International Journal of Pharmaceutical Research and Development (IJPRD)
Platform for Pharmaceutical Researches & Ideas
www.ijprd.com

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# POLYMERS: THE PRIME SPINE FOR DRUG DELIVERY SYSTEMS

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***ABSTRACT***
*Drug dosage form contains many components in addition to the active pharmaceutical ingredient to assist in the manufacturing process as well as to optimize drug delivery. The amalgamation of polymers and pharmaceuticals led to the introduction of polymers in the design and development of drug delivery system. Polymers have been used as the main tool to control the drug release rate from the formulation. Extensive application of polymers in drug delivery has been realized because polymers offer unique properties which so far have not been attained by any other material. In the common sense, polymers are 'plastics', which are used as everyday materials and are produced in huge amounts. However, with the development of biomaterials in the 1980s, specialized polymers have become increasingly used in medicines as components of medical devices. More recently, with the development of nano biotechnology, more sophisticated polymers have been developed, for instance as constituents of nano particulate systems for vaccine and drug delivery.*

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***KEYWORDS :*** *Polymer, Controlled release, Excipients, Transdermal.*

## INTRODUCTION

Synthetic and natural-based polymers have found their way into the pharmaceutical and biomedical industries and their applications are growing at a fast pace. Understanding the role of polymers as ingredients in drug products is important for a pharmacist or pharmaceutical scientist who deals with drug products on a routine basis. Having a basic understanding of polymers will give you the opportunity of not to only familiarize yourself with the function of drug products but also possibly develop new formulations or better delivery systems. This chapter will provide with the basis for understanding pharmaceutical polymers, their basic concepts, chemistry, properties, types of polymers and use of polymers in pharmaceutical and biomedical industries.

### Polymers in Pharmaceutical Products

Of the many materials used in the pharmaceutical formulations, polymers play the indispensable role.

Their applications range widely from material packaging to fabrication of the most sophisticated drug delivery devices. The important application of polymers undoubtedly resides in the development of sophisticated controlled release drug delivery systems. In conventional dosage forms, polymers are usually used as excipients, adjuvant, suspending agents, or emulsifying agents whereas in controlled release dosage forms, polymers are used mainly to control the release rate of drugs from the dosage forms. The presence of numerous polymers which are able to control the drug release profiles has been the basis for the explosive advances in the development of controlled release dosage forms during 80's. It would not be an overstatement that the future development of more sophisticated dosage forms will entirely depends on the appropriate use of existing polymers and synthesis of new polymers. One way of classifying polymers in pharmaceutical applications is to divide them into three general categories according to their common uses: (1) polymers in conventional dosage forms; (2) polymers in controlled release dosage forms; and (3) polymers for packaging.

**Classification of Polymers[2,3]**

**A. On the Basis of Interaction with Water**

a. Non Bio-Degradable Hydrophobic Polymer
Example: Polyvinyl Chloride, Polyethylene Vinyl acetate

b. Soluble Polymers
Example: HPMC.PEG

c. Hydrogels
Example: Poly Vinyl Pyrrolidine

**B. Based on Polymerization Method**

a. Addition Polymer
Example: Alkane Polymer

b. Condensation Polymer
Example: Polystyrene and polyamide

**C. Based On Polymerization Mechanism**

a. Chain Polymerization
Example: Polyesters, polyamides, polyurethanes,

b. Step Growth Polymerization
Example: Polyethylene (specifically, low density polyethylene, LDPE), polystyrene, polyvinylchloride, and polyacrylates and methacrylates,

**D. Based on Chemical Structure**

a. Activated C-C Polymer
b. Polyamides, polyurethanes
c. Polyesters, Polycarbonates
d. Polyacetals
e. Inorganic polymer
f. Natural Polymers

**E. Based On Occurrence**

a. Natural Polymers
- Protein –Collagen, Keratin
- Carbohydrates-Starch, cellulose

b. Synthetic Polymers
- Polyesters, polyamides

**F. Based On Bio-stability**

**1. Bio-Degradable Polymer**

i. Polyester
Example: PLA, PGA, PHB

ii. Poly anhydrides
Example: PCL, PMA, Polydioxanones

iii. Phosphorous Based
Example: Polyphosphazenes, Polyphosphonate

iv. Polyamide
Example: Polysebacic acid, PTA

**2. Non-Biodegradeable**

i. Cellulose Derivative
Example: CMC, EC, CA, CAP

ii. Silicones
Example: PDS, Colloidal silica

iii. Acrylic Polymers
Example: PVP, EVA, Poloxamer

**Note:** Synthetic biodegradable polymers are preferred more than the natural biodegradable polymer because they are free of immunogenicity & their physicochemical properties are more predictable & reproducible

**SELECTION CRITERIA FOR POLYMERS[4]**

- Physicochemical properties
- Need for biochemical characterization
- Chemical composition
- Micro structural Design
- Surface Properties like lubricity, hydrophilicity, surface energy etc.

**Properties of Polymers for application in DDS[5]**

- 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*

**Advantages of Biodegradeable Polymers In Drug Delivery**

1. Localized delivery of drug
2. Sustained delivery of drug
3. Stabilization of drug
4. Decrease in dosing frequency
5. Reduce side effects
6. Improved patient compliance
7. Controllable degradation rate

**Role of Polymers in Various Drug Delivery Systems:**

**Polymers in Conventional Dosage Forms[6]**

Despite the well known advantages of controlled release dosage forms, conventional dosage forms are still most widely used probably because of their low cost. More than three quarters of all drug formulations are made for oral administration because of their increasing popularity due to their ease of administration, self medication and patient compliance.

**Role of polymers in tablet Excipients[7]**

One of the major parameter during tabletting process is to produce tablets which are uniform in weight and strong enough to withstand the rigors of packaging and processing in order to provide disintegration and dissolution of the tablets upon administration for the release of the drug. Tablets with such desirable pharmaceutical properties can be prepared by using various types of polymeric excipients. It is the excipient that determines the compressibility, hardness, hygroscopicity, friability, lubricity, stability, and dissolution rate of the prepared tablets. The commonly used polymeric excipients can be divided into following four categories, such as

- Binder
- Diluents
- Disintegrant
- Lubricant.

*Table I* Lists some of the examples of polymers used in each category. In many cases where drug powders alone have poor compressibility, binding agents need to be incorporated into the formulation to form suitable hard tablets.

**Table I: *Some excipients have multiple uses*[8]**

| Function | Name of Exciepient |
|---|---|
| **Binder** | Alginic acid, Poly(acrylic acid) Carbopol, Carboxymethyl cellulose, Sodium Cellulose, Microcrystalline cellulose, Microcrystalline (Avicel), Dextrin, Ethyl cellulose, Gelatin, Guar gum, Hydroxypropl methylcellulose, Karaya gum, Methylcellulose, Polyvinylpyrrolidone (Povidone), Starch, Tragacanth gum. |
| **Diulent** | Cellulose, Microcrystalline (Avicel), Cellulose, Dextrin, Starch, Starch, pregelatinized |
| **Disintegrant** | Alginic acid (1-5%), Cellulose (1-3%), microcrystalline (Avicel) (10-20%), Gelatin, Povidone(0.5-5%), cross linked, Sodium starch glycolate (1-3%), Starch(5-20%), Starch pregelatinized(5-15%),soy polysaccharide(5-15%), Gums (3-8%), Chitin and chitosan (1-5%), Smecta (5-15%), Isapghula Husk (5-15%),Ion Exchange resin(0.5-5%), Gas Evolving (>10%),Tragacanth |
| **Lubricant** | Poly(ethylene glycol), Magnesium stearate |
| **Glidant** | Colloidal silicon dioxide (Aerosil 200 pharma) |
| **Stabilizer, Thickener, Emulsifier** | Xanthum Gum, Acacia, Agar |
| **Suspending agent, Binder** | Acacia, Carrangenan |

**Tablet Coating**

Coating of tablets is required to mask or minimize the unpleasant taste or odor of certain drugs, to protect the drug against decomposition thereby resulting in enhancing the tablet appearance. Traditionally coating of tablets was the time consuming step because of repeated application of syrup to obtain the required thickness and appearance, but this problem can be overcome by the polymer coating which is fast, simpler, and result in relatively thin layer, approximately 20 to 100 μπι, on the solid dosage forms[9], also gives better coated layer by sealing the pores and smoothing the rough texture of the core surface[10]. The stability of drugs can be greatly improved if the dosage units are coated with polymers which are hydrophobic enough to block the penetration of moisture.

The coating polymers can be divided into the two major groups:

- Enteric
- Non-enteric.

**Enteric coating polymers**

Poly acids which are water-insoluble at low pH environments, such as in the stomach, and dissolve in alkaline conditions such as those found in the intestine through ionization of the acid groups. They are used to protect acid-labile drugs which may be destroyed by the acidic gastric juice and to improve tolerability of drugs which irritate the stomach. Since the enteric coated tablets release drugs only in the intestine, the enteric coating polymers allow delayed release as well as targeted release in the intestine. The most widely used polymers for enteric coating are listed in Table II along with their pH values above which the polymer coating dissolves (dissolution pH).[11]

**Non-enteric polymers**

Polymers which are water-soluble regardless of pH of the environment. Of the synthetic polymers, polyvinyl pyrrolidone (PVP or Povidone), polyethylene glycol (PEG, Carbowax), and poly (ethylene oxide)-poly (propylene oxide) block copolymers (Pluronics and Poloxamers) are widely used as coating materials. One of the factors which determine the property of the coating is the molecular weight of the polymer. For example, high molecular weight PEG's give tough coating whereas low molecular weight PEG's are mainly used as plasticizers which prevent the film coat from becoming too brittle.[12] Plasticizers cause a decrease in both the modulus of elasticity and the glass transition temperature of the polymer.[13]

**Table II. Commonly Used Controlled Release Polymeric-Film Coating Materials[14,15]**

| Function | Name of Excipients |
|---|---|
| **A. Enteric Coating** | Cellulose acetate phthalate (CAP) pH 6.0<br>Cellulose acetate trimellitate (CAT) pH 5.2<br>Hydroxypropl methylcellulose phthalate (HPMCP) pH 4.5 - 5.5<br>Poly(methacrylic acid-co-methyl methacrylate) pH 5.5 - 7.0<br>Polyvinyl acetate phthalate) (PVAP) pH 5.0<br>Shellac (esters of aleurtic acid) pH 7.0 |
| **B. Non-Enteric Water-Soluble Coating** | Alginate sodium, Gelatin, Pluronica, Poloxamers, Polyethylene glycol) (PEG), Starch derivatives<br>Water-soluble cellulose derivatives<br>Carboxy-methylcellulose, sodium salt<br>Hydroxy ethyl-cellulose<br>Hydroxy propyl- cellulose<br>Hydroxy propyl methylcellulose<br>Methylcellulose |

**Polymers Used in Controlled Release Dosage Forms**

In modern pharmaceutics polymers has the important application such as the development of

new, advanced drug delivery systems, commonly known as controlled release drug delivery systems. The controlled release dosage forms are also important in the delivery of newly developed protein drugs. The mechanism of controlled drug delivery can be classified into the following five mechanisms: (1) diffusion (2) dissolution (3) osmosis (4) ion-exchange and (5) polymeric prodrug. In all cases, polymers function as a principal component which controls the transport of drug molecules and the way this process is utilized in the device determines the primary mechanism for each drug delivery system.

**DRUG RELEASE MECHANISM**

The release of drugs from the erodible polymers occurs basically by three mechanisms,

I. The drug is attached to the polymeric backbone by a labile bond; this bond has a higher reactivity toward hydrolysis than the polymer reactivity to break down.
II. The drug is in the core surrounded by a biodegradable rate controlling membrane. This is a reservoir type device that provides erodibility to eliminate surgical removal of the drug-depleted device.
III. A homogeneously dispersed drug in the biodegradable polymer. The drug is released by erosion, diffusion, or a combination of both.

**Table III: Literature sited regarding the Extended Release DDS**

| Drug | Polymer | Inference | Reference |
|---|---|---|---|
| Metformin HCL | HPMC K100M, Eudragit, PVP K30 | HPMC K100, Eudragit Desired release pattern | 16 |
| Cephalexin | HPMC, eudragit | Eudragit-Release for longer duration | 17 |
| Etodolac | HPMC K100, HPMC K4 | HPMC K100 Shows the better release | 18 |
| Propanlol | HPMC, HEC, Ethyl Cellulose | HPMC Shows the better release | 19 |
| Ranolazine | Hypromellose phthalate 55, HPC , HEC 250, Ethyl cellulose | HEC Shows the better release | 20 |
| Zolpidem | HPMC | Shows the better release | 21 |
| Niacin | Starch-Urea-Borate | Starch-Urea-Borate | 22 |
| Alfuzosin | HPMC, Eudragit RSPO | HPMC in sustaining drug release is more prominent than Eudragit polymer | 23 |

**Table IV: Literature Cited Regarding the Sustained Release Tablet**

| Drug | Polymer | Inference | Reference |
|---|---|---|---|
| Tramadol Hydrochloride | Carageenan Gum, Karaya Gum, HPMC K15 M | HPMC K15M & Karaya gum Retard the drug release | 24 |
| Nicorandil | HPMC, Ethyl cellulose | HPMC better drug release | 25 |
| Aceclofenac | HPMC K15, HPMC K100 | HPMC K100 Shows better sustained release | 26 |
| Tizanidine HCl | Xanthum gum, Guar gum, Glyceryl Behenate, Glyceryl monostearate, Stearic acid | Glyceryl Behenate showed the release profile similar to marketed formulation | 27 |
| Nifedipine HCl | Chitosan treated sodium | Showed sustained drug | 28 |

| | | | |
|---|---|---|---|
| | alginate | release | |
| Ranolazine | Eudragit, HPMC | HPMC showed better release | 29 |
| Domperidone | HPMC K100 LV, HPC K100 M, Ethocel | HPMC K100 LV exhibited maximum drug release | 30 |

**Diffusion-Controlled Systems**

In general, two types of diffusion-controlled systems have been used: reservoir and monolithic systems. In reservoir systems, the drug is encapsulated by a polymeric membrane through which the drug is released by diffusion. Polymer films used in the diffusion-controlled reservoir system are commonly known as solution-diffusion membranes (Table III). The polymer membrane can be either nonporous or micro porous. Drug release through nonporous membranes is governed mainly by the diffusion through the polymer. Thus, the drug release rate through the solution-diffusion membrane can be easily controlled by selecting a polymer showing desirable drug solubility and diffusivity in the polymer matrix. In case of micro porous membranes, which have pores ranging in size from 10 À (Angstrom) to several hundred mm, the pores are filled with a drug-permeable liquid or gel medium. Thus, the diffusion of the drug through the medium in the pores will dominate the drug release process. Micro porous membranes are useful in the delivery of high molecular weight drugs such as peptide and protein drugs.[31]

**Dissolution-Controlled Systems**

Polymers used in the design of dissolution controlled dosage forms are usually water-soluble, but water-insoluble polymers can also be used as long as they absorb significant amount of water and disintegrate the dosage. The dissolution-controlled systems also have both reservoir and matrix dissolution systems. In reservoir systems, the drug core particles are coated with water-soluble polymeric membranes. Polymer films used in the dissolution-controlled reservoir system are commonly known as solution-diffusion membranes. The solubility of the polymeric membrane, and thus the drug release, depends on the thickness of the membrane and the type of the polymer used. Drug release can be achieved in more controlled fashion by preparing air system with alternating layers of drug and polymeric coats or by preparing a mixture of particles which have different coating characteristics. Matrix dissolution devices are generally prepared by compressing powder mix of drug and a water-soluble or water-swellable polymer. They can also be made by casting and drying of a polymer solution containing a suitable amount of dissolved or dispersed drug. A variety of other excipients may optionally be included to aid formulation properties. In an early stage of the dissolution process, the polymer starts swelling as a result of water penetration. During swelling, outer portion of polymer matrix forms a mucilaginous barrier which retards further ingress of water and acts as a rate controlling layer to drug release. Addition to the dissolution kinetics of the polymer matrix diffusion of the drug through this barrier also contributes to the drug release rate. Various polymers used in the dissolution-controlled drug release systems are listed in Table IV. The most widely used polymers are cellulose ethers, especially, hydroxyl-propyl methylcellulose (HPMC).[32] Devices with coarser particles of HPMC result in fast drug release, since they minimize the gelling effect by swelling in water without losing the integrity of the cellulose fibers. On the other hand, finer particles of HPMC hydrate and form gel on the surface fast and this inhibits rapid penetration of water into the dosage form. Thus, the drug release is close to that of the diffusion-controlled devices.[33, 34]

**Osmotic Delivery Systems**

The osmotic device comprises of a core reservoir of drugs, with or without osmotically active salt, coated with a semi-permeable polymer membrane. The presence of salt or drug molecules creates an osmotic pressure gradient across the membrane and the diffusion of water into the device gradually forces the drug molecules out through an orifice made in the device. The mechanical strength of the semi-permeable membrane should be strong

enough to resist the stress building inside the device during the operational life time of the device. The drug release rate from the osmotic devices, which is directly related to the rate of external water diffusion, can be controlled by the type, thickness, and area of the semi-permeable polymer membrane. Substituted cellulosic polymers, such as cellulose acetate derivatives, have been most commonly used as a semi permeable membrane

**Ion-Exchange Systems**

The ion-exchange systems are useful in the controlled release of ionic or ionizable drugs. Poly electrolytes are cross linked to form water insoluble ion-exchange resins. The drug is bound to the ionic groups by salt formation during absorption and released after being replaced by appropriately charged ions in the surrounding media. Cationic drugs form complexes with anionic charges in ion-exchange resin such as sulfonic and carboxylic groups of poly (styrene sulfonic acid) and poly (acrylic acid), respectively. Hydrogen ions and/or other cations such as sodium or potassium ions activate the release of cationic drugs by replacing them from the drug-resin complex. For the delivery of anionic drugs, one can utilize cationic ion-exchange resins which contain basic groups such as amino or quaternary ammonium groups of poly (di-methyl aminoethyl methacrylate).[35] Sometimes the ion-exchange resins are additionally coated with a polymer film, such as acrylic acid and methacrylate copolymer or ethyl cellulose to regulate the swelling of the resin and to further control the drug release.[36] Example: the Pennkinetic system delivers dextromethorphan from the ethyl cellulose-coated poly (styrene sulfonate) resins by this mechanism.

**Table V: Excipients used in Diffusion-Controlled Drug Release**

| Function | Name of Exciepient |
|---|---|
| **Diffusion-Controlled Drug Release** | Cellulose<br>Chitin<br>Collagen<br>Nylon<br>Poly(alkylcyanoacrylate)<br>Polyethylene<br>Poly(ethylene-co-vinyl acetate)<br>Poly(hydroxyethyl methacrylate)<br>Poly(hydroxypropylethyl methacrylate)<br>Poly(methyl methacrylate)<br>Polyvinyl alcohol-co-methacrylate)<br>Polyvinyl chloride)<br>Polyisobutene<br>Polyurethane<br>Silicone rubber |

**Table VI: Excipients used in Dissolution -Controlled Drug Release**

| Function | Name of Exciepient |
|---|---|

| | |
|---|---|
| **Dissolution -Controlled Drug Release** | Cellulose<br>Chitin<br>Collagen<br>Nylon<br>Poly (alkylcyanoacrylate)<br>Polyethylene<br>Poly(ethylene-co-vinyl acetate)<br>Poly(hydroxyethyl methacrylate)<br>Poly(hydroxypropylethyl methacrylate)<br>Poly(methyl methacrylate)<br>Polyvinyl alcohol-co-methacrylate)<br>Polyvinyl chloride)<br>Polyisobutene<br>Polyurethane<br>Silicone rubber |

**Polymeric Prodrugs**

Many water-soluble polymers possess functional groups to which drug molecules can be covalently attached. Polymer backbone, which itself has no therapeutic effect, serves as a carrier for the drug. The drug molecules are gradually released from the polymer by hydrolytic or enzymatic cleavage. If the cleavage occurs by chemical hydrolysis, the drug release depends on the nature of the covalent bonds and pH of the environment. In the body, this occurs very slowly. If the drug molecules are released by enzymatic hydrolysis, the release is mainly dependent on the concentration of enzymes. Thus, the exact release profile depends on the in vivo condition not on the delivery system itself. To be a useful drug carrier, a polymer needs to possess certain features.[37] The polymer should remain water-soluble even after drug loading. The molecular weight of the polymer should be large enough to permit glomerular filtration but small enough to reach all cell types. The drug-carrier linkages should be stable in body fluid and yet degradable once captured by the target cells. This can be achieved by making the linkage degradable by lysosomal enzymes.[37] It is preferred that the polymer itself can be degradable by lysosomal enzymes to be eliminated from the body after releasing drugs. The polymeric carrier, of course, has to be non-toxic, non-immunogenic, and biocompatible e.g. Poly (Hydroxypropl methacrylamide)[38], PVP, starch derivatives [39], dextran[40], and poly (amino acids)[41] have been used as polymeric drug carriers.

**Polymers for Drug Packaging**

Many polymers are used as packaging materials for pharmaceutical products. Plastic packaging materials has three major properties such as flexibility, transparency, and gas permeability which are easily controllable. Flexible packages are made from thin and flexible polymer films. When they are wrapped around a product, they can easily adapt their shape to conform to the shape of the contents. The thin, flexible films are usually produced from cellulose derivatives, polyethylene, polypropylene, PVC, polystyrene, polyamide (nylon), polyesters, polycarbonate, poly (vinylidene chloride), and polyurethanes. These polymeric materials are generally heat sealable and are also capable of being laminated to other materials[42]. A tight package can be prepared by wrapping an article with these polymer films followed by a brief heat treatment. Rigid packages, such as bottles, boxes, trays, cups, vials, and various closures, are made from materials of sufficient strength and rigidity. Widely used polymers are high-density polyethylene, polypropylene, polybutene, poly(vinyl chloride), acrylic copolymers, polycarbonate, nylon, and polyethylene

terephthalate (PET)[43]. Although the primary polymer component of the end products are the same, their physical, chemical, and mechanical properties of the products can be varied greatly depending on the molecular weight, crystallinity, and alignment of the polymer chains of the polymer component. One of the important requirements of any packaging material is that it should not release any component into the drug product. Preparation of containers free of any leachables such as monomelic component is especially important for the containers of ophthalmics, parenteral products, and any liquid products.[44] Among those, chemical test is designed to give a quantitative assessment of the extractable materials in both organic solvents and water.[45] Caution should be exercised in the use of polymeric containers and other devices for the delivery of protein drugs, since proteins readily adsorb and sometimes denature on the hydrophobic polymer surface[46.]

**Table VII: Composition of colon Targeted DDS reported in Literature:**

| Sr.no | Drug used | Polymer used | Inference |
|---|---|---|---|
| 1. | 5-fluorouracil | Carrageenan | Release of 5-FU was much higher in SIF compared to SGF, indicating that the release system is controllable and can be as a release system for intestine specific drug. |
| 2. | Cyclophosphamide (Microsphere) | Eudragit S-100 | Polymer drug ratio influences the particle size, as well as drug release pattern of microspheres. The % yield and encapsulation was best for drug: polymer ratio 1:3 used polymer Eudragit S 100 is suitable polymer for Colon targeting. |
| 3. | Sodium diclofenac | Chitosan | Enteric-coated chitosan microspheres |
| 4. | Insulin | Chitosan | Enteric-coated chitosan capsules |
| 5. | Indomethacin | Pectin | Matrices |
| 6. | Paracetamol | Amidated pectin | Matrix tablets |
| 7. | Dexamethasone | Guar gum | Matrix tablets |
| 8. | Bovine serum albumin (BSA) | pH-sensitive dextran | As hydrogels |
| 9. | Radioactive tracer | Starch | Enteric-coated capsules |
| 10. | 5-ASA | Alginates As calcium salt | Double coated swellable beads |
| 11 | Theophylline | Dextran fatty acid esters (Degree of substitution 20.12–0.40) | As films |

**Table VIII: Composition of TDDS reported in Literature**:

| Sr.no | Polymer | Drug | Inference | Reference |
|---|---|---|---|---|
| 1. | HPMC | Lornoxicam | Release rate of drug | 47 |

| | | | | |
|---|---|---|---|---|
| | | | through patches increased when the concentration of hydrophilic polymer was increased. | |
| 2. | Isosorbide dinitrite | Ethyl cellulose-50 | Matrix system | 48 |
| 3. | HPMC | Hydrocortisone | Gel | 49 |
| 4. | Eudragit NE, Eudragit E100,45 Eudragit L100 | Coumarin | Matrix | 50 |
| 5. | MDX-4-421 (a silicone) | L-Timolol maleate | Matrix | 51 |
| 6. | Carboxy vinyl polymer | L-Dopa | Gel | 52 |
| 7. | Acrylic PSA emulsion ,CoTran9722 | Nicotine Drug in adhe | Drug in adhesive | 53 |
| 8. | Soybean lecithin (Epikuron 200) | Scopolamine, broxaterol | Gel matrices | 54 |
| 9. | Cariflex TR-1107 | Dihydro etorphine | Drug in adhesive | 55 |
| 10. | Acrylic adhesives Polyisobutylene solutions (Vistanex LM-MH, Vistanex MML-100) | Ketoprofen | Drug in adhesive | 56 |
| 11. | Silicone oil EVA Polyisobutylene ScotchPak 1006 | Arecoline | Reservoir Membrane Adhesive Backing film | 57 |
| 12. | 2-Ethylhexyl acrylate – and acrylic acid copolymer | PGE | Drug-in-adhesive | 58 |
| 13. | HEMA, Styrene and *N*-vinyl pyrrolidone copolymer for membrane | Cytarabine, ara-ADA | Carbopol 934 gel, reservoir | 59 |
| 14. | HPMC (Methocel K4M) Urecryl MC 808 PIB | Propranol | Matrix | 60 |
| 15. | MDX4-4210 silicone elastomer | Nitroglycerine | Matrix | 61 |
| 16. | Acrylate copolymer (Gelva-737) Silicone-2920and2675 Polyisobutylene solutions.(Vistanex LM-MS,Vistanex MML-100) | Fentanyl | Matrix | 62 |
| 17. | Plastoid E25L | Miconazole | Matrix | 63 |
| 18. | Polyvinyl alcohol (backing) HPMC (matrix) Ethylene vinyl acetate (rate-controlling membrane) | Propranolol | Membrane-controlled reservoir system | 64 |

**Safety and Recognition of New Polymers as Excipients**

Pharmaceutical excipients have a vital role in drug formulations. However, the development of new

excipients is often neglected because of a lack of mechanisms to assess the safety of excipients outside a new drug application process. Existing regulations and guidelines state that new excipients should be treated as new chemical entities with full toxicological evaluation. Therefore, successful development of new polymeric excipients depends on obtaining appropriate toxicological data on the safety and biocompatibility of such excipients. There exist specific relevant guidelines for specific delivery systems, such as implant applications, which have been developed by the United States Pharmacopoeia (USP) for testing of the polymer safety and Sample pages from Biomedical and Pharmaceutical. One example of such a test is the USP Biological Reactivity Test, in vivo, which includes the systemic injection test, the intracutaneous test and the implantation test. Such guidelines may be of relevance when developing polymer excipients for parenteral controlled-release applications. Other guidelines from the European Medicines Evaluation Agency (EMEA) and the FDA describe the type of data package required in the preclinical development of new excipients.

**CONCLUSION**

Polymeric substances are in contact with drugs not only as ingredients in final dosage forms but also as processing aids or packaging materials. In conventional dosage forms, the majority of polymers used as excipients are natural polymers and many are included in the GRAS list as a result of a long history of pharmaceutical marketing. In pharmaceutical packaging, polyethylene, polypropylene, and poly (vinyl chloride) have been used most widely. There is a trend, however, to replace them with more environment-friendly, biodegradable polymers. Of the numerous roles played by polymers in the production of pharmaceutical products, emphasis often has been placed on the use of polymers in the fabrication of controlled release drug delivery systems. The progress in the area of controlled drug delivery has been possible only as a result of incorporation of polymer science into pharmaceutics. Development of sophisticated pharmaceutical products requires the multidisciplinary efforts. Polymers with special or multiple properties are need to be developed to achieve self-regulated drug delivery, long-term delivery of protein drugs, and drug targeting to specific organs in the body. These cannot be achieved by elaborate device design alone. These require development of smart polymeric systems which recognize and respond to physiological and pathological processes in the body. Polymers will remain as the indispensable component in the development of new pharmaceutical products.

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