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POLYMERS IN PHARMACEUTICAL INDUSTRIES- A REVIEW

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ABSTRACT

The current review article focuses on polymers in pharmaceutical drug delivery of therapeutic agents. These dosage forms include tablets, patches, tapes, films, semi-solids and powders. Polymers are the backbone of a pharmaceutical drug delivery system as they control the release of the drug from the device. Biodegradable polymers attracts the attention of its use as they can be degraded to non-toxic monomers and most important, a constant rate of drug release can be achieved from a biodegradable polymer based controlled release device. Natural polymers can be used as the means of achieving predetermined rates of drug delivery and their physio-chemical characteristics with the ease of availability provide a platform to use it as a polymers for drug delivery systems. Biodegradable polymers have been widely used in biomedical applications because of their known bio-compatibility and biodegradability. In the biomedical area, polymers are generally used as implants and are expected to perform long term service. These improvements contribute to make medical treatment more efficient and to minimize side effects and other types of inconveniences for patients. The main role of polymers is to protect drug from physiological environment and prolong release of drug to improve its stability. The drug is release from polymers by diffusion, degradation and swelling. In addition to this review presents characteristics and behaviours of plant derived and mucoadhesive polymers which are currently used in drug delivery.

KEYWORDS: Polymers, excipients, synthetic polymer, natural polymers, sustained release, control release.

INTRODUCTION

From the past decades, research at the level of molecular biology has unveiled the molecular basis for many diseases. New important technologies and concepts such as Recombinant DNA and gene therapy have provided tools for the creation of pharmaceuticals and methods designed to specifically address such diseases. However progress towards the application of these medicines outside of the laboratory has been considerably slow principally due to the lack of effective drug delivery systems that is mechanisms that allow the release of the drug into the appropriate body compartment for the appropriate amount of time without seriously disrupting the rest of the organism functionality. The application of the polymeric materials for medical purposes is growing fast. Polymers have found applications in diverse biomedical fields such as drug delivering systems, developing scaffolds in tissue engineering, implantation of medical devices and artificial organs, prosthesis, ophthalmology, dentistry, bone repair, and many other medical fields. Polymers have been used as a main tool to control the drug release rate from the formulations.

These improvements contribute to make medical treatment more efficient and to minimize side effects and other types of inconveniences for patients.

The pharmaceutical applications of polymers range from their use as binders in tablets to viscosity and flow controlling agents in liquids, suspensions and emulsions.

Polymers can be used as film coatings to disguise/mask the unpleasant taste of a drug, to enhance drug stability and to modify drug release characteristics.

Pharmaceutical polymers are widely used to achieve taste masking; controlled release (e.g. extended, pulsatile and targeted) enhanced stability and improved bioavailability.

Polymers are able to

* Prolong drug availability if medicines are formulated as hydrogels or microparticles.
* Favourably alter bio distribution, if formulated into dense nanoparticles.
* Enable hydrophobic drug administration if formulated as micelles.
* Transport a drug to its usually inaccessible site of action, if formulated as gene medicines.

Characteristics of an ideal polymer

 It should be versatile and possess a wide range of mechanical, physical, chemical properties.

 It should be non-toxic and have good mechanical strength and should be easily administered.

 It should be inexpensive and easy to fabricate.

 It should be inert to host tissue and compatible with environment.

Criteria followed in polymer selection

 The polymer should be soluble and easy to synthesis.

 It should have finite molecular weight.

 It should be compatible with biological environment.

 It should be biodegradable.

 It should provide good drug polymer linkage.

CLASSIFICATION POLYMERS

Based on interaction with water

 Non-biodegradable hydrophobic Polymers:- E.g. Polyvinyl chloride,

 Soluble Polymers:- E.g. HPMC, PEG.

 Hydro gels:- E.g. Polyvinyl pyrrolidine.

Based on polymerisation method

 Addition Polymers:- E.g. Alkane Polymers.

 Condensation polymers:- E.g. Polysterene 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:- E.g. 1. Proteins-collagen, keratin, albumin, cellulose

 Synthetic polymers:- E.g. Polyesters, polyamides

Based on bio-stability

- Bio-degradable
- Non Bio-degradable

TYPES OF POLYMER DRUG DELIVERY SYSTEM8

Polymers for Drug Delivery in Tissue Engineering Several strategies have been developed in order to regenerate functional tissue, the majority of which involve the use of polymer scaffolds specifically designed to direct tissue growth. The cell transplantation method is one of the most commonly used in cartilage and bone formation.20 Polymer matrices both natural and synthetic can play a vital role in the delivery of protein growth factors and cytokines to aid angiogenesis and tissue reconstruction procedures. These molecules are essential to tissue growth as they control a number of vital cellular processes including proliferation and differentiation. It has been shown that by careful selection of the polymer and the processing method, controlled-release matrices, incorporating proteins and growth factors that induce and enhance tissue growth can be produced. The future use of gene therapy as a way of regenerating tissue is an exciting area, and despite still being in its infancy, it may yet provide a solution to the challenge of delivering drugs and proteins more effectively in all areas of medicine. Poly (lactic-co-glycolic acid) Microspheres The term microsphere refers to a small sphere with a porous inner matrix and variable surface from smooth and porous to irregular and nonporous. The drug when encapsulated is dispersed throughout the inner matrix. The size range of microspheres is typically 1 to 500 μm in diameter. Poly (lactic-co-glycolic acid) microspheres have increasingly become the focus of research efforts in the scientific community and pharmaceutical industry. Their application as drug delivery vehicles has risen in line with the expanding biotechnology sector and the promise of new drugs discovered in the wake of the human genome project and proteomics.

Polymeric Nanoparticles as Drug Carriers

Certain chemical entities are either rapidly degraded and/or metabolized after administration (peptides, proteins, and nucleic acids). This is the reason the idea that nanotechnologies may be employed to modify or even to control the drug distribution at the tissue, cellular, or sub cellular levels has emerged. Among the technologies utilized for drug targeting are polymer-based nanoparticles, which have been developed since the early 1980s, when progress in polymer chemistry allowed the design of biodegradable and biocompatible materials. Nanoparticles may be defined as being submicron (<1 μm) colloidal systems

generally composed of polymers. Thus, nanoparticles are colloidal systems with a size 7 to 70 times smaller than the red cells. They may be administered intravenously without any risk of embolization. Depending on the method used in the preparation of nanoparticles, either nanospheres or nanocapsules can be obtained. Nanospheres are matrix systems in which the drug is dispersed within the polymer throughout the particle. On the contrary, nanocapsules are vesicular systems, which are formed by a drug- containing liquid core (aqueous or lipophilic) surrounded by a single polymeric membrane.

Polymeric Micelles as Pharmaceutical Carriers

Polymeric micelles demonstrate many attractive properties as pharmaceutical carriers. They are stable both in vitro and in vivo, can be loaded with a wide variety of poorly soluble pharmaceutical agents, effectively accumulate in pathological body areas with compromised vasculature (infarcts, tumors), and can be targeted by attaching various specific ligands to their surface. Both therapeutic and diagnostic micelles can be forms results in suboptimal therapy and/or systemic side effects. Pharmaceutical scientists have attempted to overcome the limitations of conventional oral dosage forms by developing modified release dosage forms.

Extended release dosage forms

The therapeutic effect of drugs that have a short biological half-life may be enhanced by formulating them as extended or sustained 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, cellulose acetate, and polyvinyl derivative, polyvinyl acetate. Eudragit RS and RL differ in the proportion of quaternary ammonium groups, rendering Eudragit RS less permeable to water, whereas ethylcellulose is available in a number of different grades of different viscosity, with higher-viscosity grades forming stronger and more durable films.

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. Unlike a conventional extended release dosage form, which gradually releases the drug during transit along the gastrointestinal tract, such a delivery system would overcome the problems of drugs that are absorbed preferentially from specific sites within the gastrointestinal tract (for example, many drugs are absorbed poorly from the distal gut, where an extended- release dosage form may spend the majority of its time),producing nonuniform plasma time profile delivery systems do not relay on polymers present, to achieve gastroretention 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.

ROLE OF POLYMERS IN PHARMACEUTICAL DRUG DELIVERY

Immediate release dosage forms

Tablets

Polymers have been used for many years as excipients in conventional immediate-release oral dosage forms, either to aid in the manufacturing process or to protect the drug from degradation upon storage. Micro-crystalline cellulose is often used as an alternative to carbohydrates as diluents in tablet formulations of highly potent low-dose drugs. Starch and cellulose are used as disintegrants in tablet formulations, which swell on contact with water, resulting in the tablet "bursting," increasing the exposed surface area of the drug and improving the dissolution characteristics of a formulation. Polymers including polyvinyl-pyrrolidone (PVP) and hydroxypropyl methylcellulose (HPMC) also find uses as binders that aid the formation of granules that improve the flow and compaction properties of tablet formulations prior to tabletting. Occasionally, dosage forms must be coated with a "non-functional" polymeric film coating in order to protect a drug from degradation, mask the taste of an unpalatable drug or excipients, or improve the visual elegance of the formulation without affecting the drug release rate.

Capsules

Capsules are used as an alternative to tablets, for poorly compressible materials, to mask the bitter taste of certain drugs, or sometimes to increase bioavailability. Many of the polymeric excipients used to "bulk out" capsule fills are the same as those used in immediate-release tablets. Gelatin 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.

Modified-release dosage forms

It is now generally accepted that for many therapeutic agents drug delivery using immediate release dosage forms.

POLYMERS IN PHARMACEUTICAL APPLICATIONS

Water-Soluble Synthetic Polymers

 Poly (acrylic acid) Cosmetic, pharmaceuticals, immobilization of cationic drugs, base for Carbopol polymers.

 Poly (ethylene oxide) Coagulant, flocculent, very high molecular-weight up to a few millions, swelling agent.

 Poly (ethylene glycol) Mw <10,000; liquid (Mw<1000) and wax (Mw >1000), plasticizer, base for suppositories.

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

 Poly (vinyl alcohol) Water-soluble packaging, tablet binder, tablet coating.

Cellulose-Based Polymers

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

 Carboxymethyl cellulose Super disintegrant, emulsion stabilizer.

 Hydroxyethyl and hydroxypropyl celluloses Soluble in water and in alcohol for tablet coating.

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

 Cellulose acetate phthalate enteric coating. Hydrocolloids

 Alginic acid Oral and topical pharmaceutica lproducts; 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 disintegrants.

 Carrageenan Modified release, viscosifier.

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

Water-Insoluble Biodegradable Polymers

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

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.

Plastics and Rubbers

 Polyurethane Transdermal patch backing, blood pump, artificial heart, and vascular grafts, foam in biomedical and industrial products.

 Polyisobutylene Pressure sensitive adhesives for transdermal delivery.

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

 Poly (vinyl acetate) Binder for chewing gum.

 Poly (vinyl chloride) Blood bag, and tubing.

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

 Poly (methyl methacrylate) Hard contact lenses.

 Poly (hydroxyethyl methacrylate) Soft contact lenses.

General mechanism of drug release from polymer

There are three primary mechanisms by which active agents can be released from a delivery system namely.

Diffusion

Diffusion occurs when a drug or other active agent passes through the polymers that forms the controlled-release device. Diffusion occurs when the drug passes from the polymers 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 polymers matrices and bio-active agents chosen must allow for the drug to diffuse through the pores or macro-molecular structure of the polymers upon introduction of the delivery system into the biological environment without inducing any change in the polymers itself.

Degradation

Biodegradable polymers 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 polymers 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 polymers, resulting in a release rate that is proportional to the surface area of the drug delivery system.

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 polymers mesh size, enabling the drug to diffuse through the swollen network into the external environment.

FUTURE TRENDS

Despite the excessive use of synthetic polymers the need for natural bio-degradable polymers to deliver drugs continues to be area of active research. Natural polymers has numerous advantages over synthetic ones as being readily available relatively inexpensive, natural products of living organisms, possibilities of chemical modifications. The most exciting opportunities in polymers drug delivery lie in the arena of responsive delivery systems, with which it will be possible to deliver in response to a measured blood level or to deliver a drug precisely to a targeted site. Much of the development of novel materials in controlled drug delivery is focusing on the preparation and use of these responsive polymers with specifically designed macroscopic and microscopic, structural and chemical features.

Such systems include

- Co-polymers with desirable hydrophilic/hydrophobic interactions.
- Complexation networks responding via hydrogen or ionic bonding.
- Polymers as nanoparticles for immobilization of enzymes, drugs, peptides, or other biological agents.

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