AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Review on Polymers in Drug Delivery

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ABSTRACT

Polymers have been used as a main tool to control the drug release rate from the formulations. Extensive applications of polymers in drug delivery have been realized because polymers offer unique properties which so far have not been attained by any other materials. Advances in polymer science have led to the development of several novel drug-delivery systems. A proper consideration of surface and bulk properties can aid in the designing of polymers for various drug-delivery applications. These newer technological developments include drug modification by chemical means, carrier based drug delivery and drug entrapment in polymeric matrices or within pumps that are placed in desired bodily compartments. These technical development in drug delivery/targeting approaches improve the efficacy of drug therapy thereby improve human health. Polymer chemists and chemical engineers, pharmaceutical scientists are engaged in bringing out design predictable, controlled delivery of bio active agents. Biodegradable polymers have been widely used in biomedical applications because of their known biocompatibility and biodegradability. In general natural polymers offer fewer advantages than synthetic polymers. The following review presents an overview of the different biodegradable polymers that are currently being used, their properties, as well as new developments in their applications.

Keywords: Biodegradable systems, Controlled drug delivery, Natural Polymers, Novel drug delivery, Polymers, Synthetic Polymers.

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Received 08 June 2013, Accepted 18 June 2013

Please cite this article in press as: Pallerla *et al.*, Review on Polymers in Drug Delivery. American Journal of PharmTech Research 2013.

INTRODUCTION

Conventional forms of drug delivery generally rely on tablets, eye drops, ointments and intravenous solutions. Recently, a number of novel drug delivery technologies have developed. These newer technological development include drug modification by chemical means, career based drug delivery and drug entrapment in polymeric matrices or within pumps that are placed in desired bodily compartments. These technical development in drug delivery/targeting approaches improve the efficacy of drug therapy thereby improve human health. Still there are many infectious and other deadly diseases are uncured due to the problem encountered by formulation scientists in drug delivery approaches. There is a strong need to develop a proper delivery system to achieve the complete therapeutic effects of the existing drug molecules. Use of polymeric materials in novel drug delivery approaches has attracted the scientists. Polymer chemists and chemical engineers, pharmaceutical scientists are engaged in bringing out design predictable, controlled delivery of bio active agents. When the drug is delivered to the site of action by using polymer based drug delivery approaches the safety and bio compatibility is questionable. The characterization of biocompatible polymers is more focused in the field of formulation development and drug delivery approaches etc. the biodegradable polymers have properties of degrading in biological fluids with progressive release of dissolved or dispersed drug. There is various novel drug delivery approaches are developed in the pipeline of polymer based drug delivery approaches. The bio-safety and biocompatibility are the important characteristics needed for the use of polymers in the field of pharmaceutical formulation and in novel drug delivery approaches. The present paper review is focused in the advances of biodegradable polymers based drug delivery approaches.

Polymers are becoming increasingly important in pharmaceutical applications especially in the field of drug delivery. Polymers range from their use as binders and film coating agents in tablets to viscosity and flow controlling agents in liquids, suspensions and emulsions.

- To disguise the unpleasant taste of a drug,
- To enhance drug stability and
- To modify the release characteristics.

Around eighty million patients benefit from advanced drug delivery systems today, receiving safer and more effective doses of medicines that are needed to fight a variety of human ailments, including life threatening diseases.

Polymers can bind the particles of a solid dosage form and can also change the flow properties of a liquid dosage form. Extensive applications of polymers in drug delivery have been realized because polymers offer unique properties which so far have not been attained by any other materials. Polymers are macromolecules having very large chains, contain a variety of functional groups, can be blended with other low- and high–molecular-weight materials, and can be tailored for any applications. Polymers are becoming increasingly important in the field of drug delivery. Advances in polymer science have led to the development of several novel drug-delivery systems. A proper consideration of surface and bulk properties can aid in the designing of polymers for various drug-delivery applications. These newer technological development include drug modification by chemical means, career based drug delivery and drug entrapment in polymeric matrices or within pumps that are placed in desired bodily compartments. These technical development in drug delivery/targeting approaches improve the efficacy of drug therapy thereby improve human health. Use of polymeric materials in novel drug delivery approaches has attracted the scientists. Polymer chemists and chemical engineers, pharmaceutical scientists are engaged in bringing out design predictable, controlled delivery of bio active agents. Extensive applications of polymers in drug delivery have been realized because polymers offer unique properties which so far have not been attained by any other materials. New technological development in polymer-based encapsulations and controlled drug release systems offers possibilities for optimizing the administration of drugs. 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 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. Monolithic delivery devices are systems in which a drug is dispersed within a polymer matrix and released by diffusion. The rate of the drug release from a matrix product depends on the initial drug concentration and relaxation of the polymer chains, which overall displays a sustained release characteristic. In the biomedical area, polymers are generally used as implants and are expected to perform long term service. This requires that the polymers have unique properties that are not offered by polymers intended for general applications. In general, the desirable polymer properties in pharmaceutical applications are film forming (coating), thickening (rheology

modifier), gelling (controlled release), adhesion (binding), pH-dependent solubility (controlled release), solubility in organic solvents (taste masking), and barrier properties (protection and packaging).

Novel drug delivery systems:

To deliver drugs efficiently to specific organs, a range of organic systems (e.g., micelles, liposomes, and polymeric nanoparticles) novel ways have been designed. In recent decades, significant advances in drug-delivery systems have enabled more effective drug administration. To minimize drug degradation and loss, to prevent harmful side-effects and to increase drug bioavailability and the fraction of the drug accumulated in the required zone, various drug delivery and drug targeting systems are currently under research and development. Among the several drug carriers one can name soluble polymers, microparticles made of insoluble or biodegradable natural and synthetic polymers, microcapsules, cells, cell ghosts, lipoproteins, liposomes, nanoparticles, Dendrimers and micelles[6-7].

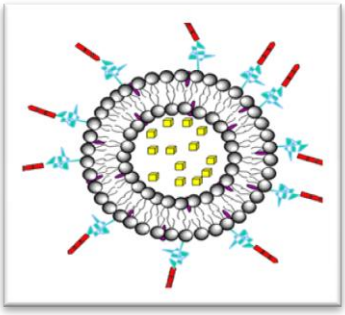

Figure 1: Drug carrier micelle

Drug delivery carriers:

Colloidal drug carrier systems such as types of polymers, micellar solutions, vesicle and liquid crystal dispersions, as well as nanoparticle dispersions consisting of small particles of 10–400 nm diameter show great promise as drug delivery systems. Whilst developing these formulations, the priority is to obtain systems with optimized drug loading and release properties, long shelf life and low toxicity. The incorporated drug participates in the microstructure of the system, and may even influence it due to molecular interactions, especially if the drug possesses amphiphilic and/or mesogenic properties.

Micelles formed by self-assembly of amphiphilic block copolymers (5-50 nm) in aqueous solutions are of great interest for drug delivery applications. The drugs can be physically entrapped in the core of block copolymer micelles and transported at concentrations that can exceed their intrinsic water- solubility. Moreover, the hydrophilic blocks can form hydrogen bonds with the aqueous surroundings and form a tight shell around the micellar core. As a result,

the contents of the hydrophobic core are effectively protected against hydrolysis and enzymatic degradation. In addition, the corona may prevent recognition by the reticulo-endothelial system and therefore, preliminary elimination of the micelles from the bloodstream. A feature that makes amphiphilic block copolymers attractive for drug delivery applications is the fact that their chemical composition, total molecular weight and block length ratios can be easily changed, which allows control of the size and morphology of the micelles. Functionalization of block copolymers with cross linkable groups the can increase the stability of the corresponding micelles and improve their temporal control. Substitution of block copolymer micelles with specific ligands is a very promising strategy to a broader range of sites of activity with a much higher selectivity[4-7].

Controlled drug delivery:

Controlled drug delivery is the use of formulation components and devices to release a therapeutic agent at a predictable rate *in vivo* when administered by an injected or non-injected route. To do this, pharmacist and analyst skills are needed to develop and measure release from the formulation, *i.e.* a polymer or device construction. Controlled Drug Delivery (CDD) occurs when a polymer, whether natural or synthetic, is judiciously combined with a drug or other active agent in such a way that the active agent is released from the material in a predesigned manner. The release of the active agent may be constant over a long period, it may be cyclic over a long period, or it may be triggered by the environment or other external events. In any case, the purpose behind controlling the drug delivery is to achieve more effective therapies while eliminating the potential for both under and overdosing. An example of Controlled drug delivery[8] was shown in figure 2.

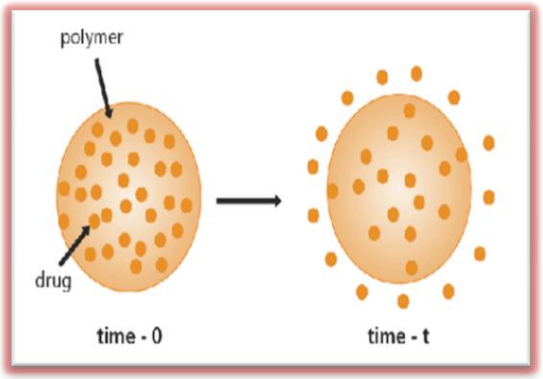

Figure 2: Example for Controlled Drug Delivery (CDD)

Controlled-release methodologies can be classified on the basis of the mechanism that controls the release of the active agent from the delivery device diffusion, osmosis, or polymer erosion.

The various polymer erosion mechanisms are of 3 basic types. Type I erosion refers to water-soluble polymers that have been insolubilized by covalent cross-links and that solubilize as the cross-links (type IA) or backbone (type IB) undergo a hydrolytic cleavage. In type II erosion, polymers that are initially water insoluble are solubilized by hydrolysis, ionization, or protonation of a pendant group. In type III erosion, hydrophobic polymers are converted to small water soluble molecules by backbone cleavage. The choice of a particular erosion mechanism is dictated by the specific application. The role of many of the original controlled-release systems was to achieve a delivery profile that would yield a high blood level of the drug over a long period of time. With traditional tablets or injections, the drug level in the blood follows the profile shown in figure 4 in which the level rises after each administration of the drug and then decreases until the next administration. The key point with traditional drug administration is that the blood level of the agent should remain between a maximum value, which may represent a toxic level, and a minimum value, below which the drug is no longer effective. In controlled drug delivery systems designed for long-term administration, remaining constant, between the desired maximum and minimum, for an extended period of time. Depending on the formulation and the application, this time may be anywhere from 24 hours (Procardia XL) to 1 month (Lupron Depot) to 5 years (Norplant)[5-10].

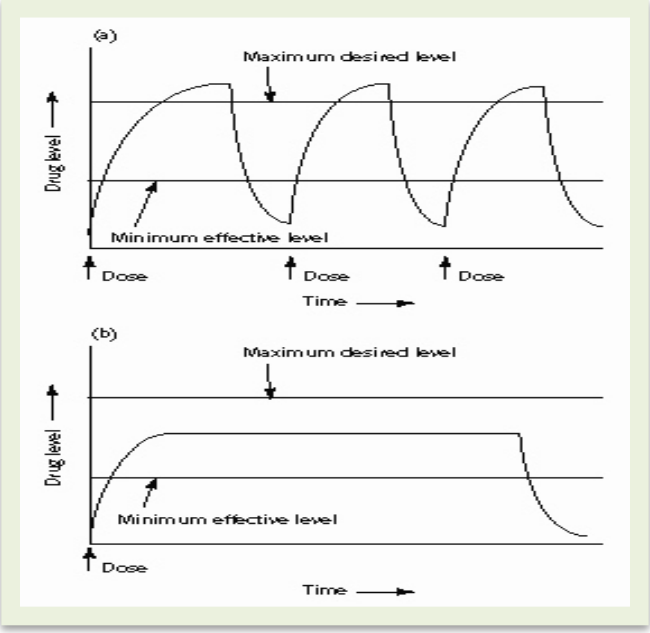

Figure 3: Drug levels in the blood with (a) traditional drug dosing and (b) controlled-delivery dosing.

Biomaterials for Delivery Systems[1-5]:

The polymers in the earlier stage were particularly used for non biological uses, and were selected because of their desirable physical properties, for example:

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

In order to be used for controlled drug delivery formulations, the polymers must be chemically inert and free of leachable impurities with appropriate physical structure, minimal undesired aging, and be readily processable. Few examples are

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

However in recent years the use of polymers were extended towards medical applications and drug targeting, few examples are

- Polylactides (PLA)
- Polyglycolides (PGA)
- Poly (lactide-co-glycolides) (PLGA)
- Polyanhydrides
- Polyorthoesters

Originally, polylactides and polyglycolides were used as absorbable suture material, and it was a natural step to work with these polymers in controlled drug delivery systems. The greatest advantage of these degradable polymers is that they are broken down into biologically acceptable molecules that are metabolized and removed from the body via normal metabolic pathways. However, biodegradable materials do produce degradation byproducts that must be tolerated with little or no adverse

reactions within the biological environment. These degradation products both desirable and potentially non desirable must be tested thoroughly, since there are a number of factors that will affect the biodegradation of the original materials. The most important of these factors are shown below a list that is by no means complete, but does provide an indication of the breadth of structural, chemical, and processing properties that can affect biodegradable drug delivery systems.

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, 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 pharmaceutical products; thickening and suspending agent in a variety of pastes, creams, and gels, as well as a stabilizing agent for oil-in-water emulsions; binder and disintegrant
- Carrageenan Modified release, viscosifier
- Chitosan Cosmetics and controlled drug delivery applications, mucoadhesive
- dosage forms, rapid release dosage forms
- Hyaluronic acid Reduction of scar tissue, cosmetics
- Pectinic acid Drug 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 Tran dermal patch backing (soft, comfortable, moderate moisture transmission), blood pump, artificial heart, and vascular grafts, foam in biomedical and industrial products

- Silicones Pacifier, therapeutic devices, implants, medical grade adhesive for transdermal delivery
- Polycarbonate Case for biomedical and pharmaceutical products
- Polychloroprene Septum for injection, plungers for syringes, and valve components
- 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
- Polystyrene Petri dishes and containers for cell culture
- Polypropylene tight packaging, heat shrinkable films, containers
- Poly (vinyl chloride) Blood bag, hoses, 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
- Acrylic acid and butyl acrylate copolymer
- Vinyl acetate and methyl acrylate copolymer
- High cohesive strength pressure sensitive adhesive for transdermal patches
- Ethylene vinyl acetate and polyethylene terephthalate

When the drug is delivered to the site of action by using polymer based drug delivery approaches the safety and bio compatibility is questionable. The characterization of biocompatible polymers is more focused in the field of formulation development and drug delivery approaches etc. the biodegradable polymers have properties of degrading in biological fluids with progressive release of dissolved or dispersed drug. There is various novel drug delivery approaches are developed in the pipeline of polymer based drug delivery approaches. The bio-safety and biocompatibility are the important characteristics needed for the use of polymers in the field of pharmaceutical formulation and in novel drug delivery approaches.

APPLICATIONS[5-13]:

Synthetic biodegradable polymers are mainly using in the biomedical area particularly in the fields of tissue engineering and controlled drug delivery. Degradation is important factor for biomedicine.

Degradation of the polymeric implant means surgical intervention may not required for removal at the end of its functional life, eliminating the need for a second surgery.

In tissue engineering, biodegradable polymers can be designed such to approximate tissues, providing a polymer scaffold that can withstand mechanical stresses, provide a suitable surface for cell attachment and growth, and degrade at a rate that allows the load to be transferred to the new tissue. In the field of controlled drug delivery, biodegradable polymers offer tremendous potential either as a drug delivery system alone or in conjunction to functioning as a medical device.

Drug products designed to reduce the frequency of dosing by modifying the rate of drug absorption have been available for many years. Regular research is going on in field of use of natural occurring biocompatible polymeric material in designing of dosage form for oral controlled release administration. Natural gums are biodegradable and nontoxic, which hydrate and swell on contact with aqueous media, and these have been used for the preparation of dosage form. Guar gum a polysaccharide derivative with glycoside linkage has been used as matrix former for controlled release of isoniazide and diltiazem. It shows synergistic effect with xanthan and kappa Carrageenan. Gellan gum has been used in pharmaceutical dosage forms as a swelling agent, as a tablet binder, and as a rheology modifier. In situ gel-forming ability of xyloglucan and borax–guar gum complexes for colon specific drug delivery have also been studied. One of the most recent applications of gums is in film forming. Recent concepts and products such as breath films, cough strips, flu, and sore throat strips have all been realized on the basis of film-forming ability of gums.

Xanthan gum is found in a number of drug formulations including cefdinir oral suspension and nitazoxanide tablets. It is a highly branched glucomannan polysaccharide with excellent stability under acidic conditions. Xanthan is generally used in solution and suspension products for its thickening property. Because of its very rigid structure, its aqueous solution is significantly stable over a wide pH range. Concentrated xanthan gum solutions resist flow due to excessive hydrogen bonding in the helix structure, but they display shear-thinning rheology under the influence of shear flow. This feature of xanthan gum solutions is critical in food, pharmaceutical, and cosmetic manufacturing processes. Xanthan gum is found in a number of drug formulations including cefdinir oral suspension and nitazoxanide tablets. It is a highly branched glucomannan polysaccharide with excellent stability under acidic conditions. Oxymorphone hydrochloride extended-release tablets contain TIMERx, which consists of xanthan gum, and locust bean gum for controlled delivery. Rectal delivery of morphine can be controlled using cyclodextrins as an absorption enhancer and xanthan as a swelling hydrogel. This combination produces a sustained plasma level of morphine and increases its rectal bioavailability. For instance, chitosan is only

soluble in acidic water, but its Carboxymethyl derivative is soluble at a wider pH range. Besides, gums are a good platform for bacteria growth, which limits their shelf life and requires sterilization[9-11].

Polysaccharides and their derivatives can be used as a rate controller in sustained release formulations due to their gelling property. They are biodegradable and their chemical composition varies greatly. The physicochemical properties of polysaccharide solutions and gels have recently been reviewed for pharmaceutical and food applications. Polysaccharides are claimed to effectively treat local colon disorders if they are used in colontargeting delivery systems, which utilize the colonic microflora. Inulin, amylase, guar gum, and pectin are specifically degraded by the colonic microflora and used as polymer drug conjugates and coating. It has been shown that drug release in the colon can be maximized if the hydrophobicity of the gums is modified chemically or physically using other conventional hydrophobic polymers. In cancer therapy, polysaccharides are used as immunemodulators. A few polysaccharides, either alone or in combination with chemotherapy and/or radiotherapy, have been used clinically in the treatment of various cancers. It was suggested that iron stabilized into a polysaccharide structure can be used to treat anemia. The product can also be used in resonance imaging as well as in separation of cells and proteins utilizing magnetic fields due to its magnetic properties[11-15].

Alginic acid and its salts are anionic polymers that can offer gelling properties. Alginic acid and its derivatives have found applications as a stabilizing agent, binding agent, drug carrier, and so on and so forth. The antibiotic griseofulvin, which is supplied as oral suspension, contains sodium alginate stabilized with methylparaben. Alginic acid and ammonium calcium alginate can be found in metaxalone tablets. Alginate microbeads can be used to entrap drugs, macromolecules, and biological cells.

Carrageenan is a sulfated linear polysaccharide of galactose and anhydrogalactose. It carries a half-ester sulfate group with the ability to react with proteins. If carrageenan is used in a solution containing proteins, the solution becomes gel or viscous due to a complex formation between carrageenan and charged amino acids of the protein. Depending on the concentration and location of the sulfated ester groups, carrageenan can be found in three different grades of kappa, iota, and lambda. Kappa carrageenan can form a strong and brittle gel, especially in the presence of potassium ions or if blended with locust bean gum. Both kappa and iota carrageenan can be used for controlled delivery application as they display gelling properties under certain circumstances. If a drug formulation needs to be thickened and does not contain proteins of any

source, a lambda carrageenan can be utilized. Donepezil hydrochloride orally disintegrating tablets and cefpodoxime proxetil oral suspension contain carrageenan. Carrageenan is shown to increase the permeation of sodium fluorescein through porcine skin as it changes the rheological properties of the drug solution. In capillary electrophoresis, a sulfated polysaccharide such as carrageenan can be used to separate the enantiomers of weakly basic pharmaceutical compounds. Different enantiomers of racemic compounds such as propranolol and pindolol have been separated using carrageenan[15-17].

Chitosan is obtained from chitin, the second most abundant natural polymer after cellulose, which can be found in shrimp, crab, and lobster shells. Chitosan is a cationic polymer and has been investigated as an excipient in controlled delivery formulations and mucoadhesive dosage forms because of its gelling and adhesive properties. The bitter taste of natural extracts such as caffeine has been masked using chitosan. Chitosan can potentially be used as a drug carrier, a tablet excipient, delivery platform for parenteral formulations, disintegrant, and tablet coating. From toxicity and safety standpoint, lower molecular weight chitosan (as an oligosaccharide) has been shown to be safer with negligible cytotoxicity. During the encapsulation process using synthetic polymers, the protein is generally exposed to the conditions which might cause their denaturation or deactivation. Because of its cationic nature, chitosan can make complexes with negatively charged polymers such as hyaluronic acid (HA) to make a highly viscoelastic polyelectrolyte complex[17-19].

Gels based on chitosan and ovalbumin protein have been suggested for pharmaceutical and cosmetic use. In veterinary area, chitosan can be used in the delivery of chemotherapeutics such as antibiotics, antiparasitics, anesthetics, painkillers, and growth promotants. As an absorption enhancer, a protonated chitosan is able to increase paracellular permeability of peptide drugs across mucosal epithelia. Chitosan can also be mixed with nonionic surfactants such as sorbitan esters to make emulsion like solutions or creams. A sustained release dosage form of salbutamol sulfate bead can be prepared using chitosan in phosphate buffer. While pectin is generally known as a suspending and thickening agent, it is also claimed to reduce blood cholesterol levels and to treat gastrointestinal disorders[19].

Pectin can be found in amlexanox oral paste HA consists of *N*acetyl-d-glucosamine and betaglucoronic acid and has been used as fluid supplement in arthritis, in eye surgery, and to facilitate healing of surgical wounds. Hyaluronan is biocompatible and nonimmunogenic and has been suggested as a drug carrier for ophthalmic, nasal, pulmonary, parenteral, and dermal routes. Pectin is a ripening product of green fruits such as lemon and orange skin. Pectins, including

high and low ester and amidated, are used in food all over the world. It is an edible plant polysaccharide, has been shown to be useful for the construction of drug delivery systems for specific drug delivery[20].

Extended release alprazolam tablet is an example of monolithic products, in which extended or sustained delivery is provided by swelling and erosion of the polymer matrix. Alternatively, a drug can be released from a drug core through a porous or nonporous membrane. While drug release through a nonporous membrane is essentially driven by diffusion, porous membrane generates an extra path for the drug release, that is, through pores. The status of drug release from membrane systems can generally be modified via membrane thickness, use of plasticizers, pore structure (size, size distribution, and morphology), and filler tortuosity (filler orientation). Membrane systems have found applications in drug stability, enteric release, taste masking, and sustained release. Enteric coated products are the ones that pass the stomach environment safely and release the drug at a higher pH environment of the intestine. These have to be coated with a pH operative coating such as an anionic polymer. Examples of enteric-coated products are duloxetine, mesalazine, naproxen, omeprazole, and amino salicylic acid. Drugs such as lutein and lycopene are more stable in membrane dosage forms. Reservoir systems have been utilized to taste mask acetaminophen and caffeine. Potassium chloride and diltiazem are also offered sustained release property if formulated in a membrane system. Many commercial oral and topical products available today have been formulated with Carbopol and Noveon polymers, as they have numerous features that provide key benefits in bioadhesive formulations[21].

POLYMER DEGRADATION[25-29]:

All the applications of biodegradable polymers benefit from the fact that the polymer "disappears" after serving its function. Two major processes are involved the degradation of bonds between monomers in the polymer chains and the erosion of bulk polymer. There are different types of polymer degradation: photo- thermal-mechanical and chemical degradation. All polymers share the property that they degrade markedly under the influence of UV light or gamma-radiation. Thermal degradation also has a great influence on non-degradable polymers. Mechanical degradation affects those biodegradable polymers that are subjected to mechanical stress, such as non-degradable polymers or biodegradable polymers used as fixture or suture material. All biodegradable polymers contain hydrolysable or oxydable bonds. This makes the material sensitive to moisture and heat. Thus the characteristics of biodegradable polymers (especially mechanical and rheological properties) are extremely sensitive to stocking, processing and use conditions.

Polymer degradation is a change in the properties tensile strength, colour, shape of a polymer or polymer based product under the influence of one or more environmental factors such as heat, light or chemicals. Deteriorative reactions occur during processing, when polymers are subjected to heat, oxygen and mechanical stress, and during the useful life of the materials when oxygen and sunlight are the most important degradative agencies. In more specialized applications, degradation may be induced by high energy radiation, ozone, atmospheric pollutants, mechanical stress, biological action, hydrolysis and many other influences. The mechanisms of these reactions and stabilization processes must be understood if the technology and application of polymers are to continue to advance. The study of all these processes has made extensive use of modern instrumental analytical methods and the various Spectrometric, chromatographic and thermal analysis techniques have been particularly prominent. Various routes for degradation of polymers and factors affecting polymer degradability (biodegradation) is shown in figure 4.

Table 1: Various routes for degradation of polymers

High molecular weight polymers • Biodegradation • Solubility • Thermodegradation • Photolysis • Hydrolysis
Low molecular weight polymers • Structure weakening • Brittleness • High surface area

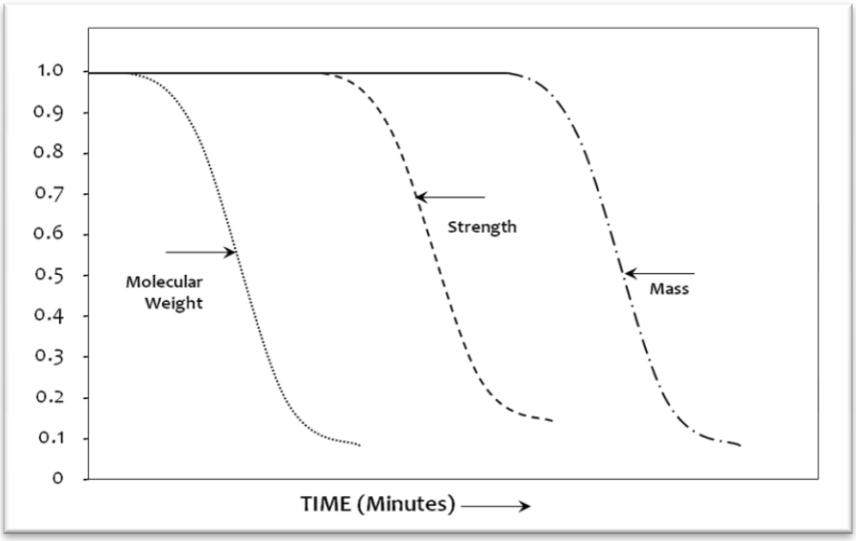

Figure 4: Factors affecting biodegradation of polymers

Some other factors which affect biodegradation of polymers are given in tables 1 and 2 Biodegradable polymers are a fairly broad region of investigation. At present the application of

the various types of biodegradable polymers in therapy, surgery, and pharmacology is considered. In practice resorbable polymers are used, as biocompatible materials as a rule, in the healing period of wounds or in the growth of injured tissues and organs and temporarily fulfill the function of the latter. A resorbable polymer may also play the role of a drug depot providing a more or less long-term supply of drug to the blood at a constant rate towards drug delivery application which enables the new advancement in the formulating new drug delivery systems which improves the therapy and treatment[31].

Table 2: Other factors affecting biodegradation of polymers

Factors affecting biodegradation of polymers		
Chemical structure. • Chemical composition. • Distribution of repeat units in multimers. • Presents of ionic groups. • Presence of unexpected units or chain defects. Configuration structure. • Molecular weight. • Molecular-weight distribution. • Annealing.	**Morphology** (amorphous/semi-crystalline, microstructures, residual stresses). • Presence of low-molecular-weight compounds. • Processing conditions. • Sterilization process. • Storage history. • Shape. • Site of implantation. • Adsorbed and absorbed compounds (water, Lipids)	**Physicochemical factors** (ion Exchange, ionic strength, and pH). • Physical factors (shape and size changes, variations of diffusion coefficients, mechanical stresses, cracking, etc.) • Mechanism of hydrolysis (enzymes versus water).

FUTURE DIRECTIONS IN POLYMER DRUG DELIVERY[33, 34]:

The most exciting opportunities in polymer drug delivery lie in the arena of responsive delivery systems, with which it will be possible to deliver drugs through implantable devices 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:

- Copolymers with desirable hydrophilic/hydrophobic interactions.
- Block or graft copolymers.
- Complexation networks responding via hydrogen or ionic bonding.
- Dendrimers or star polymers as nanoparticles for immobilization of enzymes, drugs, peptides, or other biological agents.
- New biodegradable polymers.
- New blends of hydrocolloids and carbohydrate-based polymers.

These new biomaterials tailor made copolymers with desirable functional groups are being created by researchers who envision their use not only for innovative drug delivery systems but also as potential linings for artificial organs, as substrates for cell growth or chemical reactors, as agents in drug targeting and immunology testing, as biomedical adhesives and bioseparation membranes, and as substances able to mimic biological systems. Successfully developing these novel formulations will obviously require assimilation of a great deal of emerging information about the chemical nature and physical structure of these new materials.

CONCLUSION:

Polymers have achieved a widespread use in drug delivery over the past few decades. Polymers are advantageous in the fact that they show usually an improved pharmacokinetic profile as compared to small molecule drugs with longer circulation time and they also have the potential for tissue targeting. Synthesis of novel block and copolymers and experimental design of novel combinations of polymers will henceforth expand the scope of new drug-delivery systems and achieve targeted bioavailability and controlled release profiles.

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