Review Article

Polymers Used in Pharmaceuticals: A Brief Review

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ABSTRACT
Polymer have played indispensable roles in the preparation of pharmaceutical products.their applications range widely from material packaging to fabrication of the most sophisticated drug delivery devices. This review includes various polymers used in pharmaceutics based on their applications. The review focused on the use of pharmaceutical polymers for controlled drug delivery applications. Advances in polymer science have led to the development of several novel drug delivery system. The review provides the overview of the mechanism of polymer, properties, characterization of polymer and future of polymer technology which should be considered are involved.

Keywords: Classification of polymer, Biodegradable and non-biodegradable polymer, Physical properties.

INTRODUCTION

Definition of polymer

"Polymers are long chain organic molecules assembled from many smaller molecules called as monomer."

- The polymer have been synthesized for specific need and to solve problems related with development of drug delivery system.
- Polymers have been mainly used to control the drug release rate from the formulations.
- They are also used as taste masking agent, stabilizer 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.
- Polymers are macromolecules having very large chains contain a variety of functional groups, can be blended with other low and high molecular weight material.
- Polymers are mostly applied in drug delivery because they have unique properties which have not been attained by any other material.

On the basis of surface and bulk properties polymers are have some application

1) In development of drug delivery/targeting technique to improve the efficiency of drug therapy.
2) In development of new technology in polymer based encapsulation and controlled drug release system.
3) To minimize side effect in medical treatment.
4) In pharmaceutical field polymer used as binder, emulsifying agent, thickening agent etc.
5) Polymer also used as film coating to masking the unpleasant taste to enhance drug stability and in protection and packaging.

CLASSIFICATION OF THE POLYMER[1,2]

A. Based on origin

a) Natural polymer

- Natural polymers are the substances which are obtained by natural sources like plant and animal sources.
- Proteins, enzymes, muscle fibers, polymer polysaccharide, gummy exudates are the natural polymers which are used in formulating pharmaceutical products.
- The well-known natural polymers are chitosan, carrageenan, isapghula, acacia, gelatin, agar, shellac, guar gum.
- The specific application of plant derived polymer in pharmaceutical formulations include their use in the manufacture of solid monolithic matrix systems, implants, films, beads, micro particles, nanoparticles, inhalable and injectable system as well as viscous liquid formulations.
- E.g. Proteins-collagen, keratin, albumin.

Carbohydrates-starch, cellulose, glycogen.

Collagen[1]

- Collagen is a major natural protein component in mammals that is fabricated from glycine-proline-(hydroxy) proline.
- Collagen has been widely used in pharmaceutical applications due to the fulfillment of many requirements of a drug delivery system such as good biocompatibility, low antigenicity, and degradability upon implantation.
- Collagen gels are one of the first natural polymers to be used as a promising matrix for drug delivery and tissue engineering.

Example

- The combination of liposomes and collagen-based technologies has Been used.
- In this case, drugs and other bioactive agents were firstly encapsulated in the liposomes and then embedded inside a depot composed of collagen-based systems, including scaffolds and gels.
- The combination of these two technologies (i.e., liposomes and collagen-based system) has improved storage stability, prolonged the drug release rate, and increased the therapeutic efficacy.

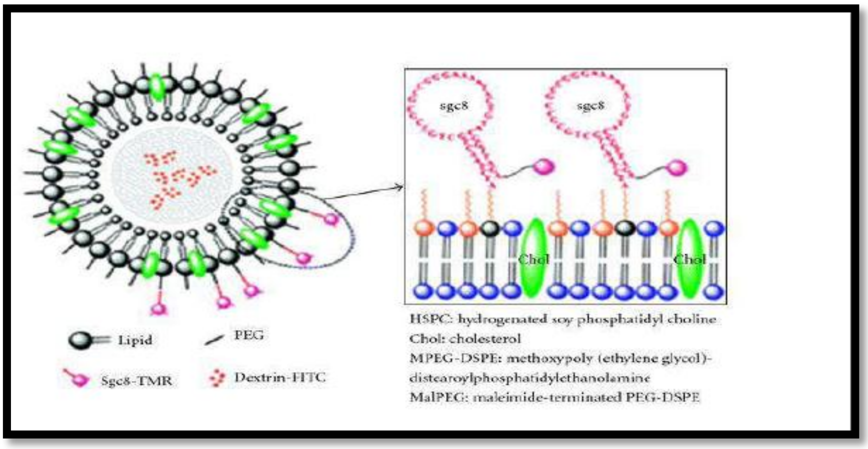

Fig. 1

b) Synthetic polymer

- Synthetic polymers are industrially produced chemical substances consisting of a number of molecules linked together with covalent bond.
- A wide variety of synthetic polymers are available with variation in main chain as well as side chain.
- The most commonly used synthetic polymer are polythene and polystyrene.
- E.g. polyester, polyanhydrides, polyamides, polyglycolic acid.

Polyglycolic acid (PGA)

- PGA is commonly obtained by ring-opening polymerization of the cyclic diester of glycolic acid, glycolide.
- PGA is a hard, tough, crystalline polymer with a melting temperature of .225 °C and a glass transition temperature, Tg, of 36 °C.
- PGA has excellent fiber-forming properties and was commercially introduced in 1970 as the first synthetic absorbable suture under the trade name Dexon™.
- The low solubility and high melting point of PGA limits its use for drug delivery applications, since it cannot be made into films, rods, capsules, or microspheres using solvent or melt techniques.

b) Based on Bio-stability

Bio-degradable Polymers[4]

- ✓ A bio-degradable polymer is a polymer in which the degradation results from the action of naturally occurring microorganisms such as bacteria, fungi.
- ✓ Biodegradable polymers are highly desirable in their conditions as they degrade in the body to biologically inert and compatible molecules.

- ✓ These polymer includes polyester, proteins, carbohydrates, etc.

Alginate

- Alginate also serves as an example of a naturally occurring linear polysaccharide.
- Alginate are widely used by many pharmaceutical scientist for drug delivery due to its many unique properties such as biocompatibility, biodegradability, low toxicity, non-immunogenicity, water solubility, relatively low cost, gelling ability, stabilizing properties, and high viscosity in aqueous solutions.
- The cross linking methodology was conducted at room temperature and physiological pH.
- The alginate based systems have been successfully used as a matrix for the encapsulation of stem cells and for controlled release of proteins, genes, and drugs.

Non-biodegradable polymer[4]

- ✓ This polymers are used in pharmaceutical formulation to increase the therapeutic efficacy of drug.
- ✓ This polymers is now days used in drug delivery system and tissue engineering.
- ✓ Following are the non-biodegradable polymers used in pharmaceutical formulation-
- ✓ E.g. ethyl cellulose, HPMC, acrylic polymer, poly (ethylene glycol).

Polyethylene glycol (PEG)

- Polyethylene glycol is synthesized by the interaction of ethylene oxide with water, ethylene glycol or ethylene glycol oligomers.
- PEG is suitable for biological applications because it is soluble in water and has low intrinsic toxicity.
- The high hydrophilic nature of PEG enhance the solubility of hydrophobic drug or carriers when conjugated with them.
- It enhances the physical and chemical stability of drug and prevents aggregation of the drugs in vivo as well as during storage.
- PEG helps in reducing the aggregation of red blood cell and also improve the blood compatibility of PEG copolymers that are implanted as cardiovascular devices such as stents.
- It is mainly used in storage of blood and organs. Both temperature responsive and chemically cross linked hydro gels have been formed from PEG.

Some linear polymers used in pharmaceuticals[3]

Repeating monomer unit	Chemical name	abbreviation
Polyolefin		
-(-CH2—CH-)- | CH3	polypropylene	PP
-(-CH2—CH-)- | Φ	polystyrene	PS
-(-CH2—CH¼CH—CH2-)-	1,4-polybutadiene	PB
-(-CH2—CH2-)-	polyethylene	PE(HDPE &LDPE)
Polyvinylics and polyvinylidenics		
-(-CH2—CHCl-)-	Poly(vinyl chloride)	PVP
-(-CH 2—CH-)- | O-CO—CH3	Poly(vinyl acetate)	PVAc
-(-CH2—CHOH-)-	Poly (vinyl alcohol)	PVAI
-(-CH2—CF2-)-	Poly(vinylidene fluoride)	PVDF
-(-CF2—CF2-)-	Polytetra-fluoroethylene	PTFE

Physical properties that contribute to the rate of biodegradation of polymer

✓ **Water permeability and water solubility**

A reflection of the free volume of the polymer and its hydrophilicity will determine the rate of hydrolysis and whether bulk or surface hydrolytic degradation occurs.

✓ **Crystallinity of the polymer**

Only the amorphous phase of the polymer is accessible to permeates (i.e. water drug) and to enzymatic attack.

✓ **Glass-transition temperature**

The glassy or rubbery nature of the polymer will be reflected in its permeability and molecular chain mobility. The chain mobility appears to be an important factor in determining the susceptibility to enzymatic attack.

✓ **Physical dimensions**

(E.g. size and surface-to-volume ratio) these appear to become significant in the advanced stages on biodegradation, when phagocytosis may come into play.

Need of biodegradable polymers[2]

- Non-biodegradable polymers are costly, invasive because require surgical removal after completion of drug release and may cause tissue toxicity if retained for longer time.
- While diffusion controlled release is an excellent means of achieving controlled drug delivery, it is limited by the polymer permeability and the characteristics of a drug increase, its diffusion coefficient decreases.
- Biodegradable polymers do not need a second surgery for removal of polymer as it undergoes auto-biodegradation.

Characterization of polymer[3]

- In general, polymers for biomedical and pharmaceutical applications are characterized in order to determine their molecular weight, composition and thermal properties. All of these characteristics may influence the properties of the final device or medicine.
- Characterization technique is mostly used to determine molecular mass, molecular structure, morphology and mechanical properties.
- The molecular weight of polymers can vary from a few hundred to several million gram per mole, while cross linked polymers have infinite molecular weight.
- Polymers obtained from chemical synthesis form a family of macromolecular species characterized by a mean molecular weight with a certain distribution, termed as “polymolecularity”.
- This effects adds heterogeneity to chemically synthesized copolymers, and the only way to appreciate this effect is to analyze the composition of the polymers at low conversion degree during polymer synthesis.

Characteristics of an ideal polymer[6]

- 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.
- It must not have tendency to retain in tissue and must be a good biodegradable material.

Characterization technique used to study polymer degradation[3]

Characterization technique	Degradation parameter	Type of polymer	outcome
GPC	Molecular weight	PDLA	Molecular weight decrease as the degradation proceeds.
DSC	Thermal changes	PLGA	Tg decreases as degradation proceeds.
TGA	Thermal changes	PDLA	Above Tg, polymer degradation faster
IR	Changes in concentration of terminal group	Poly(ethylene naphthalene-2,6-dicarboxylate)	Hydrolytic degration rate constant determined by acid catalysis reaction.

FT-IR	Absorbance peak	Polyester	Degradation rate increases with increasing polydispersity.
SEM	Surface characterization	Copolymer of sebacic acid and carboxy phenoxy propane	Crystalline region is more resistant to erosion than amorphous.
NMR	Molar fraction of monomer and degree in degradation	PDLA	Base catalyzed hydrolysis PDLA was by a random scisson mechanism; while acid catalyzed is faster chain scisson.
HPLC	Determination of monomer release	PDLA AND PLGA	GA degrade faster than LA
RAMAN SPECTROSCOPY	Chemical composition, molecular weight	Copolymer of lactide/caprolactone	Hydrolytic degradation was monitored. Crystallanity increased with time.
TOF-SIMS	Surface molecular weight and end group.	PLLA	Good linearity obtained in the kinetics study of PLLA degradation at the surface.

Mechanism of drug release from polymer[1]

1) **Erosion of the polymer surface with concomitant release of physically entrapped drug**
   - When glassy (a dry) polymer comes into contact with water or any other medium which is thermodynamically compatible, it get swallowed and diffusion takes place.

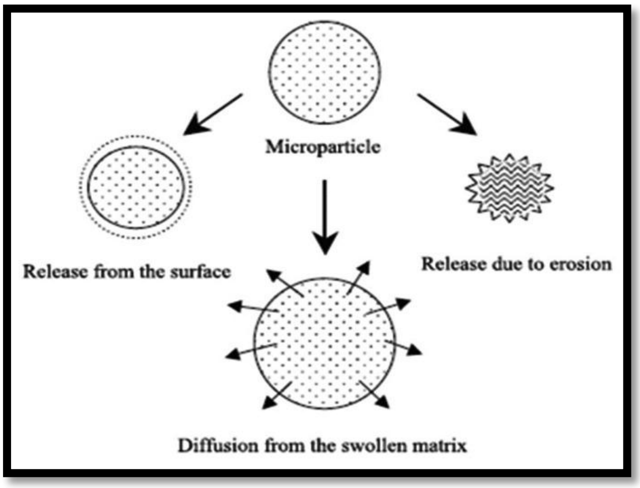

Fig. 2

2) **Cleavage of covalent bonds between the polymer and drug, occurring in the polymer bulk or at the surface, followed by drug diffusion.**
   - In these mechanism disruption of covalent bond between polymer and drug.
   - It occurs either in polymer bulk or at the surface which may lead to drug diffusion.

3) **Diffusion controlled release of the physically entrapped drug, with bio-absorption of the polymer delayed until after drug deletion.**
   - The third approach avoid any irreproducibility of the bio erosion rate and the difficulty of trying to synchronize the diffusion and bio erosion process to achieve a specified delivery rate.
   - A polymer that is to be used in biodegradable delivery system must be tailored to meet a number of requirements, the most important of which are permeability, biodegradability, and tensile strength.
   - These properties are interdependent to some degree and modifications of a polymer to optimize one property will have an effect on the other three.
   - A number of potentially biodegradable polymer system are used based on the known
   - Susceptibility of their monomer analogues to undergo cleavage under mild hydrolytic conditions

FUTURE PROSPECTS[2]

- The most exciting opportunities in polymer drug delivery lie in the arena of responsive delivery system, with which it will be possible to deliver drugs through implantable devices in response to a measured blood level to deliver a drug precisely to a targeted site.
- Much of the development novel materials in controlled drug delivery is focusing on the preparation and use of these responsive polymers with specifically designed microscopic and microscopic structural and chemical features. such system includes:

- ✓ Copolymers with desirable hydrophilic/hydrophobic interaction.
- ✓ Block or graft polymer
- ✓ Complexation networks responding via hydrogen or ionic bonding.
- ✓ Dendrites or star polymers as nanoparticles for immobilization of enzymes,drugs,peptides or other biological ingredients.
- ✓ New biodegradable polymers.
- ✓ New blends of hydrocolloids and carbohydrates –based polymer.
- ✓ Dendrimers provides a platform for the attachement of drug or gene and their release through several mechanism.
- ✓ In any case, the purpose behind controlling the drug delivery is to achieve more effective in both under and over dosing therapies.

CONCLUSION

- This review has covered the major concern about the natural and synthetic polymers, their classification, mechanism and various applications.
- Nowadays, there are few biodegradable water soluble polymers available commercially.
- Biodegradable polymers have been researched, but polymer based on renewable sources (especially on starch) are most desirable.
- The drawback associated with conventional dosage form have been overcome by utilizing polymers synthesized specifically to solve the problems.
- The use of novel polymers not only offers 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 system pass through the various phases of clinical trials and benefit to the society.
- It is believed that the advances in polymer science will revolutionize the design, development and performance of polymer based drug delivery system.
- Biodegradable polymers have proven their potential for the development of new, advances and efficient drug delivery system.

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REFERENCES

1. Jay J and Ronak P. Role of biodegradable polymers in drug delivery. International journal of current pharmaceutical research. 2012; 4(4).
2. Ankita R, Anil B and Brijesh K. Polymers in a Drug Delivery System-A review. International Journal of Pharmaceutical Research and Development. 2002; 2(8).
3. Denis L, Gilles P and Christin V. Biomedical and Pharmaceutical Polymer. published by Pharmaceutical press. 2011: 1-148.
4. Omanthanu P and Ramesh P. Polymer in Drug Delivery System. current opinion in chemical biology. 2001: 447-451.
5. Denis L, Gilles P and Christin V. Biomedical and Pharmaceutical Polymer published by Pharmaceutical press. 2011: 1-148.
6. www.PHARMATUTOR.ORG.ART-1509.