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# Applications of Polymer in Dosage Form Development

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**ABSTRACT**

Polymers have played important role in the pharmaceutical industry. The polymers are widely applicable for the formulation of the most sophisticated drug delivery systems. In the past two decades, in the pharmaceutical and biomedical field, the progress of polymeric material is considerably increased due to their biocompatibility, versatility, biodegradability properties. In medical treatment, it is more efficient and minimizes the side effect and other types of inconveniences to patients. Polymers are also called a backbone of the pharmaceutical drug delivery system as they control the release rate of the drug. The present review focuses on the role of polymers in pharmaceutical drug delivery systems, the role of polymer in pharmaceuticals like use in tablets, capsules, gastroretentive drug delivery systems, transdermal drug delivery systems, etc. In oral delivery, polymers are used as coatings, taste maskers, protective, binders, and release controlling agents. The main focus on applications of polymer in controlled drug delivery systems. The polymer mainly acts as a carrier for delivering the DNA or RNA. The main role of polymer is to protect the drug from the physiological environment and improve the stability of the drug. The future trend in pharmaceuticals and the development of nanoparticles for cancer therapy.

## INTRODUCTION:

Polymers are compounds with high molecular masses formed by monomers. In Greek word 'poly' means 'many' and 'meros' means 'units'. Polymers are played important role in novel drug delivery systems by providing therapeutic agents. The applications of polymers are found in different biomedical fields such as drug-delivering systems, implantation of medical devices, artificial organ prosthesis, tissue engineering, bone repair, ophthalmology, and many other medical fields.[1]The main purpose of polymer is to control the drug release pattern from the dosage form. Tremendous progress has been made as a result exploration of diffusion-controlled and solvent-activated formulation in drug delivery.[2] Many polymers are from natural origin like minerals, animals (chitin), or vegetal (cellulose). Some of these have been used for centuries. Protein and nucleic acid are well known as a supporter of life. Extensive biodegradable polymers have been used in biomedical applications because of their well-known biodegradability and biocompatibility. In biomedical, polymers are used for long-term treatment to make them more efficient and reduce the side effects, and for better patient compliance.

In the pharmaceutical field, polymers are playing various roles such as binders in tablet formulations, viscosity, and flow control agents in liquid formulations. Control the drug release rate of extended, pulsatile, and targeted drug delivery systems. The polymer can be used as a film coating to mask the unpleasant taste of the drug. In a sustained release drug delivery system, the rate of drug release from the matrix depends upon the initial drug concentration and relaxation of the polymer chain.

## HISTORY OF POLYMER:

The work in polymer science was started in 1811 by Henri braconnot. Macintosh used rubber gum to waterproof cotton in 1823. In 1833 John's Jabcob Berzelius described the term polymer, which described the relationship of ethylene to butane and higher homologue. A. payen identified a compound extracted from wood which he named "cellulose" in 1838. Bancklite was introduced in the market in 1909 by reacting phenol and formaldehyde at preciously controlled temperature and pressure.[3] Flory, mark, and others in the 1940s were responsible for the rapid expansion of polymers, including detailed studies of material of increasing commercial value. The first chemically synthesized cellulose was found by Kobayashi and Shodha in 1992. Then after the synthesis of cellulose, the structure is

determined by Hermann Staudinger in 1920. In 1925, confirmation of macromolecular theory by Th. Sveberg; succeeded in measuring the molar mass of polymer by ultracentrifugation.[4]

**CHARACTERISTICS OF IDEAL POLYMERS:**[5]

- It should be inert and compatible with the environment.
- It must have compatibility with most of the drugs.
- It should be easy to fabricate.
- It should be less in cost.
- It must tend to retain in tissue and must be a good biodegradable property.
- It should have good moldability.
- Low density and low coefficient of friction
- It should be versatile and possess a wide range of mechanical, physical, and chemical properties and poor tensile strength.
- It can be produced transparently or in different colors.

**Criteria followed in polymer selection**

- It should be soluble and easy to synthesis
- It should have a finite molecular weight
- It should provide good drug-polymer linkage

**CLASSIFICATION OF POLYMERS**[6,7]

1) Classification based on source:

a) Natural polymers- Protein, Cellulose, Starch.

b) Semi-synthetic polymers – cellulose derivatives, polyethylene, PGA, Polyacrylamide, Polypropylene

c) Synthetic polymer - Nylon, Teflon, Polysterylin

2) Classification based on structure:

a) Linear polymer - PVC, Polyester, Polytene

b) Chain polymer - polypropylene, Glycogen

c) Cross-linked polymer - Vulcanize rubber

3) Classification based on Nature:

a) Water-soluble polymer: Cellulose derivatives, Xanthan gum, Chitosan

b) Water-insoluble polymer - Ethylcellulose, polydimethylsiloxane

4) Based on properties:

a) Thermoplastics- polyacrylonitrile, polypropylene

b) Thermoset- Bakelite

c) Elastomer- Natural rubber

5) Based on degradability:

a) Biodegradable polymer: Polylactic acid, Polyglycolic acid, Nylon polycaprolactone

b) Non-biodegradable - ethylcellulose, polydimethylsiloxane.

6) Based on polymerization:

a) Additional polymerization: Polyethylene, polypropylene, polyvinyl, chloride, Teflon.

b) Condensation polymerization: Polyester, polyamide, polystyrene.

**ADVANTAGES OF POLYMER**

- Sustained delivery of drug
- Localized delivery of drug
- Reduce side effect
- Biodegradable and biocompatible
- Improved patient compliance

**DISADVANTAGES OF POLYMER**

- Exhibit dose dumping effect
- High initial drug release after administration

- Low mechanical properties

**SYNTHESIS OF POLYMER**


**Figure No.1: Synthesis of polymer**

**Initiation**

The first step in polymerization is initiation involve the formation of free radical. Each initiating radicle can attack the double bond of the monomer. In this way, the radicle is transferred to the moment, and a monomer radicle is produced. Addition can occur at either end of the monomer.[8]

**Propagation**

Monomer radicle also can attack another monomer and then another monomer, this step is known as propagation. By which micro radicals are formed. The entire propagation reaction usually takes place within a fraction of a second.

**Termination**

Chain termination is the chemical reaction that ceases the formation of reactive intermediates in a chain propagation step in the course of the polymerization, effectively bringing it to halt.[9]

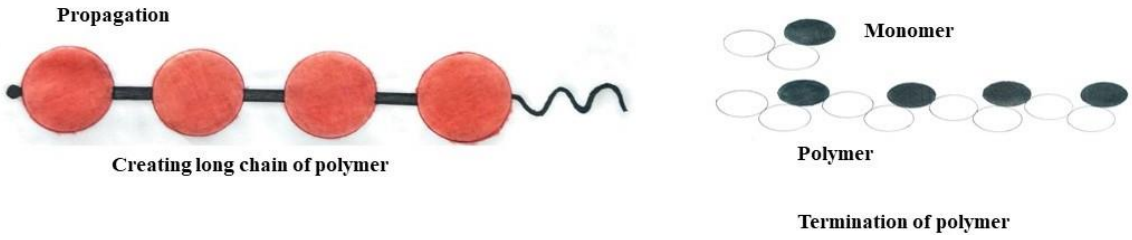


**Figure No. 2: synthesis of polymer**

## ROLE OF POLYMER IN PHARMACEUTICAL DRUG DELIVERY: -

### Immediate-release dosage form

### Tablets

In the conventional and immediate-release oral dosage forms, polymers have been used for many years as an excipient. Either to aid in a manufacturing process or to protect the drug from degradation upon the storage. The polymers are used as a binder to bind the powder particle in dump mass such as an HPMC, gelatin, polyvinylpyrrolidone, starch, alginic acid, etc. Sodium starch glycolate, cross carmellose sodium, starch is used as a disintegrant in tablets formulations when they come in contact with water they burst and increase the surface area of the drug by improving dissolution characteristics. [10]

### Capsules

Capsules are alternative dosage forms of the tablets which are filled with granules, liquids, powder, semisolids, pellets encapsulated in a polymeric shell. For the formulation of capsule shells, gelatin is commonly used in the pharmaceutical industry, either separately or combined blends according to the desired physical properties of dosage forms.[11] The soft gelatin shell of the capsule is formed by the combination of gelatin and plasticizers like glycerin or sorbitol. The cross-linked gelatin forms on the surface of the shell, a thin swollen water-insoluble membrane barrier, that decreases the dissolution rate of the API's. When the capacity of the capsule is granulated or compressed the super-disintegrant should be added to the content of hard gelatin capsules. HPMC is an alternative to animal-derived gelatin. HPMC is semisynthetic from vegetable origins, so, HPMC hard gelatin capsule is more popular among vegetarian formulation and over the counter products.[12]

### Modified release dosage forms

Pharmaceuticals developed the modified drug release dosage forms to overcome the problem of conventional dosage forms. In modified release dosage forms, the polymers like Eudragit, HPMC, PVP are commonly used.[13]

### Extended-release dosage forms

Extended-release dosage forms are formulated for those drugs which have a short biological half-life. Extended-release dosage forms prolong the time that systemic drug level is within

therapeutic range and reduce the dose frequency and increase patient compliance. For extended-release dosage form, water-insoluble polymers such as Eudragit RS & RL, ethylcellulose, cellulose acetate, polyvinyl derivatives are used. The drug release over an extended period depends upon the viscosity of the polymer or thickness of the coating layer on multi-particulates. High viscosity grades forming stronger and more durable films.[14]

**Gastrointestinal dosage forms**

In recent years, scientific advancement has been made in the research and development of rate-controlling oral drug delivery system by overcoming physiological problems, such as gastric residence time (GRT) and unpredictable gastric emptying time. For the prolongation of GRT, floating drug delivery systems are useful for retaining the therapeutic agent for prolong period and improving the bioavailability of the drug. For achieving this purpose, natural polymers like gums or synthetic polymers like HPMC are used. For the effervescent floating dosage forms, polymers such as methylcellulose, chitosan, and various effervescent agents are used such as sodium bicarbonate, tartaric acid, and citric acid.[15]

**Transdermal drug delivery system**

TDDS is a self-contained, self-discrete dosage form, which when applied to the intact skin delivers the drug at a controlled rate to the systemic circulation. In this, polymer matrix plays a major role. It releases the drug from the device to the skin. The commonly used polymers in TDDS such as; natural polymers like cellulose derivative, zein, chitosan, synthetic polymers such as polyvinylchloride, polyvinylpyrrolidone, synthetic elastomers like polybutadiene, Acrylonitrile, neoprene. Biodegradable polymers are collagen or polyglycolic acid.[16]

**Disperse system**

In biphasic systems like emulsion or suspension, the various polymers are used to mix two immiscible phases.[17] The polymers like ethylcellulose, polyvinyl pyrrolidone, etc. Oil type of emulsion is difficult to formulate but it is easily produced by using a polymer as a dispersing agent.[18]

**Application for taste masking of drugs.**

Many drugs are bitter and overcoming this problem is a major barrier in developing a successful product, especially for pediatric patients such as chewable tablets, emulsion, suspension. Water-soluble polymers are commercially available and have been used for taste

masking applications.[19] The polymer act is used for the coating to provide a physical barrier around the bitter drug. For pediatric patients, multiarticulate are coated in a fluidized bed and coated particles are incorporated into chewable or orally dispersed tablets, filled into capsules, and sprinkled onto the food. Water-insoluble polymers like Eudragit RL30D are used. [20]

**MECHANISM OF POLYMERS:**

**Diffusion**

Rate limiting step of drug diffusion through inert water-insoluble membrane barrier. There are two types i.e., Reservoir and matrix. In the reservoir diffusion system, the drug is contained in the core, which is surrounded by diffusion through this rate-controlling membrane. Examples of polymers are Poly(N-vinyl pyrrolidone), Poly(ethylene-co-vinyl acetate). In the matrix diffusion system, the drug is released either by passing through the pores or between polymer chains and these are the processes that control the release rate. Examples are Polyethylene, poly-vinyl acetate.[21]

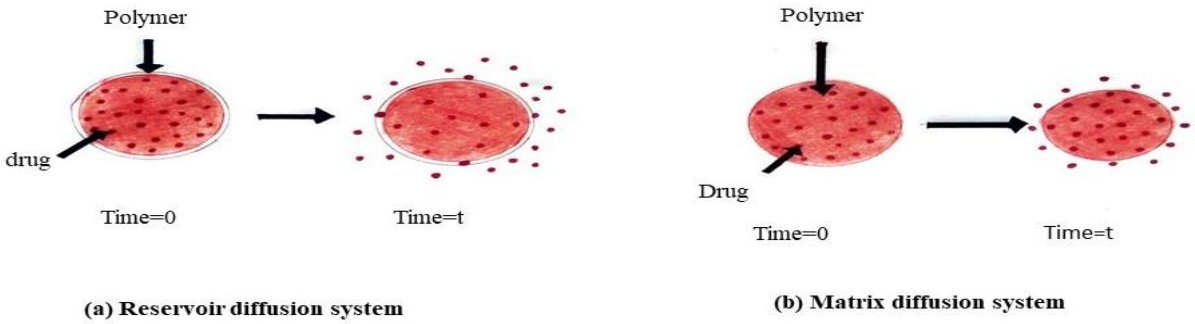


**Figure No. 3: Mechanism of the polymer by diffusion (a) reservoir system (b) matrix system**

**Degradation**

The biodegradable polymer degrades within the body by the natural biological process. The polymers are degraded biologically after the complete release of active ingredients. Most biodegradable polymers are designed to degrade by hydrolysis of polymer chain into the biologically small compound. The degradation of polyanhydrides and polyorthoesters, occurs only at the surface of the polymer, resulting in a release rate that is proportional to the surface area of the drug delivery system.[22]

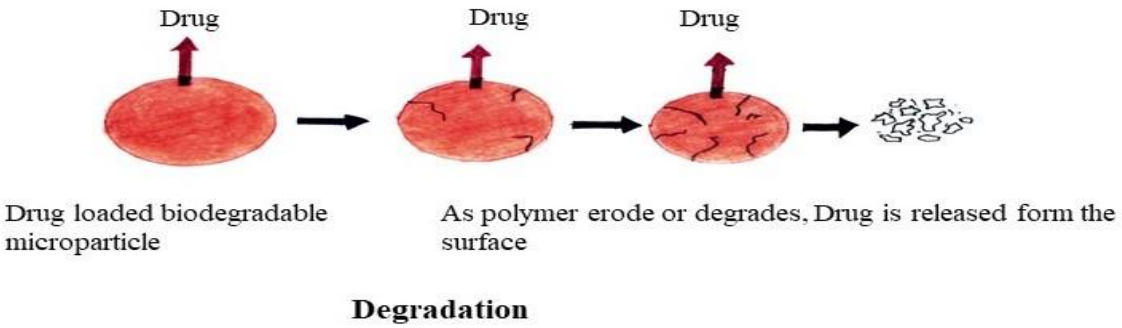


**Figure No. 4: Degradation process**

**Swelling**

They are initially dry but when placed in the body they get swelled by absorbing the water or body fluids. The swelling increases the aqueous solvent content within the formulation as well as the polymer mesh size, enabling the drug to diffuse through the swollen network into the external environment.[23]

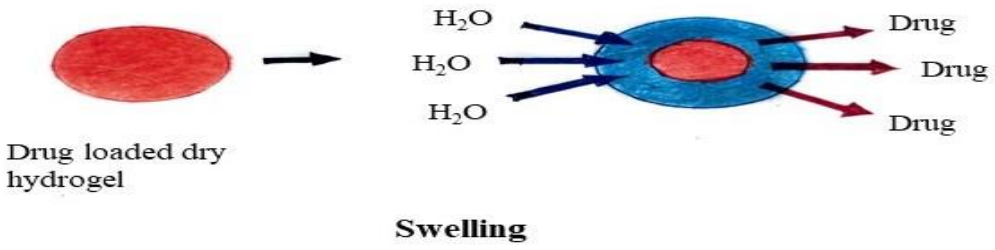


**Figure No. 5: swelling process**

**POLYMERS IN PHARMACEUTICAL APPLICATIONS**

**Collagen**

Collagen is a natural polymer protein component in mammals that are fabricated from glycine-proline-(hydroxy) proline. Collagen gels are one of the first natural polymers to be used as a promising matrix for drug delivery and tissue engineering.[24]Collagen is widely used in pharmaceutical applications as drug delivery system are collagen shields in ophthalmology, sponges for burn/ wounds, gel formulations, used in protein delivery in the form of mini-pellets, tablets, in sustained drug delivery system, by formulating gel formulation in combination with liposome, as a controlling material for transdermal delivery of nanoparticles for gene therapy. Also, used in the cell culture as basic material. For the

tumorigenic study, the collagen film is developed as a matrix system for the evaluation of calcification and the embedding of a single cell suspension.[25]

**Polyglycolic acid**

Polyglycolic acid is the synthetic polymer that is obtained by ring-opening polymerization of the cyclic diester of glycolic acid, glycoside. PGA has been used as a degradable suture DEXON due to its characteristics including a melting point of 200℃, a glass transition temperature between 35℃ and 40℃, and a very high tensile strength. PGA is incorporated into scaffolds for various tissue engineering applications such as tendon, bones, cartilage, tooth, and spinal regeneration. PGA adheres to wound and helps to prevent postoperative bleeding as well as inspire epithelization. Initially, the sheet was used only on hard tissue and have since been used on hard tissue as well.[26]

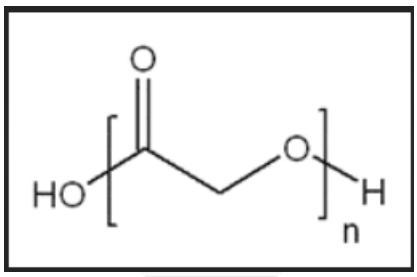


**Figure No. 6: Polyglycolic acid**

**Alginate**

Alginate is an example of a naturally occurring linear polysaccharide. Due to the unique property of Alginate, widely used by many pharmaceutical scientists for drug delivery systems. The properties such as, low toxicity, non-immunogenicity, biocompatibility, biodegradability, water-solubility, gelling ability, stabilizing property, high viscosity in aqueous solution, relatively low cost. Alginate is used as a blood chelator, to remove heavy metals-toxins from the bloodstream simply by binding them.[27] In a study, found that the specified dose of sodium alginate reduces the absorption of strontium, which is a cause of bone marrow cancer, leukemia, bone cancer, etc. Alginate is also used as a diet supplement, for the reduction of body fat level. In cosmetics, the use of alginate is a moisture retainer or thickener. Retaining a lipstick's color on the lip surface, is also applicable as a tablet binder or dissolver, in heartburn and reflux treatment. Another use of alginate is in the controlled release formulations.[28]

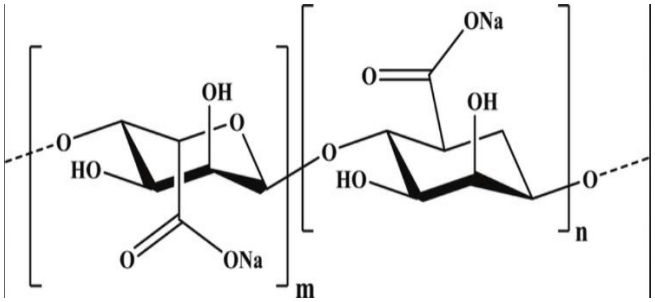


**Figure No. 7: Structure of Alginate**

**Starch**

Starch is used as a pharmaceutical excipient. Starch is used in the formulation of several dosage forms. Its function is depending upon a specific dosage form. Starch is commonly used as a binder in the production of tablets, capsules, and other solid dosage forms. It is commonly used as disintegrants. At very low dosages for masking to very difficult to process compress then into tablets or other dosage forms. It is also used as an adsorbent. Starch also helpful in delivering proteins or peptides drug orally.[29]

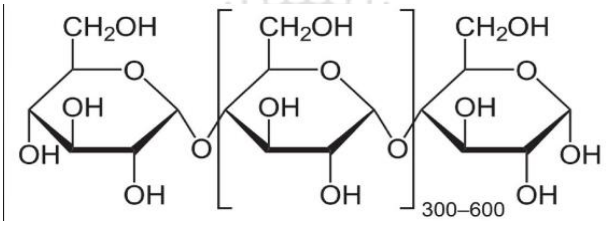


**Figure No. 8: Structure of starch**

**Chitin and chitosan**

Chitin is the second most important natural polymer in the world which is abundant in mucopolysaccharide and consists of 2-acetoamido-2-acetamido-2-deoxy-b-D-glucose. Chitin can be degraded by chitinase. Chitosan is soluble in acidic aqueous media, used for food, cosmetic, biomedical, and pharmaceutical applications.[30] Chitin and chitosan have their property such as, biodegradability, non-toxicity, ability to form film, etc. Chitosan and chitins are also applied for the nanotechnology technique. The microencapsulation technique is under increasing investigation for the delivery of drugs, biologics, and vaccines. Chitosan can also be used in solutions such as hydrogels or nanoparticles. [31]

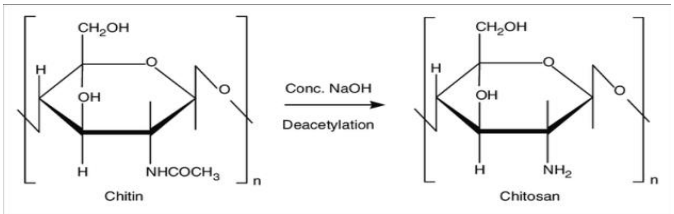


**Figure No. 9: Structure of Chitin and chitosan**

**Polyethylene glycol**

Polyethylene glycol is synthesized by the interaction of ethylene oxide with water, ethylene glycol, or ethylene glycol oligomers. Due to its solubility property and low toxicity, it is suitable for biological applications. PEG is high hydrophilic; it enhances the solubility of hydrophobic drugs or carriers when conjugating with them. PEG enhances the physical and chemical stability of the drug and prevents the aggregation of the drug *in vivo* as well as during storage. PEG helps to reduce the aggregation of RBCs. It is also used in the storage of blood and organs. [32]

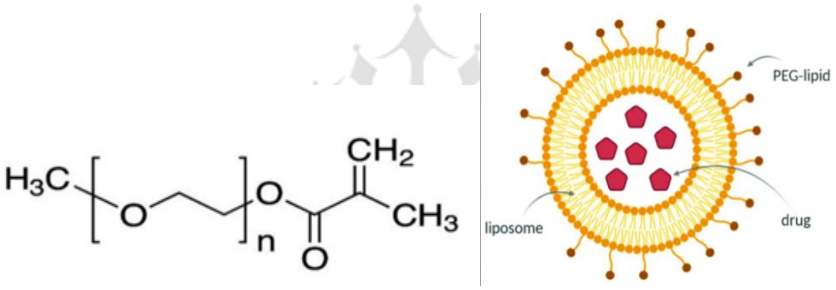


**Figure No. 10: Structure of Polyethylene glycol**

**Albumin:**

Albumin is about 65k Da in weight, non-toxic, and non-immunogenic. It is mainly applicable in nanoencapsulation, conjugate with proteins (condense albumin with paclitaxel). Microencapsulation of insulin, doxorubicin, 5-fluorouracil, and small molecules. [33]

**Table No. 1: Some polymer and their specific applications**

| POLYMERS | APPLICATIONS |
|---|---|
| **Polyethylene glycol** | Swelling agent |
| **Polyethylene oxide** | Cosmetic use |
| **PVP** | Tablet granulation |
| **Polyvinyl alcohol** | Tablet binder and coating |
| **HPMC** | Coating and binder |
| **Ethylcellulose** | Sustained release system |
| **Carboxymethylcellulose** | Superdisintigrating agent |

**Table No. 2: polymers use different methods and drug formulations.**

| Drug use | Category | Method use | Polymer used |
|---|---|---|---|
| **Venlaflexine** | Anti-depressant | Wet granulation | Bees wax, carnauba wax |
| **Zidovudine** | Anti-viral | Direct compression | HPMC-K4M, carbapol-93, EC |
| **Ibuprofen** | Anti-inflammatory | Wet granulation | EC, HAP |
| **Sulphathiazole** | Antibiotic | Solid dispersion | Polyethylene glycol, PVP |
| **Miconazole** | Anti-fungal | Direct compression/ wet granulation | Pectin, HPMC |
| **Verapamil** | $Ca^{+2}$ channel blocker | Direct compression / formulation of pellets | HPMC K4M, HPMC phthalate, ethyl cellulose |
| **Captopril** | ACE inhibitor | Direct compression | Ethyl cellulose, PVP K30 |
| **Amlodipine** | Anti-arrythmatic | Wet granulation | Guar gum, HPMC-E15LV |
| **Albendazole** | Anti-fungal | Nanosuspension | PVP K30, PVP K90 |

## FUTURE TREND

For altering the pharmacokinetic and release characteristics of drugs there is a requirement of a proper drug delivery system for promoting tissue specificity and biocompatibility. A more sophisticated drug delivery system is designed as a multifunctional all-in-one system that offers simultaneously improved pharmacokinetic, decreased toxicity, facilitate targeting and programmed profile of drug release. Delivering two or more drugs in combination or simultaneously incorporating the diagnostic agent offers a chance of more effective therapy. In advance biotechnology, proteomics, and genomics have allowed to development of novel drugs such as proteins, peptides, and nucleic acid as therapeutic strategies for the future Polymers are multicomponent, nano-sized formulate in the clinic as an anticancer compound.[34] For the treatment of cancer, they have the potential to improve pharmacological therapy. Polymer-drug conjugation promotes passive tumor targeting by enhanced permeability and retention effect and allows for lysosomotropic drug-delivering endocytic capture. The technology platform of polymer therapeutics allows the development of both new and exciting polymeric material, the incorporation of novel bioactive agents, and a combination thereof to address recent advances in drug therapy. The rational design of polymer conjugates is expected to formulate the “nanomedicines” which show true potential. In the biomedical sciences, the promising challenge in the future is the development of new and intelligent drug delivery systems for more controlled and targeted applications. Biocompatibility and acceptability are the major challenges for drug delivery systems because the interaction of synthetic material with human body cells is entirely different from the biological system. Different strategies are adopted to ensure targeted and controlled drug delivery, such as encapsulation, biomarker, and artificial nanocarriers.[35]

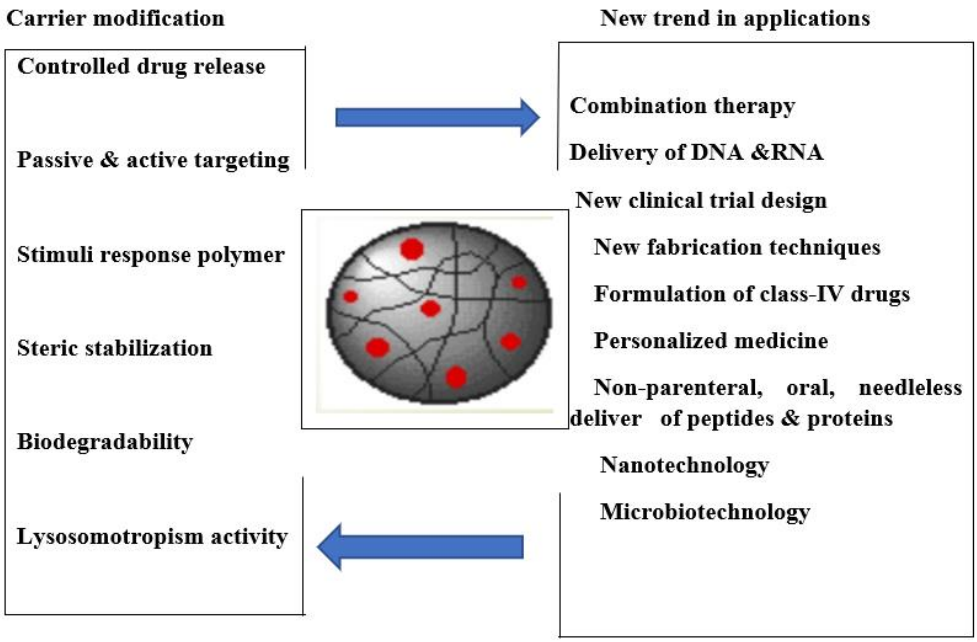


**Figure No. 11: Multifunctional polymer-based drug delivery system and trend in which influence the future strategies for development of new and improved polymer and carriers.**

## CONCLUSION:

Polymers have been used as the main tool in pharmaceuticals, to release the rate of the drug in a controlled manner. Polymer helps in improving the taste of the bitter drug, acts as a stabilizer and protective agent in the drug delivery system. Polymers are also useful in the formulation of nanoparticles or carry the proteins and peptides. The basic concept provides the foundation for further understanding of drugs and designing a better delivery system. Extensive applications of polymer in drug delivery are because it offers a unique property that so far has not been attended to by any other material. This review has covered the major concerns about the classification of polymers, the role of polymers in the drug delivery system, mechanism of polymer including diffusion, degradation, and swelling. Biodegradable polymers also have major advantages. Polymers in pharmaceuticals are also involved in this review. future trend of polymers in nanoparticles, in gene therapy, is more important research about polymers.

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