

## REVIEW ARTICLE

## ROLE OF POLYMERS IN DRUG DELIVERY

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## ABSTRACT

This review focus on the role of polymers used in pharmaceutical drug delivery of therapeutic agents. The polymers are used as carriers for delivery of drug at target site. Biodegradable polymers are widely used in delivery of drugs at specific site of the body because they can be degraded at constant rate of drug release. Natural polymers are also used for drug delivery at predetermined rates. The release mechanism of the drug from these polymers is by Degradation, Diffusion and Swelling. For controlled drug delivery of the therapeutic agents, they are used in pharmaceutical industry as binders, as film coating to mask the unpleasant taste, to enhance the drug stability and to modify the release characteristics of the drug.

**Key words:** Natural and synthetic polymers, drug delivery, mechanism, applications

## INTRODUCTION

Polymers are macromolecules having very large chains, contain a variety of functional groups, can be blended with other low- and high-molecular-weight materials, and can be tailored for any applications. Polymers are the backbone of pharmaceutical drug delivery systems. They have been found extensive applications in drug delivery because they offer unique properties which have not been attained by any other materials. Polymers have been used as a important tool to control the drug release rate from the formulations and they are also enhance used as stabilizer, taste-masking agent, and protective agent in oral drug delivery. Polymers can bind the particles of a solid dosage form and also change the flow properties of a liquid dosage form.<sup>1</sup> Advances in polymers led to development of several novel drug delivery systems due to proper consideration of surface and bulk properties of polymers. Due to this reason, polymers have been widely used in developing new technologies by many researchers. These new technologies contribute to make medical treatment more efficient and side effects are also reduced. Polymer play an important role in the Drug delivery system in terms of materials to assist delivery, excipients, and technology which allow fast or slow release of drugs from the formulation.<sup>2</sup>

## Classification of polymers:-

## Based on source:-

1. Natural:- Chitosan, Alginate, Gelatin, Albumin, Collagen, Dextran
2. Semi-Synthetic:- Hydroxy Propyl Methyl Cellulose (HPMC), Methyl Cellulose (MC), Hydroxy Propyl Cellulose (HPC)
3. Synthetic:- Polyethylene, Polylactic acid, Polypropylene, Polyglycolic acid, Polyhydroxy Butyrate

## Type of Polymerization:-

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Addition Polymer:- Polyethylene, Polypropylene, Polyvinyl Chloride

Condensation Polymer:- Polyurethane, Polyester

## Degradability:-

Biodegradable:- Polylactic acid, Polyglycolic acid, Polycaprolactone, Polyanhydrides

Non-Biodegradable:- Polydimethyl Siloxane, Polyether Urethane, Ethyl Cellulose

## Nature of Polymer Water Interaction:-

Hydrophobic Polymer:- Ethyl Cellulose, Polydiethyl Siloxane Hydrophilic Polymer :- Cellulosic: MC, HPMC, HPC, HEC, NaCMC. Cellulosic: Sodium Alginate, Xanthun gum, chitosan Hydrogel Material :- Cross-linked Polyvinyl Alcohol, Polyethylene Oxide, Polyacrylamide<sup>3</sup>

## Role of polymers in drug delivery:-

**1. Immediate release dosage forms Tablets:** Polymers including polyvinyl-pyrrolidone and hydroxypropyl methylcellulose (HPMC) find uses as binders that aid the formation of granules that improve the flow and compaction properties of tablet formulations prior to tableting.

**Capsules:** Many of the polymeric excipients used to “bulk out” capsule fills are the same as those used in immediate release tablets. Gelatine has been used almost exclusively as a shell material for hard (two-piece) and soft (one-piece) capsules. HPMC has recently been developed and accepted as an alternative material for the manufacture of hard (two-piece) capsules.

## 2. Modified-release dosage form

To achieve gastro retention mucoadhesive and low-density, polymers have been evaluated, with little success so far, for their ability to extend gastric residence time by bonding to the mucus lining of the stomach and floating on top of the gastric contents respectively.

### 3. Extended release dosage forms

Extended and sustained release dosage forms prolong the time that systemic drug levels are within the therapeutic range and thus reduce the number of doses the patient must take to maintain a therapeutic effect thereby increasing compliance. The most commonly used water-insoluble polymers for extended-release applications are the ammonium ethacrylate copolymers (Eudragit RS and RL), cellulose derivatives ethylcellulose, and cellulose acetate, and polyvinyl derivative, polyvinyl acetate.

### 4. Gastroretentive Dosage Forms

Gastroretentive dosage forms offer an alternative strategy for achieving extended release profile, in which the formulation will remain in the stomach for prolonged periods, releasing the drug *in situ*, which will then dissolve in the liquid contents and slowly pass into the small intestine.<sup>4</sup>

## TYPES OF POLYMERS IN PHARMACEUTICAL DRUG DELIVERY:

### Polymers as floating drug delivery system

Polymers are generally employed in floating drug delivery systems so as to target the delivery of drug to a specific region in the gastrointestinal tract i.e. stomach. Natural polymers which have been explored for their promising potential in stomach-specific drug delivery include chitosan, pectin, xanthan gum, guar gum, gellan gum, karaya gum, psyllium husk, starch, alginates etc.<sup>5</sup>

### Polymers used in mucoadhesive drug delivery system

The new generation mucoadhesive polymers for buccal drug delivery with advantages such as an increase in the residence time of the polymer, penetration enhancement, site-specific adhesion, and enzymatic inhibition, site-specific mucoadhesive polymers will undoubtedly be utilized for the buccal delivery of a wide variety of therapeutic compounds. This class of polymers has enormous potential for the delivery of therapeutic macromolecules. Application of lectin and "lectinomimetics" appears to be the most promising area of current research efforts aimed at the safe and effective delivery of drugs via the buccal mucosa.<sup>6</sup>

### Polymers used as Colon Targeted Drug Delivery

Polymer plays a very important role in the colon targeted drug delivery system. It protects the drug from degradation or release in the stomach and small intestine. It also ensures abrupt or controlled release of the drug in the proximal colon. For example Wong *et al.* studied the dissolution of dexamethasone and budesonide from guar gum-based formulations and observed that the drug release in simulated colonic fluid was markedly increased at galactomannanase concentrations >0.01 mg/ml. A novel colon targeted tablet formulation using pectin as a carrier and diltiazem hydrochloride and

indomethacin as model drugs has been developed. *In vitro* study showed that prepared dosage forms have limited drug release in stomach and small intestine and released maximum amount of drug in the colon. McLeod *et al.* synthesized glucocorticoid-dextran conjugates in which dexamethasone and methylprednisolone were attached to dextran using dicarboxylic acid linkers (succinate and glutarate). Dextran conjugates resisted hydrolysis in upper GI tract contents but were rapidly degraded in cecal and colonic contents where the bacterial count is high. Chitosan capsules were used for colonic delivery of an antiulcerative colitis drug. 5-Aminosalicylic acid (5-ASA) was used as model drug. A marked increase in the release of drug from chitosan capsule was observed in the presence of the rat cecal content.<sup>7</sup>

### Polymers for Sustained Release

Polymer used in the sustained release system by preparing biodegradable microspheres containing a new potent osteogenic compound. In order to achieve the sustained release of 3-ethyl-4-(4-methylisoxazol-5-yl)-5-(methylthio) thiophene-2-carboxamide, a new potent osteogenic compound for the treatment of bone disorders, prepared a microspheres containing BFB0261 and newly synthesized three poly (d, l-lactic acid) (PLA), four poly (d, l-lactic acid-co-glycolic acid) (PLGA), and eight poly (d, l-lactic acid)-block-poly(ethylene glycol) (PLAPEG) biodegradable polymers or copolymers, and evaluated the release pattern of microspheres.<sup>8</sup>

### Polymers in implantable drug delivery

Polymer micro-needles are of interest for implantable drug delivery due to their enhanced biocompatibility, and capability to conform to tissue without shattering during the insertion or tissue reconfiguration processes. These devices have been fabricated using several polymers including polydimethylsiloxane (PDMS), polylactic and polyglycolic acid (PLGA), block copolymer hydrogels, SU-8 photoresist, and polyimide. Bernardo *et al.* 2010 developed a device that incorporates the flexibility and biocompatibility of polymer microneedles while still offering the advantages of active fluidic delivery devices in simple microfluidic architecture. This device uses a similar electrochemical release and dose control mechanism as our previous work (Chung and Erickson) but is now integrated into a flexible system as opposed to its silicon predecessor.<sup>9</sup>

### Polymeric micelles

Polymeric micelles (PMs) are developed in response to the immediate needs of high selectivity of drug carriers. Nowadays many life threatening diseases, such as cancer, current chemotherapy of which, still face a most serious problem of lack of selectivity of anticancer drugs toward proliferative cells, thus, resulting in the cytotoxic action of these drugs. PMs formed from an amphiphilic block copolymer are suitable for encapsulation of poorly water-soluble, hydrophobic anticancer drugs. Importantly, critical features of the PMs as drug carriers, including particle size, stability, loading capacity and release kinetics of drugs allow PMs to be targeted to the tumor site by a passive mechanism called the enhanced permeability and retention effect.<sup>10</sup>

## Polymers in tissue engineering

A wide range of natural-origin polymers with special focus on proteins and polysaccharides might be potentially useful as carriers systems for active biomolecules or as cell carriers with application in the tissue engineering field targeting several biological tissues.

Protein-based in the tissue engineering field are:-

- collagen,
- gelatin
- silk fibroin, fibrin (fibrinogen) and
- Other proteins such as elastin or soybean are used.

Several polysaccharides based polymers used in tissue engineering are:-

- Chitosan
- Starch
- Alginate
- Chondroitin sulphate<sup>11</sup>

## Polymers used in micro and nanoparticles for targeted drug delivery

Micro- and nanospheres fabricated from a biodegradable polymer for drug delivery systems have become increasingly important owing to the fact that such systems enable controlled drug release at desired sites. A number of polymers have been investigated for formulating biodegradable nanoparticles, such as polylactide (PLA), polycaprolactone (PCL) and poly(lactide-co-glycolide) (PLGA). These are biocompatible and biodegradable polymers which have recently been the subject of extensive investigation. Polymeric nano carriers such as poly(DL-lactide-co-glycolide) have shown promising pharmacokinetics both at the whole-body and cellular levels (passive targeting). The active drug targeting is usually achieved by the chemical attachment onto a targeting component that strongly interacts with antigens (or receptors) displayed on the target tissue, leading to the preferential accumulation of the drug in the targeted organ, tissue, or cells.<sup>12</sup>

## Polymer drug conjugate

Polymer-drug conjugates achieve tumour-specific targeting by the enhanced permeability and retention (EPR) effect these macromolecular prodrugs comprise a minimum of three components: a natural or synthetic, water-soluble polymeric carrier (usually of 10 000–100 000 Da), a biodegradable polymer-drug linkage (often a peptidyl or ester linkage) and a bioactive antitumour agent. Phase I/II clinical trials involving *N*-(2-hydroxypropyl)methacrylamide (HPMA) copolymer-doxorubicin (PK1; FCE28068) showed a four- to fivefold reduction in anthracycline-related toxicity, and, despite cumulative doses up to 1680 mg/m<sup>2</sup> (doxorubicin equivalent), no cardiotoxicity was observed.<sup>13</sup>

## MECHANISM OF DRUG RELEASE FROM POLYMERS

### Diffusion

Diffusion occurs when a drug or other active agent passes through the polymer that forms the

controlled-release device. Diffusion occurs when the drug passes from the polymer matrix into the external environment. As the release continues its rate normally decreases with this type of system since the active agent has a progressively longer distance to travel and therefore requires a longer diffusion time to release. In these systems, the combinations of polymer matrices and bioactive agents chosen must allow for the drug to diffuse through the pores or macromolecular structure of the polymer upon introduction of the delivery system into the biological environment without inducing any change in the polymer itself.<sup>14</sup>

### Degradation

Biodegradable polymer degrades within the body as a result of natural biological processes, eliminating the need to remove a drug delivery system after release of the active agent has been completed. Most biodegradable polymers are designed to degrade as a result of hydrolysis of the polymer chains into biologically acceptable and progressively smaller compounds. For some degradable polymers, most notably the polyanhydrides and polyorthoesters, 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.<sup>15</sup>

### Swelling

They are initially dry and when placed in the body will absorb water or other body fluids and swell. The swelling increases the aqueous solvent content within the formulation as well as the polymer mesh size, enabling the drug to diffuse through the swollen network into the external environment.<sup>16</sup>

## APPLICATIONS OF POLYMERS IN DRUG DELIVERY:-

### Application in conventional dosage forms:-

1. Tablets:- As binders to mask unpleasant taste for enteric coated tablets
2. Liquids:- Viscosity enhancers For controlling the flow
3. Semisolids:- In gel preparation
4. In Ointments
5. In transdermal Patches<sup>17</sup>

### Application in biomedical field:-

#### A. Water-Soluble Synthetic Polymers

1. Poly (acrylic acid) Cosmetic, pharmaceuticals, immobilization of cationic drugs, base for Carbopol polymer.
2. Poly (ethylene oxide) as Coagulant, flocculent, very high molecular-weight up to a few millions, swelling agent
3. Poly (ethylene glycol) MW <10,000; liquid (MW <1000) and wax (MW >1000) as plasticizer, base for suppositories

4. Poly (vinyl pyrrolidone) aUsed to make betadine (iodine complex of PVP) with less toxicity than iodine, plasma replacement, tablet granulation.

5. Poly (vinyl alcohol) Water-soluble packaging, tablet binder, tablet coating Polyacrylamide Gel electrophoresis to separate proteins based on their molecular weights, coagulant, absorbent.

6. Poly (isopropyl acrylamide) and poly (cyclopropyl methacrylamide)

### B. Cellulose-Based Polymers

1. Ethyl cellulose Insoluble but dispersible in water, aqueous coating system for sustained release applications

2. Carboxymethyl cellulose Super disintegrant, emulsion stabilizer

3. Hydroxyethyl and hydroxypropyl celluloses

4. Soluble in water and in alcohol, tablet coating

5. Hydroxypropyl methyl cellulose Binder for tablet matrix and tablet coating, gelatin alternative as capsule material

6. Cellulose acetate phthalate enteric coating

### C. Hydrocolloids

1. Alginic acid Oral and topical pharmaceutical products; thickening and suspending agent in a variety of pastes, creams, and gels, as well as a stabilizing agent for oil-in-water emulsions; binder and disintegrant

2. Carrageenan: - Modified release, viscosifier

3. Chitosan:- Cosmetics and controlled drug delivery applications, mucoadhesive dosage forms, rapid release dosage forms

4. Hyaluronic acid Reduction of scar tissue, cosmetics

5. Pectinic acid Drug delivery

### D. Water-Insoluble Biodegradable Polymers

Lactide-co-glycolide polymers Microparticle–nanoparticle for protein delivery.

### E. Starch-Based Polymers

Starch Glidant, a diluent in tablets and capsules, a disintegrant in tablets and capsules, a tablet binder Sodium starch glycolate Super disintegrant for tablets and capsules in oral delivery

### F. Plastics and Rubbers

1.Polyurethane Transdermal patch backing (soft, comfortable, moderate moisture transmission), blood pump, artificial heart, and vascular grafts, foam in biomedical and industrial products Silicones Pacifier, therapeutic devices, implants, medical grade adhesive for transdermal delivery

2.Polycarbonate Case for biomedical and pharmaceutical products

3. Polychloroprene Septum for injection, plungers for syringes, and valve components

4. Polyisobutylene Pressure sensitive adhesives for transdermal delivery

5. Polycyanoacrylate Biodegradable tissue adhesives in surgery, a drug carrier in nano- and microparticles

6. Poly (vinyl acetate) Binder for chewing gum.

7. Polystyrene Petri dishes and containers for cell culture

8. Polypropylene Tight packaging, heat shrinkable films, containers

9. Poly (vinyl chloride) Blood bag and tubing.

10. Polyethylene Transdermal patch backing for drug in adhesive design, wrap, packaging, containers

11. Poly (methyl methacrylate) hard contact Lenses Poly (hydroxyethyl methacrylate) Soft contact lenses <sup>18</sup>

### Applications of polymers for controlled drug delivery

1. Reservoir Systems

2. Ocusert System

3. Matrix Systems

4. Swelling Controlled Release Systems

5. Biodegradable Systems

6. Osmotically controlled Drug Delivery

7. Introduction: Principles of Controlled Drug Delivery

8. The Progestasert System

9. Reservoir Designed Transdermal Patches

10. Matrix Systems

11. Stimulus Responsive Drug Release

12. Ultrasound Responsive Drug Release

13. Temperature Responsive Drug Release

14. pH Responsive Drug Release

15. Electric Current Responsive Drug Release

16. Polymer-Drug Conjugates <sup>19</sup>

### Future prospective of advanced drug delivery using polymers:-

### Engineered Polymers for Advanced Drug Delivery

**Smart polymers:** - Modern drug delivery technology has been made possible by the advances in polymer science. Advancement in polymer science and engineering has developed new polymers for well-controlled delivery of therapeutic drugs. One of them will be the smart polymer (stimuli-sensitive polymer), which possesses active responsiveness to environmental signals and changes the physicochemical property as designed. Physical (temperature, ultrasound, light, electricity, mechanical stress), chemical (pH, ionic strength), and biological signals (enzymes, biomolecules) have been used as triggering stimuli.

### Smart polymeric systems

Passive targeting based on the EPR effect uses a unique physiological property of a disease (physiological targeting), while conjugation of targeting moiety to drug carriers is a biochemical targeting strategy. Smart polymeric systems also provide a targeting strategy,

which is activated and triggered by a specific environmental signal (triggered targeting)

### Polymeric systems for molecular imaging

Advancement in imaging technology has shifted conventional invasive and anatomical diagnosis to non-invasive and physiological/molecular imaging technique. Applying the molecular imaging technique to clinical imaging modalities, such as magnetic resonance imaging (MRI), positron emission tomography (PET), fluorescent optical imaging, and ultrasound imaging, however, has been hampered by poor sensitivity, specificity, and targeting ability of current imaging probes. Small molecules that are directly labeled with a wide range of chemicals have been limited in use due to their lack of specificity, instability, toxicity, and rapid clearance. Recently, combination of polymer chemistry and imaging realm has led to novel polymeric probes for clinical diagnosis. Polymeric probes for molecular imaging take all advantages of polymer-based drug delivery systems, which can significantly increase plasma half-life and blood stability, reduce systemic toxicity, and especially improve contrasting ability by introduction of targeting moiety<sup>20</sup>

### CONCLUSION

The use of novel polymers not only offers benefits but also can prove to be harmful because of the toxicity and

other incompatibilities associated with them. Care should be taken to properly select polymers while designing a delivery system. The ultimate goal is to introduce cost effective, biocompatible, multifunctional, less toxic polymers so that the delivery systems pass through the various phases of clinical trials and benefit the society. Among various types of polymer hydrogels, polymer blends of natural and/or synthetic polymers are used in the pharmaceutical formulations, in that controlled drug delivery systems having advantages over conventional therapy fall into various categories such as diffusion-controlled, chemically controlled, solvent activated and modulated release systems. The new generation mucoadhesive polymers for buccal drug delivery With advantages such as an increase in the residence time of the polymer, penetration enhancement, site-specific adhesion, and enzymatic inhibition, site-specific mucoadhesive polymers will undoubtedly be utilized for the buccal delivery of a wide variety of therapeutic compounds for that lectin and "lectinomimetics" appears to be the most promising area of current research efforts aimed at the safe and effective delivery of drugs via the buccal mucosa. MIP [molecular imprinting] in fully aqueous environments, imprinting of very polar molecules and bio-macromolecules, mass transfer, binding site population, capacity and template bleed. On the whole, polymers are being extensively used in pharmaceutical industry due to their vast applications.

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