

Review article

Polymers in the Biomedical Field, Types, and Applications

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ARTICLE INFO:

Received: 15 July 2022
Accepted: 22 Aug 2022
Published: 31 Aug 2022

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ABSTRACT:

The use of polymer has been increasing day by day because of its benefits in delivering drugs to specific organs to treat or diagnose diseases. This review article describes, in brief, the polymer's introduction, its history, and role in the biomedical field, and also used as an implant to perform persistently. These enhancements add to make medical treatment more productive and limit side effects and different sorts of inconveniences for patients. The major role of polymers is to protect drugs from the physiological environment and prolong the release of drugs thus improving their overall stability. It also derives the classification and types of polymers in use. As we are using a drug along with a polymer, it also has some conjugations, which is briefly described. The use of polymers in formulating a drug will help in targeted action and also in the mediated release of the drug. Since polymers have shown an increase in the bioavailability of drugs, several polymers are being used.

Keywords: Melatonin, nephrotoxicity, therapeutic, chemicals, drugs.

1. INTRODUCTION

A polymer is any of a group of a natural or manmade substance called macromolecules, which are multiples of monomers, which are smaller chemical units with two or more binding sites which it forms covalent linkages to form a macromolecule. Thus, they act as building blocks of polymers. Various changes in the administration of medical supplements have led to the immense use of polymeric material in the biomedical field. Polymers applications have spread to the biomedical fields such as drug delivery systems, developing scaffolds in tissue engineering, implantation of medical devices, artificial organs, prosthesis, ophthalmology, dentistry, bone repair, and many other medical fields.[1] various levelled progress in present-day drug conveyance starts with the utilization of polymer transporters to evoke spatiotemporal arrival of therapeutic in both pulsatile portion conveyance items and embedded repositoryframework. Enormous headway has been made because of the investigation of dissemination controlled furthermore, dissolvable enacted details in drug conveyance. Hydro-gels and other polymer-based transporters have been credited to give safe entry to drugs through unwelcoming physiological places. Polymers of controlled molecular design can be designed to give a clear-cut reaction to outside conditions because of a strong comprehension of the basic systems and the idea of behavioural transitions. Polymers consolidated with therapeutics can be bioactive to give their own medical benefit or can be biodegradable to further develop discharge energy and prevent carrier accumulation. pharmaceutical agents have been formed into polymers to

alter transport or circulation half-life characteristics simultaneously to allow for passive and active targeting. Lastly, the most recent medication conveyance research utilizing polymeric materials has delivered recognition frameworks and polymer transporters that work with cytoplasmic conveyance of novel therapeutics [2]. This review aims to provide unique coverage of use of polymers in biomedical field, addressing the foundations of polymeric use in a conceptual context and critically reviewing its recent developments, polymer therapeutics and any other advancements.

2. HISTORY OF POLYMERS [3]:

The utilization of polymers in the clinical field isn't a novelty, natural polymers have been utilized as parts of ayurvedic remedies for hundreds of years. With regards to man-made polymers anyway the circumstance is altogether different. Since polymer science is a generally a novel exploration man-made water-soluble polymers as macromolecular drugs or as a feature of medication conveyance frameworks connected with immunization can be viewed as a cutting-edge accomplishment.

The first polymer-drug forms showed up around 1955, being mescaline-N-vinylpyrrolidone form. Around a decade after the fact Frank Davis and Abraham Abuchowski had anticipate the capability of forming poly(ethylene glycol) (PEG) to proteins causing the introduction of a procedure called PEGylation. PEGylation comprises in the covalent obligation of poly(ethyleneglycol) polymer chains to another

particle typically a medication or then again, a protein with remedial impacts.

In 1994, the main manufactured polymer-drug form intended to treat malignant growth was clinically tested. It comprised on a HPMA (N-(2-hydroxypropyl) methacrylamide) copolymer form of doxorubicin. Designated arrival of anticancer agents can likewise be made utilizing block copolymer micelles which can entrap the medication or to covalently connection to it.

During the 2000s, two polymer-protein conjugates, PEG-interferon- (an antiviral medication expected to treat ongoing hepatitis C and hepatitis B) and PEG-GCSF (Stake granulocyte colony-stimulating factor) were set on the lookout and after five years the principal helpful nanoparticles (albumin-entrapped paclitaxel) was supported as a therapy for metastatic breast malignant growth. All profoundly component that prompted the improvement of polymer-based drugs to be specific polymeric medications, polymer-drug conjugates and polymer-protein conjugates. The clinical preliminaries of these new advances at last lead to the resolution of numerous other unforeseen difficulties that immediately showed up, , the assembling of the polymers at a modern scale and the speedy and aggregate solubilization of the drugs for safe vaccination. The enhancement of these clinical tests regarding dosage and frequency is still being assessed today for production of large variety of products.

3. ROLE OF POLYMERS IN DRUG DELIVERY[4]:

➤ Immediate release dosage forms

• TABLETS :

Microcrystalline cellulose is frequently utilized as an option in contrast to starches as diluents in tablet formulation of exceptionally potent low-dose drugs. Starch and cellulose are utilized as disintegrants in tablet formulation, which grow on contact with water, bringing about the tablet "disintegrating" expanding the uncovered surface region of the medication and working on the dissolution qualities of a formulation. Polymers including polyvinyl-pyrrolidone and hydroxypropyl methylcellulose(HPMC) additionally track down utilizes as binders that help in the development of granules that work on the flow and compaction properties of tablet formulations preceding tableting (Figure 1). Every so often, measurements structures should be covered with a "non-functional "polymeric film covering to safeguard a drug from degradation, cover the flavour of an unpalatable drug or excipients, or work on the visual polish of the formulations without influencing the medication discharge rate [5].

• CAPSULES :

A large number of the polymeric excipients used to "mass out"capsules fills are equivalent to those utilized in intermediate discharge tablets. For hard and soft-shell gelatin has most frequently utilized. By recent advances HPMC has

been acknowledged as elective material for hard and soft capsules.[6]

➤ Modified-release dosage forms

To accomplish gastro retentive mucoadhesion and low density, polymers have been assessed, with little achievement up until this point their capacity to broaden gastric residence time by attaching to the mucus layer of the stomach and floating on top of the gastric substance individually.[7], [8]

➤ Extended-release dosage forms:

Broadened and supported discharge dose forms extend the time that' systemic medication levels are inside the therapeutic reach and in this way decrease the quantity of dosages, the patient should produce to keep a therapeutic result there by expanding compliance.[9], [10] The most normally involved water insoluble polymers for broadened discharge applications are the ammonium ethacrylate copolymers cellulose subsidiaries ethyl cellulose and cellulose derivation, and polyvinyl subsidiary, polyvinyl acetate.[11]–[13]

4. BIOMATERIALS FOR DELIVERY SYSTEMS:

The polymers in the extremely beginning stage they were especially utilized for non-natural purposes, and were chosen in view of their advantageous actual properties, for instance:

- Poly (methyl methacrylate) for physical strength transparency.
- Poly (vinyl alcohol) for hydrophilicity and strength.
- Poly (urethanes) for elasticity.
- Poly (ethylene) for toughness and lack of swelling.
- Poly (siloxanes) or silicones for insulating ability.
- Poly (vinyl pyrrolidone) for suspension capabilities.

For controlled drug conveyance definition, the polymers should be chemically inert and free from contaminations with suitable actual structure, insignificant undesired maturing, and to promptly processable.[9], [14] Few examples :

- Poly (ethylene-co-vinyl acetate)
- Poly (methyl methacrylate)
- Poly (vinyl alcohol)
- Poly (N-vinyl pyrrolidone)
- Poly (acrylic acid)
- Poly (2hydroxy ethyl methacrylate)
- Polyacrylamide
- Poly (methacrylic glycol)
- Poly (Ethelene glycol)

However in recent years the use of polymers were to words medical applications and drug targeting few examples :

- Polyrthoesters
- Poly (lactide-co-glycolides) (PLGA)
- Polylactide (PLA)
- Polyanhydride
- Polyglycolides (PGA)

CLASSIFICATION POLYMERS[15]:

Basis on interaction with water

Non-biodegradable

Soluble Polymers

Hydro gels

hydrophobic Polymers

E.g. HPMC, PEGE.g. Polyvinyl pyrrolidine

E.g. Polyvinyl chloride

Based on polymerisation method

Addition Polymers Condensation polymers

E.g. Alkane Polymers E.g. Polystyrene and Polyamide

Based on polymerization mechanism

Chain Polymerization

Step Growth Polymerization

Based on chemical structure

Activated C-C Polymer

Inorganic Polymers

Natural polymers

Based on occurrence

Natural polymers

Synthetic polymers

E.g. 1. Proteins-collagen,E.g. Polyesters, polyamides

keratin, albumin, cellulose

Based on bio-stability

Bio-degradable

Non Bio-degradable

TYPES OF POLYMER DRUG DELIVERY SYSTEM:

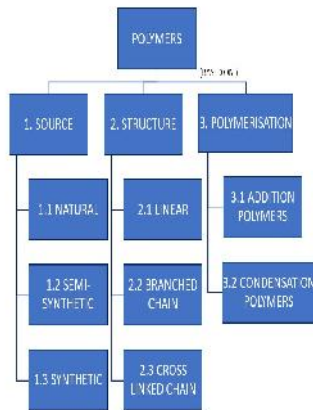


Fig 1: Diagram showing various classification of polymers.

SOURCE[16]:

Based on their occurrence in nature, polymers have been arranged in three sorts

Natural polymer :

The polymers, that occur in nature are called natural polymer otherwise called biopolymers (Figure 2, 3, 4).

Examples:

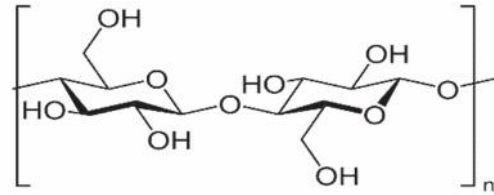


Fig 2: Cellulose

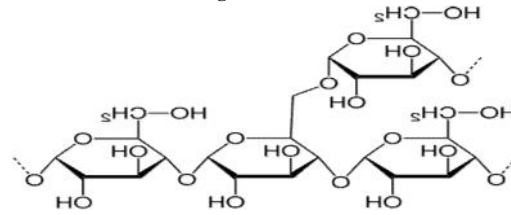


Fig 3: Starch

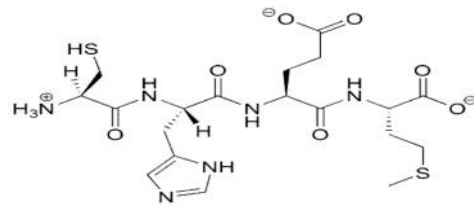


Fig 4: Protein

Semi-synthetic polymer:

They are the artificially changed natural polymers (Figure 5, 6)

Examples:

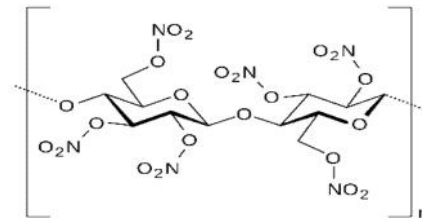


Fig 5: Cellulose nitrate

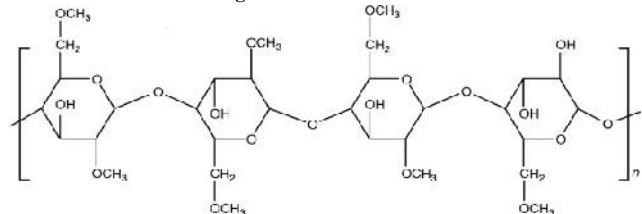


Fig 6: Methyl cellulose

1.3 Synthetic polymer:

The polymer which has been blended in the research facility is known as synthetic polymer. These are otherwise called man-made polymers (Figure 7, 8, 9).

Examples:

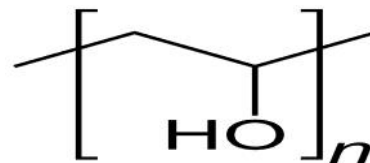


Fig 7: Polyvinyl alcohol

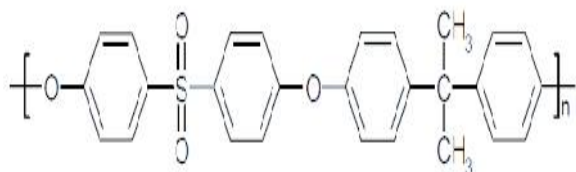


Fig 8: Polysulfone

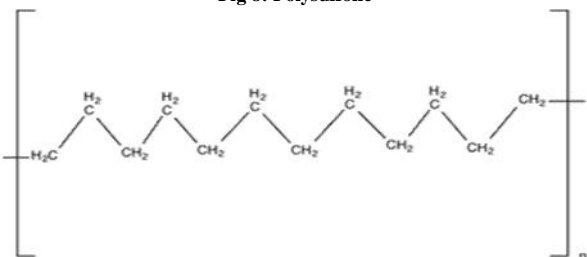


Fig 9: Polyethylene

STRUCTURE[17] :

Based on structure, polymers are of three types.

- **Linear polymer :**

Polymers in which the monomer molecules have been connected together in one constant length to shape the polymer particle.

- **Branched chain :**

Branched polymer molecules are those wherein there are side parts of connected monomer molecules projecting from different focal branch fixed along the principle polymer chain.

- **Cross-linked chain polymer :**

Whenever polymers are created in which, the polymer molecules are connected to one another at points other than their closures, the polymers are supposed to be crosslinked. Crosslinking can be made to happen during the polymerization interaction by the utilization of suitable monomers (Figure 10).

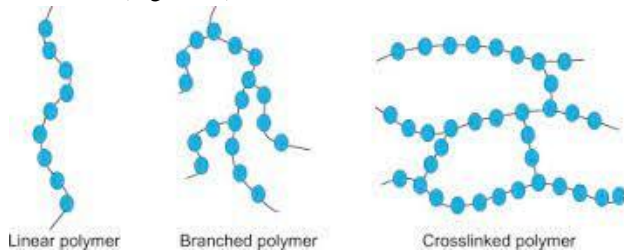


Fig 10: Polymerization chain reaction

POLYMERISATION[18] :

On the basis of polymerisation, polymers are classified in two types.

- **Addition polymer :**

They are made from olefinic, diolefinic, vinyl and related monomers. They are made from basic expansion of monomer molecules to each other in a fast progression by a chain system. This interaction is called addition polymerization.

Examples : Polyethylene

- **Condensation polymer :**

They are framed from intermolecular responses between bifunctional or polyfunctional monomers molecules having receptive practical gatherings such as -OH, -COOH, -NH₂, -NCO etc...'

5. POLYMER THERAPEUTICS :

Polymer therapeutics is a term used to depict an inexorably significant area of biopharmaceutics in which a linear or branched polymer chain acts either as the bioactive (a polymeric medication) or, all the more normally, as the inactive transporter to which a therapeutics covalently connected, as on account of polymer-drug forms, polymer-protein conjugates, polymeric micelles, and multicomponent polyplexes.[19] Formation of the remedial to the polymer works on the phenomenon of pharmacokinetic and pharmacodynamic properties of biopharmaceuticals through an assortment of measures, including expanded plasma half-life(which further develops patient compliance in light of the fact that less continuous dosages are required), assurance of the restorative from proteolytic enzymes, decrease in immunogenicity, upgraded stability of proteins, upgraded solvency of low MW drugs, and the potential for designated conveyance.[19]–[21] Most of polymer forms are planned as anticancer therapeutics, Even though othersicknesses have additionally been designated, including rheumatoid joint inflammation, diabetes, hepatitis B and C, also, ischemia.[22] The notoriety of forms for anticancer specialists is an aftereffect of a detached cancer focusing on peculiarity initially termed by Matsumura and Maeda as the enhanced permeation and retention (EPR) impact.[23]

Polymer conjugation:

Conjugation of polymers can occur either with the drug molecule or with the protein molecule.

➤ Polymer-drug conjugation :

Quite possibly the most regularly concentrated on areas of polymer therapeutics is polymer-drug conjugates in which the low molecular weight therapeutic and polymeric transporter are most frequently an anticancer agent and HEMA copolymer, separately. This region was brought into the world from a milestone research paper by Ringsdorf in 1975[24] and afterward further spearheaded during the 1980s by Duncan and Kopecek, who planned the principal designated man-made polymer-anticancer conjugates to progress to clinical study.[25], [26] This work was exhaustively surveyed as of late.[27], [28] Rather than free medications, which ordinarily disseminate arbitrarily all through the body and consequently apply pernicious incidental effects, connection of the therapeutic to polymer transporters limits cell take-up to endocytosis, stretches out dissemination times to a few hours, and works with latent focusing of growths through the EPR impact.[20]

➤ Polymer-protein conjugation :

Spearheading studies distributed by Davis and partners in 1970s laid the establishment for the area presently known as

PEGylation in which proteins and peptides are covalently conjugated to PEG. This procedure has turned into the strategy for decision over the recent years to work on the pharmacokinetic and pharmacodynamic properties of protein therapeutics.[19], [20] PEG is ordinarily utilized as the favoured transporter in this application on account of an absence of immunogenicity, antigenicity, and toxicological aspects (PEG is endorsed by the FDA for injectable, topical, rectal, and nasal drug delivery systems). Besides, it is incredibly hydrophilic, which assists with safeguarding the protein from a resistant reaction of the immune system, and it can be combined to work with targeted formation without crosslinking the protein, which permits the drug to be delivered.[29] Also, despite the fact that PEGylation can prompt a decline in protein movement, the expanded bioavailability time can make up for this to in any case give drug concentration at important levels. The effect of PEGylation on drugs has been broadly evaluated somewhere else.[21], [29], [30] In spite of the triumphs and future guarantee of PEGylation in polymer-protein forms, PEG is restricted because of an absence of biodegradability, and conjugation can decrease or change protein movement.

Duncan et al. report a clever methodology for polymer-protein formation called polymer-unmasking protein therapy (PUMPT) in which a model enzyme (catalyst), trypsin, was conjugated to dextrin, a characteristic polysaccharide that is biodegradable and has been clinically endorsed for an assortment of purposes.[31]

IDEAL CHARACTERISTICS OF POLYMERS BEING USED IN BIOMEDICAL FIELD:

- ❖ It should possess low density.
- ❖ It should be less liable of friction.
- ❖ It should possess good corrosion resistance.
- ❖ They must have good module ability.
- ❖ They must obtain excellent surface finish.
- ❖ They can be produced with close dimensional tolerance.
- ❖ They must be economical.
- ❖ Should possess poor tensile strength.
- ❖ Low mechanical properties.
- ❖ Poor temperature resistance.
- ❖ It can be produced transparent or in different colours.
- ❖ It should be biodegradable.
- ❖ It must provide good linkage with drug molecules.
- ❖ Its production should be easy and accurate.

6. APPLICATION OF POLYMERS IN BIOMEDICAL FIELD:

Polymers are widely used in our daily life .

Ø **General application of polymers**[18] :

- In pharmaceutical industries, polymers are applied in manufacturing of containers and also for the manufacturing of syringe, vials, catheter’s.
- They are used as excipient in various drug formulations of tablets, capsules and liquid orals.

- They are also used as excipient in novel drug delivery system for formulating nanoparticles, liposomes, microencapsulation...etc (Table 1).
- They are used to construct artificial replacement for human organ.
- They are used to repair, sustain and augment function of organ.
- They are also used to provide biochemical function.

Ø **Application in conventional dosage forms**[15] :

- In tablets, they are used as binder’s, diluent’s, disintegrating agents.
- They are used in the process of tablet coating.
- In liquids, they are used to impart viscosity to liquid formulations.
- They are also used for controlling the flow of liquids.
- In semi-solids, they are used in oral preparation and ointment preparation.

Table 1: Table containing different polymers used in different medicinal products.

Product	Drug Name	Polymer used	Type of polymer	Brand Name
Cesamet®	Nabilone	PVP	Water soluble	Eli Lilly and Company
Certican®	Everolimus	HPMC	Non-ionic cellulosic polymer	Novartis
Gris-PEG®	Griseofulvin	PEG 6000	Hydrophilic	Pedinol/Valeant Pharmaceuticals
Intelence®	Etravirine	HPMC	Non-ionic cellulosic polymer	Tibotec/Johnson & Johnson
Isoptin SR-E®	Verapamil	HPC/HPMC	Water soluble/Non-ionic cellulosic polymer	Abbott
Kaletra®	Lopinavir, Ritonavir	PVP	Water soluble	Abbott
Nivadil®	Nivalidipine	HPC/HPMC	Water soluble/Non-ionic cellulosic polymer	Fujisawa Pharmaceuticals Co., Ltd.
Prograf®	Tacrolimus	HPMC	Non-ionic cellulosic polymer	Fujisawa Pharmaceuticals Co., Ltd.
Rezulin®	Troglitazone	PVP	Water soluble	Pfizer, Inc.
Sporanox	Itraconazole	HPMC	Non-ionic	Janssen

®	e		cellulosic polymer	Pharmaceuticals, Inc.
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7. DISCUSSION

As the use of polymers is going on increasing in biomedical field it is still under research, as a result many modified polymers have been discovered which are intensively used in controlled drug delivery system and also in artificial organ lining, parenteral preparation, chemical reactors. Beside of all these uses, the most potent opportunity for these polymers lies in the field of responsive delivery system. The health care workers can recover the patient's diseases faster. With ongoing research novel combination of polymers will show the way to a new drug delivery system, which will increase the action rate of drug in curing diseases in future.

8. CONCLUSION

There is tremendous research going on the polymers about how it is going to help in therapeutical aspects like enhancing drug delivery time, pattern, stability, targeting and much more future aspects are awaiting to be known. The research references highlighted in this review have shown the great achievement so far in terms of enhancing drug delivery through various techniques been mentioned in this review so far. The progressing demands of modern drug delivery systems has led to finding novel properties of polymers and many researches has even failed due to lack of compatibility but overcoming them is an new approach we should work on and find the better ways to do the research. Even though, we have succeeded in finding the value of polymers in therapeutics we need to go for the core knowledge of polymers in future.

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ACKNOWLEDGEMENT: None

CONFLICT OF INTEREST: The authors declare no conflict of interest, financial or otherwise.

SOURCE OF FUNDING: None.

AVAILABILITY OF DATA AND MATERIALS: Not applicable.

CONSENT FOR PUBLICATION: Not applicable.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE: Not applicable.