The aim of this article is to provide a wide-angle prospect of the different uses of pharmaceutical polymers in pharmaceutical drug delivery. The several types of polymeric excipients are discussed, with special attention paid to how they work in oral delivery of drug. to completely exploit their various qualities and possible impact on medication delivery in an effort to create better pharmaceutical goods overall.

INTRODUCTION

Polymers, a remarkably versatile group of materials, have undergone significant advancements over the past few decades, leading to a profound impact on our everyday lives. Their utilization in polymer and pharmaceutical medication delivery systems stems from their ability to exert precise control over drug release, either in terms of space or time. Extensive research conducted over several decades has showcased the diverse applications of polymers in various biomedical domains such as prosthetics, ophthalmology, dentistry, bone regeneration, and numerous others. Furthermore, their use extends to the development of tissue engineering scaffolds, pharmaceutical drug delivery systems, as well as the implantation of synthetic organs and medical devices. Consequently, the utilization of polymeric materials in the medical field is experiencing a rapid and escalating growth trajectory [1].

Author for Correspondence:
Email: kedar.bavaskar@gmail.com

A polymer is a complex molecule made up of repeated structural units, joined together by strong chemical bonds. Polymers can be categorized as natural, synthetic, or semi-synthetic. In the field of pharmaceuticals, polymers serve various purposes such as facilitating the manufacturing process of drug delivery systems, safeguarding and improving stability, increasing bioavailability and patient acceptance, aiding in product identification, and enhancing overall safety, effectiveness, and drug delivery during storage and usage [2, 3].

Polymers have been extensively employed as a primary means of regulating the rate at which drugs are released from formulations, notably in the context of Gastroretentive drug delivery systems. The notable utilization of polymers in drug delivery is mainly attributed to their exceptional properties, which remain unmatched by other materials. The progress made in polymer science has facilitated the emergence of numerous innovative drug delivery systems. The diverse applications of polymers in the pharmaceutical field include their use as binders in tablets and as agents to control viscosity and flow in liquids, suspensions, and emulsions. Polymers can also serve as film coatings to mask

the unpleasant taste of drugs, enhance drug stability, and modify drug release properties. Within pharmaceuticals, polymers find extensive use in achieving taste masking, controlled release (such as extended, pulsatile, and targeted release), improved stability, and enhanced bioavailability. Monolithic delivery systems involve dispersing a drug within a polymer matrix, with drug release occurring through diffusion, regulated by the drug concentration and relaxation of the polymer chains, resulting in a sustained release pattern. Biodegradable polymers have gained significant traction in biomedical applications due to their biocompatibility and ability to degrade naturally. These advancements contribute to enhancing the efficiency of medical treatments while minimizing adverse effects [1-4].

Historical Background [1-4]

The word "polymer" comes from Greek roots meaning "many parts." Polymers have high molecular weights and consist of repeating units called monomers. They are considered a subset of macromolecules. Monomers are small molecules that combine with other molecules to form a polymer. Around 1955, the first polymer-drug conjugates were discovered, with the mescaline-N-vinylpyrolidine conjugation being one of the first. A decade or so later, Frank Davis and Abraham Abuchowski saw the promise of conjugating poly (ethylene glycol) (PEG) to proteins, leading to the development of a process known as PEGylation.

Ideal Characteristics of Polymer [4]

- It should be inert and compatible with the environment.
- It should be non- toxic and physiologically inert.
- It should be easily administrable.
- It should be easy to fabricate and must be inexpensive.
- It should have good mechanical strength.
- It must have compatibility with most of the drugs.
- It must not adversely affect the rate of release of the drug.

Classification of Polymers [1, 4, 5]

Polymers can be classified into different ways on the basis of their chemical structure, physical properties, polymerization method and source of origin.

1. Based on the Origin:

Natural Polymers

a) Protein-based: Albumin, Collagen, gelatin.
b) Polysaccharides: Agarose, alginate, carrageenan, chitosan, cyclodextrins, dextran, hyaluronic acid, polysialic acid.

Synthetic Polymers

Biodegradable Polymers

a) Polyesters: Poly (lactic acid) (PLA), poly (glycolic acid) (PGA), poly (hydroxyl butyrate) (PHB), poly (Ɛ-caprolactone) (PCL), poly (β-malic acid) (PMA).
b) Polyanhydrides: Poly (sebacic acid) (PSBA), poly (adipic acid) (PAPA), poly (terephthalic acid) (PTA) and various copolymers.
c) Polyamides: Poly (imino carbonates) (PIC), poly amino acids (PAA) etc. Phosphorus-based: Polyphosphates, poly phosphonates, poly phosphagens.
d) Others: Poly (cyano acrylates) (PCA), polyurethanes, poly ortho esters, poly dihydropyrans, polyacetals.

Non-biodegradable Polymers

a) Cellulose derivatives: Carboxymethyl cellulose (CMC), ethyl cellulose (EC), cellulose acetate (CA), cellulose acetate propionate (CAP), hydroxypropyl methylcellulose (HPMC).
b) Silicones: Polydimethylsiloxane (PDS), Colloidal silica etc. Acrylic polymers: Polymethacrylates (PMA), poly (methyl methacrylate) (PMMA), poly hydro (ethyl methacrylate) (PHEM).
c) Others: Polyvinyl pyrrolidone (PVP), ethyl vinyl acetate (EVA), poloxamers, poloxamines.

Semi-synthetic Polymer

Hydrogenated natural rubber, Cellulose nitrate, methyl cellulose etc are chemically modified polymers.

2. Based on the Polymerization Process:

Carothers in 1929 classified polymers into two types on the basis of mechanism of polymerization reaction:

Addition Polymers

The creation of polymer is caused by addition polymerization reactions. Some monomer molecules have double and triple bonds. E.g. polythene, polypropene, polystyrene, polyvinyl chloride.

Condensation Polymers

Polymerization occurs through a condensation polymerization process. This polymerization process eliminates tiny molecules like water, alcohol, and hydrogen chloride. Its monomers are poly functional or bifunctional. E.g. Polystyrene and Polyamide

3. Based on Interaction With Water

- Non-biodegradable hydrophobic Polymers: E.g. Polyvinyl chloride,
- Soluble Polymers: - E.g. HPMC, PEG
- Hydro gels: E.g. Polyvinyl pyrrolidine

4. Based on Physical Properties

- Elastomers: E.g., Natural rubbers, synthetic rubber.
- Plastic: E.g., polyethylene, polystyrene.
- Fibres: E.g., saran, vinyon, orlan.

5. Based on Stimuli Response

- Photo responsive polymers: E.g., PAA, PHPMAm and PNIPAM.
- pH responsive polymers: E.g., Chitosan, albumin, gelatin.
- Inflammation responsive polymers: E.g., Hyaluronic acid.
- Temperature responsive polymers: E.g., Poly N- alkyl substituted acrylamide.
- Enzyme-Responsive Polymers: E.g., Pectin, chitosan, amylase/amylopectin, cyclodextrin and dextrin.

Different Types of Polymeric Pharmaceutical Drug Delivery System

1. Drug Delivery using Polymeric Materials in Tissue Engineering

The subject of biomedical engineering has made significant strides in the last few years, primarily in the area of creating innovative approaches to boost tissue regeneration or enhance therapeutic effects. Polymers (natural, synthetic, or blended formulations) are an essential part of the most recent advancements because of their unquestionably broad range of characteristics and functions, which make them perfect for creating scaffolds for tissue engineering or drug delivery systems.

Polymers are extensively employed in tissue engineering to create biomimetic scaffolds that can replace damaged tissue while preserving an environment that is conducive to healing [5]. In tissue engineering, an in vivo-like microenvironment is generated using stem cells, polymers, and a physical, chemical, or biological stimuli. A biocompatible and biodegradable polymeric structure has been created using a variety of natural and synthetic polymers in order to achieve this aim. Natural polymers are the least poisonous and have the best biodegradability and biocompatibility of all the polymers. In bone tissue engineering, the most absorbable natural polymers—such as chitosan, collagen, silk fibroin, gelatin, cellulose, alginate, and starch are employed [6].

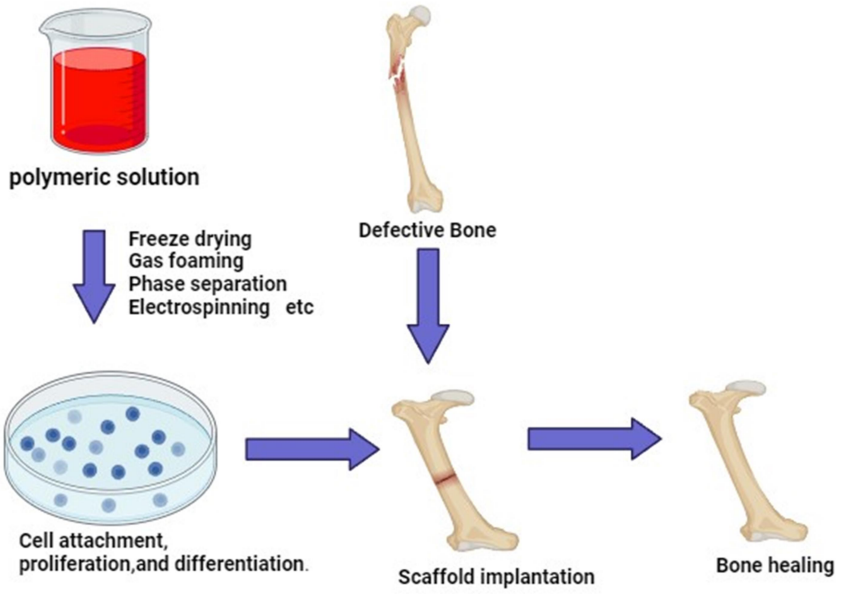

Figure 1: Drug Delivery using Polymeric Materials for creating scaffold in Tissue Engineering

2. Polymeric Nanoparticles

Particles classified as polymeric nanoparticles (NPs) range in size from 1 to 1000 nm. They can contain active chemicals that are either surface-adsorbed onto the polymeric core or trapped inside the particles [7]. Due to their excellent biodegradability, biocompatibility, and high drug-loading capacity, polymeric nanoparticles, or PNPs, are frequently utilised as drug carriers. Polymeric micelles, liposomes, dendrimers, polymeric sponges, and colloidal carriers are examples of PNPs, which are widely used nanocarriers. Since PNPs are frequently utilised as drug delivery systems, they have the capacity to load both natural and synthetic substances, such as growth factors, proteins, peptides, DNA, mRNA, and medications. Because of their tiny size, polymer-based nanoparticles usually exhibit unique characteristics. PNPs are particularly effective at increasing drug delivery to the intended cell or tissue, extending the half-life of the medication, lowering cytotoxicity, and improving pharmacokinetics [8]. The pH shift that happens when nanoparticles are endocytosed into a cell has piqued the curiosity of researchers studying pH-responsive nanoparticles [9].

Several types of synthetic and natural biomaterials can be used to create PNPs., including chitosan, albumin, gelatin, collagen, polylactic acid, polylactide co-glycolic acid, polylactic acid (PLA) (PLGA), polyethylene glycol, (PEG) polycaprolactone, (PCL), respectively. They are stabilized in numerous forms, such as polymeric nano systems, nanoparticles, vesicles, micelle, and dendrimers.

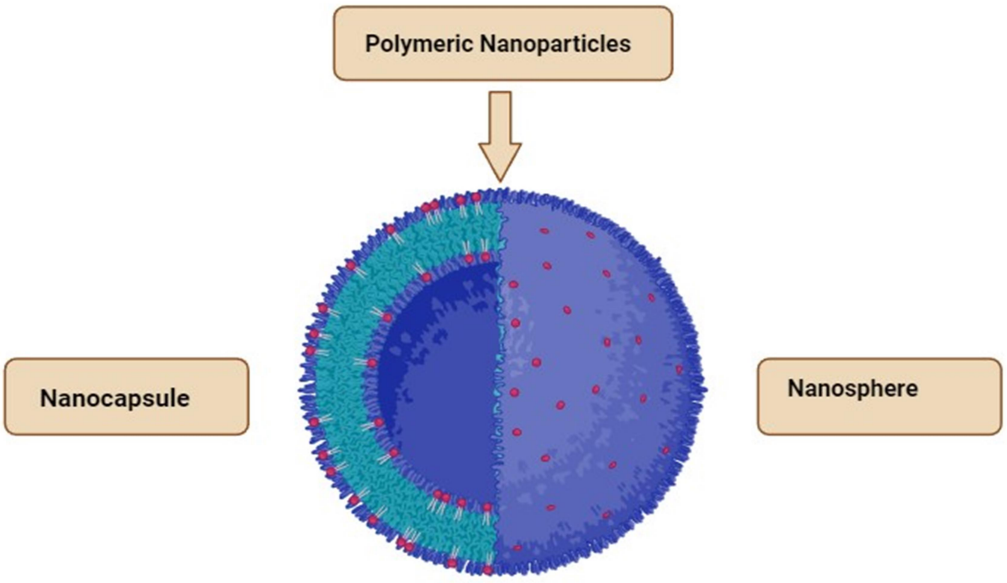

Figure 2: Polymeric Nanoparticles comprising Nanocapsule and Nanosphere.

3. Polymeric Micelle

In the field of nanosystems, polymeric micelles are multifunctional nanoparticles that have the ability to modify the release kinetics of embedded pharmaceutical medicines. The polymeric micelle enhances their ability to solubilize a poorly water-soluble drug in their micellar core and increases their permeability and retention to healthy cells with less harm [8].

Poly (lactic-co-glycolic acid) (PLGA) is the most widely used polymer for the synthesis of micelles as DDSs because of its excellent biocompatibility and biodegradability. As a novel type of nanoparticle for the delivery of hydrophobic chemotherapeutics, polymeric micelles have appeared. Nowadays polymeric micelles are a great medication delivery technology because of their many benefits [10].

4. Polymers Based Gene Delivery (Polyplexes)

Gene-based therapies are a novel approach to treating a wide range of diseases which are now incurable. However, gene therapies' intermittent nature has severely limited their potential in biomedical applications. Therefore, the invention of gene-delivery vectors is essential to the success of gene-based treatments. Gene delivery

has been accomplished using a range of gene-delivery vectors created to date. They can be divided broadly into viral and non-viral vectors. Non-viral vectors have recently garnered significantly greater research attention due to safety concerns related to viral vectors. Polymeric vectors are a great substitute for viral vectors among these non-viral vectors because of their low immunogenicity, ease of manufacture, regulated chemical composition, and high chemical adaptability. Particularly, biodegradable polymers, which have the several benefits [11].

Compared to other applications, gene therapy is one area where the use of biodegradable polymeric vectors is comparatively more significant. Resources suggest that there are two main categories of biodegradable polymers: natural and manmade polymers. Getting nucleic acids and genes into cells is a difficult task. Using polyplexes provides a compelling way around this challenge. The development of innovative polyplexes has greatly evolved in the past several decades [12].

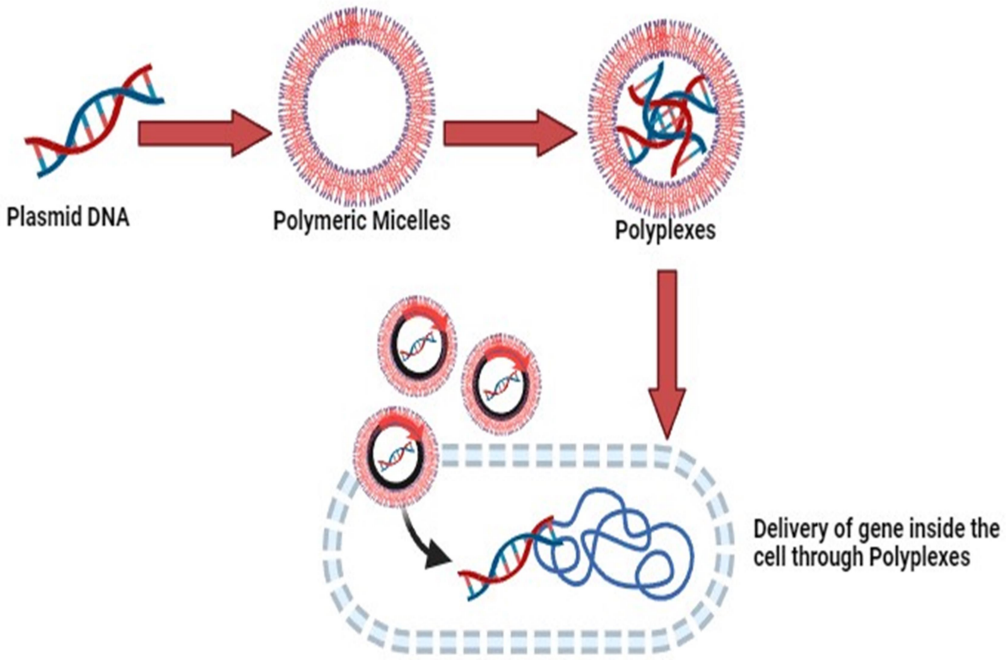

Figure 3: Polyplexes for gene delivery.

5. Polymers in Oral Solid Dosage Forms [1-13]

Solid oral dosage forms can be categorized into two main categories: modified-release technologies and immediate-release dosage forms, where medication disintegration and subsequent release and dissolution take place in the body. Numerous polymeric excipients seen in immediate-release tablets are also utilised to "bulk out" capsule fills. When medications with short biological half-lives are formulated as extended- or sustained-release dosage forms, their therapeutic impact may be improved. The duration of release is prolonged by sustained and extended-release dose formulations. Tablet and capsules are the most common forms of solid oral drug products, which may be defined as solid pharmaceutical dosage forms in which the active agents are blended with excipients. Oral tablets and capsules are widely used for the delivery of a range of drugs. For a long time, polymers have been utilised as excipients in traditional oral dosage forms, either to facilitate the production process or to protect the drug from degradation during storage. In order to attain desired dosage form properties including drug content, hardness or crushing strength, disintegration time, friability, tensile strength, and dissolution time, polymeric excipients are mixed with an API and processed using various methods.

Furthermore, solid oral dose formulations including polymeric inert excipients can overcome the challenges associated with some medicines' low bioavailability. Moreover, innovative technologies utilising polymer

excipients facilitate the creation of numerous novel solid formulations that exhibit superiority over traditional dosage forms.

6. Gastroretentive Dosage Forms

The oral drug delivery systems encounter various difficulties, including limited bioavailability as a result of the gastrointestinal tract's heterogeneity, commensal flora's pH, the dosage form's stomach retention time, surface area, and enzymatic activity [14]. Several Gastroretentive drug delivery systems (GRDDS) have been employed to enhance the therapeutic effectiveness of medications with limited absorption window, unstable at alkaline pH, soluble in acidic environments, and localised stomach activity. The main mechanism of GRDDS includes floating, sinking, swelling, effervescence, mucoadhesion, and magnetic properties [15].

A variety of physiochemically distinct polymers provide potential uses for the design of GRDDS. A specific type of GRDDS is best suited for a particular class of polymers based on their chemical characteristics. Therefore, a deeper comprehension of polymers and GRDDS procedures should aid in the establishment of effective Gastroretentive delivery systems, and efforts should be undertaken to expand the use of polymers in novel GRDDS approaches [16].

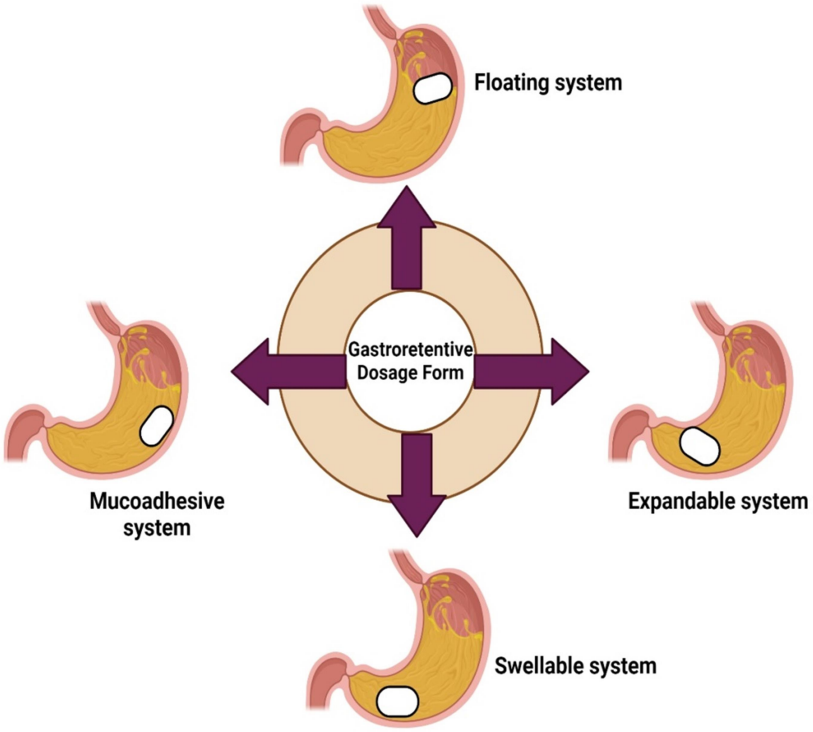

Figure 4: Various Gastroretentive drug delivery system.

7. Polymeric Micelles For Ocular Drug Delivery

Following topical administration, polymeric micelles have emerged as a promising nanocarrier to get over these restrictions and deliver therapeutic drug concentrations in the anterior and posterior portions of the ocular tissues. A majority of polymeric micelles utilised in drug delivery are composed of amphiphilic di-block polymers, tri-block polymers (hydrophilic-hydrophobic-hydrophilic), graft polymers (hydrophilic-hydrophobic), and ionic copolymers (hydrophilic-ionic). The main hydrophilic component in most of these systems is poly (ethylene glycol) (PEG).

Polymeric micelle formulations are a highly effective drug delivery system. Medications that are very soluble in water, for instance, mostly bind to micelle surfaces, whereas drugs that are poorly soluble in water primarily bind to micelle cores. Furthermore, the interface between hydrophilic and lipophilic micelles is where amphiphilic medicines are primarily soluble. One sort of polymer with good water solubility is polyethylene glycol (PEG). It is frequently

utilised in the hydrophilic blocks of polymer micelles since it is stable, non-toxic, viscous, and simple to get. The PEG–PCL polymeric micelle is the alternative most popular micelle. During ocular transport, the negatively charged PEG-PCL micelles are able to penetrate deeper than the chitosan-coated micelles. Because PCL is biocompatible and biodegradable, PEG–PCL micelles are a secure and efficient method of drug administration [17].

8. Polymers in Parenteral

Parenterally administered different polymers, such as methyl acrylate, function as interferon inducers, causing interferon to be induced in diseases like cancer. When a medication is mixed with a polymer and present in the body, methacrylic acid alkyl amide acts as a plasma expander, raising the level of plasma in the body. Certain vaccines, like methyl methacrylate, are administered using polymers that break down in the gastrointestinal tract [18].

Key Role of Polymers as a Multifunctional Excipient

1. Polymer as a Diluent

Diluents are fillers or bulking agent that are used to make up the volume of tablet if tablet is unable to produce the sufficient volume. Example: Lactose, Spray dried lactose, Micro crystalline cellulose (Avicel 101 and 102), Pvpk30 (Pearlitol SD200 and 25C), Sorbitol, Dibasic calcium phosphate dehydrate, Calcium sulphate dehydrate etc. Excipients are therefore added in order to boost mass and volume, which makes administration easier, accurate metering possible, and production feasible. A good bulking agent should be affordable, tasteless, and compatible with the other ingredients in the recipe. The hardness of the solid dosage form and the pace at which the tablet dissolves in the gastrointestinal tract can both be impacted by the physicochemical characteristics of the diluents [19].

2. Polymer as a Binder

Binders for tablets or capsules facilitate the powders' adherence to one another. Granulation binders facilitate granule agglomeration and cohesiveness, hence encouraging suitable compatibility and free-flowing qualities. They are utilised in graduation procedures.

Numerous polymer binders, both synthetic and natural, are frequently utilised in solid drug delivery systems. Several well-known examples include: alginates, carbomer, microcrystalline and powdered cellulose, cellulose derivatives (sodium carboxymethyl cellulose sodium [CMC], ethyl cellulose [EC], methyl cellulose [MC], hydroxyethyl cellulose, hydroxyethyl methylcellulose, hydroxypropyl methylcellulose [HPMC]), chitosan, gelatin, copovidone, crospovidone, maltodextrin, polyethylene glycol (PEG), polycarbophil, polydextrose, polyvinyl pyrrolidone (PVP) [13].

3. Polymer as a Disintegrating Agent

After oral ingestion, disintegrants are needed to encourage drug fragmentation and maximise drug release in the GI tract's aqueous environments. A solid oral dosage form's disintegration and the active ingredient's subsequent dissolving are recognised to be essential and may be the rate-limiting stage for drug absorption. Disintegrants have been added to solid oral dosage forms to speed up the process of disintegration, which in turn has increased the percentage of dissolution, bioavailability, and pharmacological impact of several active substances. Alginic acid, alginates, starch, and pregelatinized starch are polymeric disintegrants [13-14].

4. pH Responsive Polymer

When the pH of a solution changes, pH-responsive polymers are likely to alter their structural makeup and physical characteristics, such as solubility, surface activity, and chain arrangement. Consequently, a pH-responsive polymeric system that is exposed to a stimulating systemic pH may experience a variety of phenomena, including coating, gelling, shrinking, and swelling. 20 pH-responsive polymers are unusual in that they can be used for medication delivery, particularly targeted and controlled distribution. Examples of Some pH responsive polymer are Chitosan, Carrageenan, Hyaluronic acid, Alginate, Agar, Eudragit. [20]

5. Polymer as a Solubalizer

The amorphous drugs are thermodynamically unstable, during the process of manufacturing, storage, and product use, they frequently recrystallize. In order to resolve this problem, amorphous pharmaceuticals have been stabilised through the use of polymeric carriers to create amorphous solid dispersions (ASDs), which are thought to be among the best ways to administer poorly soluble medications. Therefore, the most important element influencing the development of ASD is the choice of polymer. In order to

resolve this problem, amorphous pharmaceuticals have been stabilised through the use of polymeric carriers to create amorphous solid dispersions (ASDs), which are thought to be among the best ways to administer poorly soluble medications. Therefore, the most important element influencing the development of ASD is the choice of polymer. Polymers typically used in forming ASDs include polyvinyl lactam polymers such as polyvinylpyrrolidone (PVP), polyvinylpyrrolidone-vinyl acetate copolymer (PVP/VA) and Soluplus, cellulose derivatives such as hydroxypropyl cellulose (HPC), hydroxypropyl methylcellulose (HPMC), hydroxy ethyl cellulose, Hypromellose acetate succinate (HPMCAS), hydroxypropyl methylcellulose phthalate (HPMCP), cellulose acetate phthalate (CAP) and polymethacrylates (Eudragit R E, L, S) [21].

6. Polymer as a Mucoadhesive Agent

The mucoadhesive polymeric strategy has become highly significant since it provides a number of benefits for overcoming obstacles. Due to its many benefits, this method has been utilised to transport drugs to a variety of organ locations, including the buccal, gastrointestinal, nasal, rectal, vaginal, and ophthalmic. One benefit of using mucoadhesive polymers is that they can produce prolonged medication administration by extending the residence time at the application site. Examples of Some Mucoadhesive polymer is Carbopol, Chitosan, hydroxypropyl methyl cellulose (HPMC), gellan gum [22].

General Mechanism of Drug Release from Polymer [1, 18, 23]

There are three primary mechanisms by which active agents can be released from a delivery system are as follows:

1. Diffusion

When an active ingredient, such as a drug, diffuses through the polymer that makes up the controlled-release device, it happens. The drug diffuses when it leaves the polymer matrix and enters the surrounding environment. With this kind of system, the rate of release often reduces as it goes on since the active agent needs more time to diffuse into the system due to its increasing distance to travel. Diffusion occurs when a glassy (dry) polymer comes into contact with water or any other thermodynamically suitable liquid. The polymer is ingested.

2. Degradation

Biodegradable polymer degrades itself within the body as a result of natural biological processes, removing the requirement for a drug delivery system to be removed once the active agent has been released. The majority of biodegradable polymers are made to hydrolyse into increasingly smaller, physiologically acceptable molecules as the polymer chains break down. For some degradable polymers, most notably the polyanhydrides and poly Ortho esters, the degradation occurs only at the surface of the polymer, resulting in a release rate that is proportional to the surface area of the drug delivery system.

3. Dissolution

When a drug is released via the polymer dissolving and being absorbed by the dissolution fluid. Slowly dissolving polymers are used to encapsulate the drug (reservoir system) or spread it (matrix system) in sustained or controlled drug delivery systems. The drug's dissolution and subsequent release are determined by the rate at which the dissolution fluid penetrates the matrix.

Current Status and Future Prospects of Polymers in Pharmaceutical Drug Delivery System

Pharmaceutical Polymers are the heart of pharmaceutical formulations in conventional and novel drug delivery system with the progress in all spheres of science and technology, Dosage forms have changed over time, moving from basic mixtures and pills to immensely complicated, scientifically advanced drug delivery systems called as Novel Drug Delivery Systems (NDDS). Since the early 1980s, the use of polymers in innovative drug delivery systems (NDDS) has gained momentum in an effort to improve therapeutic outcomes from the same medicine due to the NDDS's many benefits over traditional dosage forms. Since then, a number of Polymeric Novel Drug Delivery Systems have been created, accounting for a significant fraction of the worldwide market. Producing and utilising these responsive polymers with precisely engineered macroscopic and microscopic structural and chemical properties is a major area of focus for the development of novel materials in controlled drug delivery systems. The future possibilities for innovative drug delivery systems will be increased by the design and production of unique combinations of polymers. It goes without saying that a lot of new

information regarding the chemistry and physical makeup of these novel materials will need to be acquired [1, 18, 24, 25].

CONCLUSION

Polymer based pharmaceutical drug delivery system have been used to treat many lethal diseases such as Cancer, Viral diseases, Hepatitis and Genetic disorders. When designing dosage forms for efficient drug distribution, a number of polymers have been effectively employed as excipients, and more are currently being researched. Biocompatibility, biodegradability, and bioavailability are the main features of natural polymers. Natural biodegradable polymers have drawn a lot more attention in recent years because of their uses in the sectors of environmental conservation and physical health maintenance. From the discussion, it can be inferred that pharmaceuticals can be incorporated into polymers to create a range of shaped and sized dosage forms that release the medication gradually. Meanwhile In terms of toxicity, drug compatibility, and degradation pattern, polymer selection is crucial during the drug-making process. This article provides a broad overview of the potential use of pharmaceutical polymers in drug delivery systems. Polymers with distinct properties, whether synthetic, semisynthetic, or natural, are widely used in pharmaceutical sciences. Polymeric excipients for drug delivery systems are now widely available due to the rapid advancements in medicinal engineering.

REFERENCES

[1] Gandhi. K, Deshmane. S, Biyani. K. Polymers in Pharmaceutical Drug Delivery System: A Review. Int. J. Pharm. Sci. 2012;14(2):57-66.

[2] Rajeswari. S, Prasanthi. T, Sudha. N, Swain. N, Panda. S, Goka. V. Natural Polymers: A Recent Review. World Journal of Pharmacy and Pharmaceutical Sciences. 2017;6(8):472-494.

[3] Gupta. A, Sharma. N, Khinchi. M.P, Agrawal. D. A Review on Natural Polymer. Asian Journal of Pharmaceutical Research and Development. 2013;1(5): 134-145.

[4] Sivakumar. *P, et al.* Overview on Pharmaceutical Polymers. World Journal of Pharmacy and Pharmaceutical Sciences. 2015;10(5):953-975.

[5] Hudita. A, Galateanu. B. Polymer Materials for Drug Delivery and Tissue Engineering. Polymers MDPI. 2023; 15: 3103.

[6] Guo. L, Liang. Z, Yang. L, Du. W, Yu. T, Tang. H, *et al.* The role of natural polymers in bone tissue engineering. Journal of Controlled Release. 2021;338; 571–582.

[7] Zielinska. A, Carreiro. F, Oliveira. A, Neves. A, Pires. B, Venkatesh. N, *et al.* Polymeric Nanoparticles: Production, Characterization, Toxicology and Ecotoxicology. Molecules MDPI. 2020; 25: 3731.

[8] Bhardwaj. H, Jangde. R.K, Current updated review on preparation of polymeric nanoparticles for drug delivery and biomedical applications. Next Nanotechnology. 2023; 2: 2949-8295.

[9] Deirram. N, Zhang. C, Kermaniyan. S, Johnston. S, Such. G. pH-Responsive Polymer Nanoparticles for Drug Delivery. Macromolecular Rapid Communication journal. 2019: 40: 1800917.

[10] Begines. B, Ortiz. T, Aranda. M.P, Martinez. G, Merinero. M, Alcudia. A. Polymeric Nanoparticles for Drug Delivery: Recent Developments and Future Prospects. Nanomaterials MDPI Journal. 2020; 10:1403.

[11] Chen.CK, Huang. PK, Law. WC, Chu. CH, Chen. NT, Lo. LW. Biodegradable Polymers for Gene-Delivery Applications. International Journal of Nanomedicine. 2020;15: 2131-2150.

[12] Ita. K. Polyplexes for gene and nucleic acid delivery: Progress and bottlenecks. European Journal of Pharmaceutical Sciences. 2020; 150:105358.

[13] Debotton. N, Dahan. A. Applications of Polymers as Pharmaceutical Excipients in Solid Oral Dosage Forms. Medicinal Research Reviews. 2016;00(0): 1-46.

[14] Merwe. J.V, Steenekamp. J, Steyn. D, Hamman. J. The Role of Functional Excipients in Solid Oral Dosage Forms to Overcome Poor Drug Dissolution and Bioavailability. Pharmaceutics MDPI Journal. 2020; 12: 393.

[15] Tripathi. J, Thapa. P, Maharjan. R, Jeong. S.H. Current State and Future Perspectives on Gastroretentive Drug Delivery Systems. Pharmaceutics MDPI Journal. 2019;11: 193.

[16] Patil. S, Rathi. M, Misra. A. Applications of Polymers in Gastric Drug Delivery. Elsevier Inc. 2021.

[17] Mandal. A, Bisht. R, Rupenthal. I.D, Mitra. A.K. Polymeric micelles for ocular drug delivery: From structural frameworks to

recent preclinical studies. Journal of Controlled Release. 2017; 12-15.

[18] Sivakumar. P. Overview on Pharmaceutical Polymers. World Journal of Pharmacy and Pharmaceutical Sciences. 2015;10(5):953-975.

[19] Varma. K. Excipients used in the Formulation of Tablets. Research and Reviews: Journal of Chemistry. 2016; 143-145.

[20] Mutalabisin. M, Chatterjee. B, Jaffri. J. pH Responsive Polymers in Drug Delivery. Research J. Pharm. and Tech. 2018; 11(11): 5115-5122.

[21] Zhang. J, Guo. M, Luo. M, Cai. T. Advances in the development of amorphous solid dispersions: The role of polymeric carriers. Asian Journal of Pharmaceutical Sciences. 2023; 18: 100834.

[22] Pandey. M, Choudhury. H, Aziz. Ab, Bhattamisra. U.K, Gorain. B, Ting Su. J.S, et al. Potential of Stimuli-Responsive in Situ Gel System for Sustained Ocular Drug Delivery: Recent Progress and Contemporary Research. Polymers MDPI Journal. 2021; 13: 1340.

[23] Pawar. D, Patrekar. P, Dhanawade. P, Dongare. S, Mali S. Polymers Used in Pharmaceuticals: A Brief Review. International Journal of Pharma and Chemical Research. 2016; 2(4): 233-238.

[24] Chaudhari. T, Desale. V, Patil. T, Patil. T, Shaikh. H, Ahmad. S. A Review on Polymer Used in Drug Delivery System. International Journal of Advanced Research in Science, Communication and Technology. 2023; 3(1): 585-594.

[25] Zaki. N.M, Saeed. B. Smart Pharmaceutical Polymers Classification and Applications: A Review. ACE Journal of Clinical Chemistry and Laboratory Medicine. 2021; 1 (2): 7-17.