Available online on 15.10.2024 at <http://jddtonline.info>

# Journal of Drug Delivery and Therapeutics

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Review Article

## Synthetic and Natural Polymers Enhancing Drug Delivery and Their Treatment: A Comprehensive Review

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### Article Info:



#### Article History:

Received 08 July 2024  
Reviewed 04 Sep 2024  
Accepted 30 Sep 2024  
Published 15 Oct 2024

### Cite this article as:

Saini L, Dubey A, Pal R, Pandey P, Mandal RK, Synthetic and Natural Polymers Enhancing Drug Delivery & Their Treatment: A Comprehensive Review, Journal of Drug Delivery and Therapeutics. 2024; 14(10):153-165  
DOI: <http://dx.doi.org/10.22270/jddt.v14i10.6802>

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### Abstract

Polymers, both synthetic and natural, play a critical role in modern drug delivery systems by enhancing the efficacy, targeting, and release profiles of therapeutic agents. This comprehensive review delves into the various types of synthetic polymers such as poly (lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), and polyvinyl alcohol (PVA), as well as natural polymers like chitosan, alginate, and gelatin. These polymers are explored for their potential to improve solubility, bioavailability, and controlled release of drugs. Moreover, their application in targeted drug delivery, particularly for cancer, cardiovascular, and inflammatory diseases, is highlighted. The review also compares the advantages and limitations of synthetic versus natural polymers, discussing their biodegradability, biocompatibility, and regulatory considerations. Advances in polymer-based drug delivery platforms such as nanoparticles, hydrogels, and micelles are also examined, offering insights into future directions in personalized medicine. The highlights of provide in the review article, initially basics of drug delivery, polymer, polymerization with role of polymer in polymerization. At intermediate, classification, sources of polymer with that some advanced approached in drug delivery and lastly, marketed, recent available products with future challenges and current status in the drug delivery.

**Keywords:** Biodegradable polymer; natural; compatible; drug delivery; treatment; enhancing; polymers.

## 1. Introduction

Drug delivery refers to the method or process of administering a pharmaceutical compound to achieve a therapeutic effect in humans or animals. The goal of drug delivery systems is to control the rate, time, and place of drug release, ensuring that the drug reaches the target area in the body efficiently and at the right concentration. These systems can be tailored to enhance the stability, bioavailability (BA), and solubility of drugs, improving patient outcomes and minimizing side effects <sup>1-2</sup>.

Polymers play a crucial role in drug delivery by acting as carriers for the drug, allowing for controlled and sustained release. Biodegradable and biocompatible polymers like polylactic acid (PLA), polyethylene glycol (PEG), and polycaprolactone (PCL) are often used to create matrices, nanoparticles, or hydrogels that encapsulate the drug<sup>3</sup>. These polymers protect the drug from degradation, enhance its solubility, and enable targeted delivery to specific tissues or organs, reducing the need for frequent dosing and improving therapeutic efficacy. By using polymers, drug delivery systems can be

fine-tuned for various applications such as cancer therapy, pain management, and infectious diseases like tuberculosis <sup>4</sup>. The word polymer derived from Greek word “poly” means many and “meros” means pieces. Polymers are the substance which are used in pharmaceutical preparation. A polymer is a material consisting of large molecules called macromolecule, which are made by joining of repeating units called monomers. Polymers can be natural or synthetics are found in living organism minerals (proteins, cellulose, and nucleic acid) and man- made materials (concrete, glass, plastics, rubbers) <sup>5-6</sup>.

The process formulation of polymers from monomers called polymerization. Polymers both natural and synthetic are created via polymerization of small molecule known as monomers. When the number of monomers is very large, the compound called a high polymer <sup>7</sup>.

Pharmaceutical polymer is frequently employed to produce controlled release, increased stability, and improved bioavailability (BA). The initial drug

concentration and polymer chain relaxation determine the rate of a drug release from a matrix product, which in general exhibits a sustained release characteristic<sup>8</sup>. Polymeric drug delivery systems based on natural and synthetic polymer are rapidly emerging in pharmaceutical fields. Polymers play an important role in the advancement of drug delivery technology by allowing the release of two types of drugs, hydrophilic and hydrophobic<sup>9-10</sup>.

### 1.1. Drug delivery system:

A drug delivery system is a method designed to transport therapeutic agents to specific areas in the body to achieve optimal drug concentration for treatment<sup>11</sup>. These systems aim to control the timing, dosage, and location of drug release, enhancing the therapeutic effect while minimizing side effects<sup>12</sup>. Modern drug delivery systems include various technologies such as nanoparticles, liposomes, hydrogels, and implants, which improve the stability, solubility, and targeting of drugs. This targeted approach helps in treating conditions more effectively, reducing the need for frequent dosing, and increasing patient compliance<sup>13</sup>.

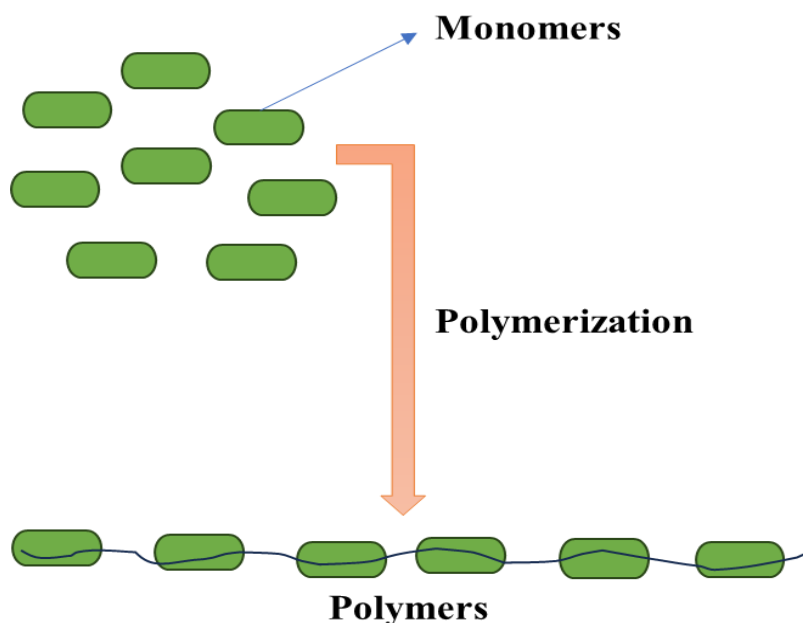
Drug delivery systems is defined technologies that carry drugs into the body. These technologies include method of delivery, such as a pills that swallow or a vaccine that

is injected. A variety of polymers used to create a variety of drug delivery system, including tablets, capsules, injectable, transdermal patches and topical formulations<sup>14-15</sup>.

In pharmaceutical formulation polymers are used as an excipient. Excipients are ingredients other than active pharmaceutical ingredients [API] in a pharmaceutical dosages form. Excipients are inactive ingredients are added in formulation to improve the stability<sup>16</sup>. They may be used to enhance the active ingredient therapeutic properties, to facilitate drug absorption, to reduce viscosity, to enhance solubility, or to add bulk to solid formulation that have small amounts of potent active ingredient<sup>17</sup>. During manufacturing process, excipients can improve the handling of active substances.

### 1.2. Polymerization:

Polymerisation is a chemical process in which formation of polymers from monomers. Monomers are chemically bonded together to form a long chain or three-dimension network structure called as polymer<sup>18</sup>. The polymers are used in pharmaceutical industry as excipient in tablet binding, emulsion, suspension and mechanical supports and protective and stabilizing agents. Pharmaceutical polymers are increased stability and more bioavailability (BA) of formulation<sup>19</sup>.



**Figure 1: Representation of polymerization from monomers**

*Types of polymerisations:* Polymerization is the chemical process in which monomers combine to form a polymer<sup>20</sup>. There are several types of polymerizations, each with distinct mechanisms:

#### 1) Chain polymerisation:

Chain polymerization, also known as addition polymerization, is a process where monomers containing a double bond or another reactive group link together in a stepwise fashion to form a polymer chain<sup>21</sup>. The

reaction occurs in three key stages: initiation, propagation, and termination. During initiation, a reactive species like a free radical, cation, or anion is generated, which opens the double bond of the monomer. In the propagation step, this reactive site transfers to the newly formed end of the growing chain, allowing additional monomers to rapidly attach, forming long polymer chains<sup>22</sup>. The process continues until termination, where the reactive chain end is neutralized, either by combination or disproportionation. Chain

polymerization is fast and efficient, making it useful for creating high molecular weight polymers like polyethylene, polystyrene, and PVC <sup>21-23</sup>. The resulting polymers are usually thermoplastic, with characteristics such as strength, flexibility, or transparency, depending

on the monomers and conditions used in the polymerization process. In this reaction, monomers are added to proceed the growth of polymer chain <sup>22</sup>. Chain polymerization can be divided in three main types in the Table 1 as below.

**Table 1: List of types of chain polymerization with suitable details** <sup>21-25</sup>

Type of Chain Polymerization	Key Features	Example
Free Radical Polymerization	<ul style="list-style-type: none"> <li>- Initiated by free radicals</li> <li>- Requires heat, light, or a chemical initiator</li> <li>- Rapid reaction</li> <li>- Broad range of monomers can be used</li> </ul>	Polyethylene (PE), Polystyrene (PS)
Cationic Polymerization	<ul style="list-style-type: none"> <li>- Initiated by an electrophile (cation)</li> <li>- Highly sensitive to impurities</li> <li>- Often used for monomers with electron-rich double bonds</li> </ul>	Polyisobutylene (PIB), Polyvinyl ether
Anionic Polymerization	<ul style="list-style-type: none"> <li>- Initiated by nucleophiles (anions)</li> <li>- Highly controlled (living polymerization)</li> <li>- Suitable for monomers with electron-deficient double bonds</li> </ul>	Polybutadiene, Polystyrene (living polymer)

The each type of chain polymerization differs in its initiation mechanism and is suitable for specific kinds of monomers, which influences the properties of the resulting polymers.

## 2) Step polymerization

Step polymerization, also known as condensation polymerization, is a process where bi-functional or multi-functional monomers react to form a polymer through a series of stepwise reactions. Unlike chain polymerization, in step polymerization, any two reactive monomers,

oligomers, or polymer chains can combine at any stage of the reaction <sup>26</sup>. As the monomers react, small by-products like water, alcohol, or hydrogen chloride are often released. The polymer chains grow gradually, and high molecular weight polymers are only formed towards the end of the reaction. In this process, multifunctional monomers react together to form covalent bonds, to release small molecules <sup>27</sup>. The several types of polymerization mentioned in the Table 2 as below.

**Table 2: List of types of polymerizations, brief description and few examples** <sup>26-28</sup>

Types of polymerizations	Description	Example
Addition polymerization	Monomers add together without loss of any atom	Polyethylene, Polypropylene, polyvinyl chloride
Condensation polymerization	Monomers react together with the loss of small molecules, such as water or alcohol.	Nylon, polyester, polyurethane
Ring -opening polymerization	A cyclic monomer is opened up and the monomer units are added together to form a polymer chain	Polystyrene, polyisoprene
Crosslinking	Polymer chains are joined together to form a three - dimensionless network	Vulcanized rubber

## 3) Ring -opening polymerization

Monomer is broken, typically by the action of a catalyst or initiator, which generates an active species that

propagates the polymer chain <sup>29</sup>. The reaction continues as more monomer rings open and attach to the growing polymer chain. ROP is often used to synthesize polymers with controlled structures and properties.

This technique is widely employed for creating biodegradable polymers such as polylactic acid (PLA), polycaprolactone (PCL), and other aliphatic polyesters<sup>30</sup>. These materials are used in medical devices, drug delivery systems, and environmentally friendly packaging due to their biodegradability and tunable mechanical properties. The ROP method allows precise control over molecular weight and polymer architecture, making it an essential tool in modern polymer chemistry<sup>28-31</sup>.

#### 4) Crosslinking polymerization

Crosslinking polymerization is a process in which polymer chains are interconnected by covalent bonds, forming a three-dimensional network structure<sup>32</sup>. This occurs when multifunctional monomers or crosslinking agents, containing more than two reactive sites, react with polymer chains, linking them together at multiple points<sup>33</sup>. The result is a polymer with enhanced mechanical properties such as increased strength, elasticity, and resistance to solvents and heat. Polymer chain is joined together to form a three -dimensionless network<sup>34</sup>.

#### 1.3. Role of Polymers in Drug Delivery:

Polymers play a critical role in drug delivery systems by enhancing the effectiveness, safety, and targeting of therapeutic agents. Their unique properties allow for controlled and sustained release of drugs, improving bioavailability, reducing side effects, and increasing patient compliance<sup>33-34</sup>. The several key roles of polymers in drug delivery discussed as following:

- **Immediate release dosage forms Tablets:** Polymers including polyvinyl -pyrrolidone (PVP) and hydroxypropyl methylcellulose (HPMC) used as binders in formation of granules and improve flow property of tablets<sup>32</sup>.

- **Capsules:** Polymers used as excipient to increases the bulk weight in capsules. Mostly Gelatin is used as a shell material for hard and soft capsules.
- **Control release drug:** Polymers are used to release the drug in a controlled manner.
- **Enhance bioavailability:** Polymer can improve the BA of drug<sup>32-35</sup>.

Polymers are versatile tools in drug delivery, enabling the development of more effective, patient-friendly, and targeted therapies. They are used in various forms, including microspheres, nanoparticles, hydrogels, and liposomes, across a range of medical applications<sup>36</sup>.

## 2. Classification of Polymers and Sources of Polymers

Polymers facilitate controlled and sustained release of drugs, ensuring that medications are delivered at optimal rates and concentrations to target sites in the body. Additionally, polymers can be engineered for targeted delivery, allowing for specific interactions with tissues or cells, which minimizes side effects and maximizes therapeutic efficacy<sup>37</sup>. The types of polymers used in drug delivery systems include biodegradable polymers (like polylactic acid and polycaprolactone), which break down safely in the body; natural polymers (like chitosan and alginate), which are biocompatible and often derived from biological sources; and synthetic polymers (like polyethylene glycol and polyvinyl alcohol), which can be customized for specific drug formulations and release profiles. These versatile materials enable the development of advanced drug delivery systems such as NPs, hydrogels, and microspheres, significantly improving the effectiveness of various therapies<sup>38</sup>.

Polymers can be classified based on different criteria, such as their source, structure, polymerization process, or properties as below following Fig. 2.

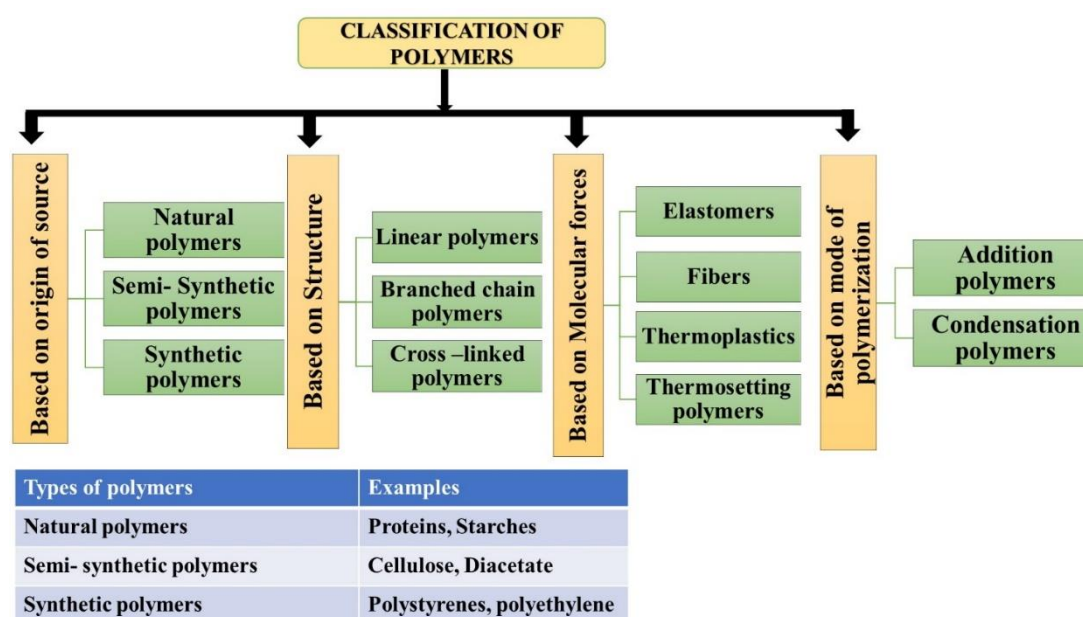


Figure 1: Classification of polymers with their listed examples

## 2.1 Types/Classification of Polymers:

The classification of polymers on the basis of their few parameters discussed in the below description:

**2.1.1 Natural polymers:** Natural polymers are polymers that are present in nature and extracted from natural resources as plant and animals. They are composed of repeating units of monomers, such as sugars, amino acids, or nucleotides, and play essential roles in biological processes<sup>39</sup>. Common examples of natural polymers include cellulose, which provides structural support in plants; chitin, found in the exoskeletons of insects and crustaceans; proteins, which are vital for cellular functions and structures; and DNA, the genetic material that carries hereditary information.

- **Natural polymers from plant origin:** Polysaccharides (Cyclodextrins, cellulose, starch, pectin, gum etc.
- **Natural polymers from animal origin:** polysaccharides (chitosan, chondroitin, sulphate)
- **Natural polymers from microbial origin:** Polysaccharides (Alginate, Dextran), Polyesters (phase), Polyamides 9 (Poly-glutamate) etc.

**2.1.2 Semisynthetic polymers:** semi synthetic polymers are polymers are obtained by chemical and physical process of natural polymers Examples; cellulose acetate (rayon), cellulose nitrate and vulcanized rubber etc. Semisynthetic polymers are derived from natural polymers through chemical modification or processing, combining the beneficial properties of both natural and synthetic materials. These polymers undergo transformations to enhance their performance, stability, or applicability while retaining some characteristics of their natural precursors. The common examples include cellulose derivatives such as cellulose acetate and carboxymethyl cellulose, which are used in applications like films, coatings, and pharmaceuticals<sup>40</sup>.

**2.1.3 Synthetic polymers:** synthetic polymers are polymers obtained from low-molecular compounds (monomers) in laboratories. Examples: nylon, terylene, polyethylene, PS and Teflon.

### 2.1.4 Classification of polymers based on polymerization

- **Additional polymerization:** For example, poly ethane, Teflon, polyvinyl chloride, etc.
- **Condensation polymerization:** Examples include nylon-6,6, perylene, polyesters, etc.

### 2.1.5. Classification of polymers based on structure

- **Linear polymer:** The structure of polymers containing long and straight chains.
- **Branched-chain polymers:** when linear chains of polymer form branches.
- **Cross-linked polymers:** They are composed of bifunctional and trifunctional monomers. They have a stronger covalent bond in comparison to other linear polymers.

### 2.1.6. Classification of polymer based on molecular forces

- **Elastomers:** These are rubber like solids, and weak interaction forces are present in them. For example, rubber.
- **Fibres:** Strong, tough, high tensile strength and strong forces of interaction are present. For example, nylon-6,6.
- **Thermoplastics:** These have intermediate forces of attraction. For example, polyvinyl chloride.
- **Thermosetting polymers:** These polymers greatly improves the material's mechanical properties. For example, phenolics and silicones<sup>38-41</sup>.

## 2.2 Sources of Polymers:

The origins from which polymers are obtained, categorized into three main types: natural, synthetic, and semi-synthetic sources. Natural polymers are derived from living organisms, including plants (e.g., cellulose and starch), animals (e.g., proteins and chitin), and microorganisms (e.g., polysaccharides like alginate and xanthan gum)<sup>42</sup>. Synthetic polymers are artificially created through chemical processes, primarily from petrochemical sources, such as polyethylene, polystyrene, and nylon. Semi-synthetic polymers are modified versions of natural polymers, created by chemically altering their structure to enhance certain properties, like cellulose acetate<sup>43</sup>. The origin and sources of polymers mentioned in the Table 3 with complete description and details. These are the different types of polymers Table 3 as below.

**Table 3: List of types of polymers and their sources** <sup>42-45</sup>

Type of Polymer	Characterization	Examples	Sources
Natural Polymers	Biodegradable, biocompatible, derived from living organisms.	Cellulose, Chitin, Proteins	Plants, Animals, Microorganisms
Synthetic Polymers	Man-made, often non-biodegradable, produced through chemical processes.	Polyethylene, Nylon, Polystyrene	Petrochemicals
Semi-Synthetic Polymers	Modified natural polymers, enhanced properties through chemical alteration.	Cellulose Acetate, CMC	Natural sources (e.g., cellulose)
Addition (Chain-Growth) Polymers	Formed by adding monomers with unsaturated bonds in a chain reaction.	Polyethylene, Polystyrene	Petrochemical sources
Condensation (Step-Growth) Polymers	Formed through stepwise reactions releasing small molecules (e.g., water).	Nylon, Polyester	Natural & petrochemical sources
Cross-linked Polymers	Formed by creating a three-dimensional network, enhancing strength and durability.	Vulcanized Rubber, Epoxy Resins	Natural and synthetic sources
Elastomers	Flexible, rubber-like materials with high elasticity.	Natural Rubber, Silicone	Natural and synthetic sources

This table categorizes the types of polymers based on their characteristics, providing a clear overview of examples and their respective sources.

### 2.3. *Ideal characteristics of Polymers: in Drug Delivery:*

The ideal characteristics of polymers for drug delivery systems include biocompatibility, ensuring that the material does not elicit an adverse immune response; biodegradability, allowing for safe and gradual breakdown in the body without toxic residues; and controlled release properties, enabling sustained and targeted delivery of therapeutic agents to enhance efficacy while minimizing side effects <sup>46</sup>. Additionally, the polymers should possess adequate mechanical strength to withstand physiological conditions, as well as solubility and swelling behavior to facilitate drug release.

The few important key role and ideal characteristics of polymers describe as follows:

- Polymer should be non-toxic, non-immunogenic.
- Polymer should have good mechanical strength.
- Polymer should be compatible with the environment.
- Polymer can be soluble in organic solvents to mask taste <sup>44-47</sup>.

They should be easily processable to form various delivery systems such as NPs, hydrogels, and microspheres, allowing for versatile applications in different therapeutic areas <sup>47</sup>. These characteristics are crucial in developing effective, safe, and patient-friendly drug delivery systems.

## 3. Advanced Approaches of Polymers In Drug Delivery

Advanced approaches in the use of polymers for drug delivery have revolutionized therapeutic strategies by

enhancing the precision and efficacy of treatments. One prominent method is nanoparticle-based drug delivery, where polymeric nanoparticles encapsulate drugs, enabling targeted delivery to specific cells or tissues, such as tumor sites, while minimizing systemic side effects. Another approach is the development of smart polymers, which respond to environmental stimuli (such as pH, temperature, or specific biomarkers) to release drugs in a controlled manner, ensuring that the therapeutic agents are delivered precisely when and where needed <sup>48</sup>. Additionally, polymer-drug conjugates can improve solubility and stability of poorly soluble drugs, enhancing their bioavailability. Hydrogels are also gaining attention for their ability to swell and retain large amounts of water, providing sustained release of drugs while mimicking biological tissues. Furthermore, 3D printing of polymeric drug delivery systems allows for customization and optimization of drug formulations and release profiles <sup>49</sup>. Collectively, these advanced polymeric approaches hold the potential to improve patient outcomes and transform the landscape of drug delivery in various therapeutic areas.

The various advanced approaches used in polymers in the several drug delivery systems, these are discussed in the below description:

### 3.1. *Biodegradable and biocompatible polymers:*

Biodegradable polymers are typically categorized into two groups: synthetic and natural polymers <sup>46</sup>. Biocompatible synthetic polymers are often designed to be biodegradable, and their degradation products can be absorbed by the human body. In contrast, natural polymers are metabolized into metabolites that the kidneys can easily eliminate. Common synthetic

biodegradable polymers include polyglycolic acid (PGA), polylactic acid (PLA), poly(lactide-co-glycolide) (PLGA), and polycaprolactone (PCL) <sup>50</sup>. Additionally, several natural polymers, such as cellulose, gelatin, and chitosan, are well-known for their degradability and biocompatibility. A range of antimicrobial techniques has been developed using these degradable biocompatible polymers. Polyglycolic acid (PGA) is a biodegradable and biocompatible aliphatic polyester that is widely utilized in medical applications. It can be synthesized from glycolic acid through ring-opening polymerization <sup>49-51</sup>.

Similarly, polylactic acid (PLA) is a biodegradable, bioabsorbable thermoplastic aliphatic polyester derived from renewable resources. Lactic acid exists in two optical isomers, L- and D-lactic acid, and PLA is produced from lactide via ring-opening polymerization <sup>52</sup>. PLA is commonly used in medical implants, including screws, pins, rods, and orthopedic devices. Due to its biodegradability, PLA has also been employed in the production of semipermeable microcapsules, generating non-toxic metabolites in the body upon degradation.

**Table 4: List of biodegradable polymers used in the drug delivery** <sup>48-52</sup>

Biodegradable Polymer	Application	Examples in Drug Delivery
Polyglycolic Acid (PGA)	Sutures, drug delivery systems	Used in drug-loaded microspheres for sustained release
Polylactic Acid (PLA)	Medical implants, tissue engineering	Employed in controlled release formulations and implants
Poly(lactic-co-glycolic acid) (PLGA)	Drug delivery, tissue engineering	Utilized in nanoparticles and microspheres for targeted delivery
Polycaprolactone (PCL)	Sutures, drug delivery systems	Used in slow-release drug formulations and implants
Chitosan	Wound dressings, drug delivery	Formulated into nanoparticles and hydrogels for mucosal delivery
Gelatin	Drug delivery, scaffolds for tissue engineering	Used in microspheres for sustained release and controlled drug delivery
Alginate	Drug delivery, tissue scaffolds	Employed in hydrogels and beads for encapsulating drugs
Hyaluronic Acid	Drug delivery, dermal fillers	Used in targeted delivery systems and as carriers for anti-cancer drugs
Starch	Drug delivery, food applications	Formulated into tablets and films for controlled release

This table 4 provides an overview of various biodegradable polymers, their applications, and examples of their use in drug delivery systems.

### 3.2. Targeted drug delivery system polymer in nanoparticle (NPs):

The nanoparticle is coated by polymer, the release is then controlled by diffusion of the drug from the polymeric membrane. Membrane coating acts as a drug release barrier; drug solubility and diffusion in the polymer membrane becomes a determining factor in drug release <sup>53</sup>.

**Polymeric NPs:** Polymeric nanoparticles (NPs) are solid particles composed of macromolecular polymers, specifically designed for targeted drug delivery. These nanoparticles typically range in size from 10 to 100 nanometers, making them ideal for penetrating biological barriers and facilitating cellular uptake. They are fabricated from biodegradable and biocompatible polymers, ensuring safety and minimizing adverse reactions within the body. Polymeric NPs have gained significant attention in the medical field for their versatility in treating a wide array of diseases, including cancer, neurodegenerative disorders, and cardiovascular

diseases <sup>54</sup>. Their unique properties allow for enhanced drug solubility, controlled release, and targeted action, improving therapeutic efficacy while reducing side effects. The utilizing polymeric NPs, researchers aim to optimize drug delivery systems, leading to more effective and patient-friendly treatment options <sup>55</sup>.

**Dendrimers:** Dendrimers play a significant role in drug delivery systems due to their unique branched structure and nanoscale size, which allow for enhanced drug solubility, stability, and targeted delivery. These highly branched, tree-like macromolecules provide numerous functional groups that can be modified to improve their compatibility with various therapeutic agents. Dendrimers can encapsulate drugs within their internal cavities or conjugate them on their surface, enabling controlled release and minimizing systemic side effects <sup>56</sup>. Their precise architecture facilitates the attachment of targeting ligands, such as antibodies or peptides, ensuring that the drug is delivered specifically to diseased cells while sparing healthy tissues. Additionally,

dendrimers exhibit excellent BA and can overcome biological barriers, such as cell membranes, enhancing cellular uptake. This combination of properties makes dendrimers an attractive option for various applications, including cancer therapy, gene delivery, and vaccines, significantly improving the efficacy and safety of therapeutic interventions<sup>57</sup>. Example: Poly (amidoamine) (PAMAM).

### 3.3. *Hydrogels for drug delivery:*

Hydrogels are highly hydrated mesh networks formed from natural, synthetic, or semi-synthetic polymers, which are covalently crosslinked. This material is used for local drug delivery because they provide high biocompatibility, drug protection<sup>55-57</sup>. Hydrogels enable the encapsulation. Hydrogels and hydrogel drug delivery systems are traditionally defined as being natural or synthetic. Hydrogels are naturally origin include; chitosan, alginate, fibrin, gelatin, or hyaluronic acid-based hydrogels; polyethylene (PEG), or polyvinyl alcohol are common synthetic hydrogels. The semi-synthetic hydrogels like gelatin methacryloyl hydrogels. Which are gelatin -based but functionalized by synthetic methacryloyl groups<sup>58</sup>.

### 3.4. *3D printed drug delivery system:*

The one or more multiple drug dosage forms manufactured by one type of 3D printing technology. In more and more research, three-dimensional bioprinting was which a new era of 3D is printing technologies where researches aim to build living tissue models. The first publication of 3D -printed tablet in 1996 when solid samples were created with a desktop printer from PCL and PEO polymers containing blue and yellow dyes<sup>59</sup>. A 3D printed drug delivery system refers to the innovative application of 3D printing technology to create customized pharmaceutical formulations and devices that enhance the precision and efficiency of drug delivery. This approach allows for the fabrication of complex geometries and personalized designs that can be tailored to the specific needs of individual patients<sup>60</sup>. By utilizing materials such as biodegradable polymers, hydrogels, and even bioinks, 3D printing enables the production of dosage forms with controlled release profiles, thereby improving drug bioavailability and therapeutic outcomes.

### 3.5. *Techniques used 3D Printing:*

There are several different 3D printing techniques: Fused deposition modelling (FDM), Powder bed fusion, Material jetting, Binder jetting, Vat polymerization, Direct energy deposition, Laminated object manufacturing (LOM)<sup>61</sup>.

### 3.6. *Polymers drug conjugates:*

Polymer-drug conjugates (PCDs) are nanosized drug delivery systems that combine drug molecules with polymers. They are developed for a variety of uses in cancer treatment, Alzheimer's disease treatment and drug delivery system with low toxicity. PDC's can improve the solubility of drugs and designed to release drug at a controlled rate polymer drug conjugates have a longer half - life other than drug delivery systems<sup>62</sup>. PDC's made up of polymeric backbone, linker, targeting ligand components. Polymer used in PDC's: Poly(caprolactone) (PCL), Polyethylene glycol (PEG), and Hyaluronic acid (HA).

Moreover, polymer-drug conjugates can be engineered for targeted delivery, as the polymer can be functionalized with specific targeting ligands (e.g., antibodies, peptides, or small molecules) that direct the conjugate to particular cells or tissues, such as tumor cells. This targeted approach can enhance the therapeutic effect while reducing systemic toxicity, a critical consideration in cancer therapy and other diseases<sup>63</sup>. The use of biocompatible and biodegradable polymers in these conjugates also contributes to their safety profile, as they can be broken down into non-toxic metabolites after the drug has been released. Polymer-drug conjugates represent a promising strategy in modern drug delivery systems, offering a versatile platform for improving the efficacy and safety of various therapeutic agents<sup>61-64</sup>.

## 4. Recent Marketed and Current Products in Drug Delivery

Recent advancements in drug delivery systems have led to the development and marketing of several innovative products that utilize polymers to enhance therapeutic efficacy and patient compliance<sup>65</sup>. One notable example is Abraxane, a nanoparticle albumin-bound formulation of paclitaxel, which employs a polymeric carrier to improve solubility and facilitate targeted delivery in cancer treatment. Another significant product is Neulasta, which utilizes a PEGylated form of filgrastim; the polyethylene glycol (PEG) polymer extends the drug's half-life, allowing for less frequent dosing in patients undergoing chemotherapy. Lantus, an insulin formulation, employs a polymeric approach to provide a prolonged release of insulin, ensuring stable blood glucose control for diabetic patients<sup>66</sup>. Moreover, Sutent, a cancer medication, uses a polymer-based delivery system to optimize the bioavailability of sunitinib, thereby enhancing its therapeutic effects<sup>64-65</sup>.

The various marketed products of polymer loaded products discussed in the Table 5 as below following description.

**Table 5: List of marketed products with following polymer details**

Drug/API	Brand Name	Use/Application Drug	Polymer Type/Class	Dosage Form	Ref.
Tolvamer	K-BIND®	treatment of hyperkalemia	Calcium, polystyrene	Powder, suspension	[67]
Colestipol	Cloestid®	Used to lowering cholesterol level in blood	Copolymer of diethylenetriamine	Tablet	[68]
Diclofenac	Voltaren XR	To treat a mild -to - moderate pain	Sodium Carboxymethyl cellulose, Sodium alginate	Tablet	[69]
Amoxicillin	Amoxil, Moxilin	To treat bacterial infection	PAM, PVA	Powder for oral suspension, dispersible tablets	[70]
Paracetamol	Panadol, Tylenol	Used to treat pain and fever	Cellulose	Tablet, suspension	[71]
Verapamil	Verasol*	Used to treat high blood pressure	Sodium alginate, chitosan	Tablet	[72]
Morphine sulphate	Vermor®10	Used to treat pain	HPMC	Injection, Tablet	[73]
Clonidine	Arkamin®	To treat high blood pressure	PVP	Powder, tablet	[74]
Ivermectin	Iverhope	Used to treat parasitic disease such as hookworm	PCL	Injection, Tablet	[75]
Cetirizine	Cetzine®	Used to treat allergies, hay fever	Chitosan	Tablet	[76]
Rabeprazole	Rabekind®	Used to treat in duodenal ulcers	CMC, HPC	Tablet	[77]
Cefixime	Zifi®	To treat bacterial infection	Ethyl cellulose, chitosan	Tablet	[78]
Metformin	Metford- 500	Used to treat high blood sugar level	Polyacrylate, xanthan gum	Injection, Tablet	[79]
Telmisartan	Telmidax-40	To treat high blood pressure	PEG, PVP	Injection, Tablet	[80]
Myo-inositol	Mychiro	PCOS	Polythioether, polyuethanes	Tablet	[81]
Amlodipine	Amlip®-5	Used as hypertensive drug	PVA, sodium alginate	Tablet	[82]
Salbutamol	Asthalin	To treat chest tightness, cough	EC, sodium carboxy methyl cellulose	Inhalers, Tablet	[83]

These products exemplify how polymer-based drug delivery systems can improve the pharmacokinetics of drugs, leading to better treatment outcomes and increased patient satisfaction. As research continues to evolve, the integration of polymers in drug delivery is expected to yield even more innovative therapies tailored to meet specific clinical needs <sup>67-69</sup>.

## 5. Future Prospects and Current Status

The future prospects for the utilization of polymers in enhancing drug delivery are promising, with ongoing research and technological advancements paving the way for more effective and personalized therapeutic approaches. Current innovations in polymer science, such as the development of smart polymers that respond to specific physiological stimuli (like pH or temperature), are expected to significantly improve controlled and targeted drug release systems. These advancements could lead to therapies that deliver drugs precisely where and when they are needed, thereby maximizing efficacy while minimizing side effects <sup>84</sup>.

Moreover, the integration of 3D printing technologies with polymer drug delivery systems holds potential for creating customized dosage forms tailored to individual patient needs. This could revolutionize how medications are formulated, allowing for the combination of multiple drugs into a single delivery system, thus improving patient compliance and treatment outcomes <sup>85</sup>.

Research is also focused on developing biodegradable and biocompatible polymers that can safely degrade in the body, eliminating concerns about toxicity and long-term accumulation. As regulatory frameworks evolve to accommodate novel drug delivery systems, the market is

likely to see an increase in approved polymer-based therapeutics<sup>86</sup>.

Additionally, the application of nanotechnology in polymer drug delivery systems is set to expand, with ongoing studies exploring the use of polymeric NPs, micelles, and liposomes for improved solubility and

bioavailability of challenging drug candidates. The combination of polymeric materials with biologics and gene therapies is another area of growth, offering exciting possibilities for treating complex diseases like cancer and genetic disorders<sup>87</sup>. The various advance approaches utilized in the enhancing the drug delivery in Table 6 as below description.

**Table 6: List of future recent approaches in the drug delivery**<sup>83-86</sup>

Type of Polymer	Example	Features/Use/Application
Synthetic Polymers	Poly(lactic-co-glycolic acid) (PLGA)	Biodegradable and biocompatible copolymer used in controlled drug release; employed in cancer therapies and vaccines for sustained release and improved bioavailability.
	Polyethylene Glycol (PEG)	Enhances solubility and circulation time of drugs; used in PEGylated formulations like Pegasys for hepatitis C, improving pharmacokinetics and reducing immunogenicity.
	Polycaprolactone (PCL)	Biodegradable polyester used in slow-release formulations; applicable in orthopedic and tissue engineering devices.
Natural Polymers	Chitosan	Biodegradable and biocompatible; used in nanoparticles and hydrogels for drug delivery, particularly in cancer treatment and wound healing, leveraging its mucoadhesive properties for enhanced absorption.
	Alginate	Forms hydrogels for controlled drug release; utilized in oral and injectable formulations, particularly for localized treatment of anti-inflammatory drugs.
	Gelatin	Biocompatible and biodegradable; used in microspheres for sustained drug release and as scaffolds in tissue engineering.
Hybrid Approaches	Dendritic Polymers	Highly branched synthetic polymers that encapsulate drugs; improve solubility and target delivery, particularly for cancer and gene therapies through ligand attachment.
	Natural-Synthetic Polymer Blends	Combining natural (e.g., gelatin) and synthetic (e.g., PLGA) polymers; used to create scaffolds for tissue engineering and localized drug delivery, offering controlled release and enhanced biocompatibility.
	Smart Polymers	Responsive polymers that release drugs upon environmental stimuli (e.g., pH or temperature); utilized in targeted delivery systems for improved efficacy.

This table outlines various approaches in utilizing synthetic and natural polymers for enhancing drug delivery, highlighting their features and specific applications in therapeutic treatments<sup>88</sup>.

The recent advancements in synthetic and natural polymers for drug delivery systems reflect a growing trend toward personalized and targeted therapies. By harnessing the unique properties of these materials, researchers are developing innovative formulations that enhance drug solubility, stability, and release profiles, ultimately improving treatment outcomes across a wide range of medical conditions<sup>89-90</sup>. Continued exploration and development in this field promise to further revolutionize drug delivery, making it more effective and patient-centered.

## Conclusion

In conclusion, the comprehensive review of synthetic and natural polymers in enhancing drug delivery underscores the significant advancements in pharmaceutical technology aimed at improving therapeutic efficacy and patient outcomes. The unique properties of synthetic polymers, such as

biocompatibility and controlled release capabilities, combined with the inherent advantages of natural polymers, such as biodegradability and non-toxicity, create versatile platforms for drug delivery systems. The recent innovations, including the development of hybrid approaches and smart polymers, highlight the potential for tailored therapies that can respond to specific physiological conditions, thereby optimizing drug release and minimizing side effects. As research continues to evolve, the integration of these polymers in drug delivery systems holds great promise for revolutionizing treatment paradigms across various medical fields, ultimately leading to more effective and personalized therapeutic solutions.

## List of Abbreviations:

**PEG:** Polyethylene glycol; **PVP:** Polyvinyl pyrrolidone; **PCOS:** Polycystic ovary syndrome; **PVA:** Polyvinyl alcohol; **HPMC:** Hydroxypropyl methylcellulose; **PAM:**

Polyacrylamide; **PAL**: Polycaprolactone; **EC**: Ethyl cellulose; **CMC**: Carboxymethyl cellulose; **HPC**: Hydroxypropyl cellulose

**Ethical Approval**: Not applicable.

**Consent for Publication**: Not applicable.

**Human and Animal Ethical Right**: Not applicable.

**Conflict of Interest**: The authors declare no conflict of interest, and no funding was required to conduct these review data.

**Acknowledgments**: The corresponding authors would like to thank, all involved members and faculty staff for their collaboration.

**Availability of Data and Materials**: The data supporting this study's findings will be available in the cited references.

**Funding**: The research received no external funding.

**Author Contribution**: All authors have equal contribution in the compilation of data.

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