REVIEW ARTICLE JPAR 2019

Journal of Pharmaceutical Advanced Research

(An International Multidisciplinary Peer Review Open Access monthly Journal)

Available online at: www.jparonline.com

Application of Polymers in Pharmaceutical Formulation – A concise review

Tikesh Agrawal[1]*, Updesh Lade[1], Rakesh Tiwle[2]

[1]Chhatrapati Shivaji College of Pharmacy, Chichgadh Road, Deori, Gondia, Maharashtra – 441901, India.
[2]Shri Rawarpura Sarkar Institute of Pharmacy, Power grid Kumhari, Chhattisgarh – 490042, India.

Received: 06.10.2019 Revised: 14.09.2019 Accepted: 20.10.2019 Published: 31.10.2019

ABSTRACT: Polymers play a vital role in the development of the pharmaceutical formulations in industry due to their bulk availabilities and surface properties. The polymers can be used in the colloidal drug as well as in carrier drug delivery system. The polymer is consisting of small particle in a delivery system and optimized the drug releasing property. The polymers are obtained from the natural origin or various sources or it can be syntheses in the laboratory. Polymers are giant molecules of high molecular weight which acts as a supplement towards the active pharmaceutical ingredients (API) and not give any side effects in the formulation. In this review the Eudragit polymer has been extensively discussed as it is the first choice of the polymer in the pharmaceutical industry for formulating various novel formulations. The natural polymers gain access for its tremendous used in the pharmaceutical and biomedical formulations due to their easy of availability, biodegradability and having a widely used in the biocompatibility. The purpose of this study is to give the general idea of the different types polymers along with their applications in the various dosage forms used in the drug delivery system. This study also provides the information on ongoing research activities and future trends for the developments of medicine using various advanced form of polymers.

Corresponding author*
Mr. Tikesh Agrawal
Lecturer
Chhatrapati Shivaji College of Pharmacy,
Chichgadh Road, Deori, Gondia,
Maharashtra – 441901, India.
Tel: +91-7972554829
Mail ID: tikeshagrawal150@gmail.com

Keywords: Eudragit, Polyesters, Sustained release, Cellulose Easters, Natural Polymers.

INTRODUCTIONS:

In a Greek words, poly means many or units of high molecular mass each molecule of which consist a very large number of single structural units joined together. Polymers are giant molecules of high molecular weight, known as more molecules, which are coupling to a large number of small molecules, called monomers [1]. Monomers combine to form polymer is known as polymerization [2]. A biodegradable polymer is a part of biomedical applications in light of their known biocompatibility and biodegradability [3].

DEVELOPMENT OF POLYMERS:

Thomas Hancock gave an idea about the modification of natural rubber [4]. In eighteenth century, the naturally-occurring polymers as materials for providing tools, decoration, weapons, clothing, shelter, writing materials and other requirements [5]. Polymers have existed in natural form since life activated and those such as DNA, RNA, proteins and polysaccharides play crucial roles in animal and plant life. The use of polymers in the medical field is not a novelty. The natural polymers have been used as integral of herbal remedies for centuries [6]. The first polymer-drug conjugates appeared around 1955 that is polyethylene glycol (PEG) to proteins causing technique called PEGylation.

CLASSIFICATION OF POLYMERS:

Polymer is a high molecular weight. It gives the different physical properties, chemical structure and mechanical behavior to the dosage form. The polymers can be classified as natural, semi synthetic and synthetic polymers.

Table 1. Classification based on chemical nature [7].

Poly-mers	Example of Polymer
Vinyl Poly-mers	Polymethacrylates, Polyvinyl Alcohols, Polyvinyl Pyrrolidone (Povidone), Poly(Acrylic Acid) (Carbomer)
Cellu-lose Ethers	Methycellulose, Ethycellulose, Hydroxy ethyl cellulose (HEC), Hydroxy propyl cellulose (HPC), Hydroxy propyl methyl cellulose (HPMC):Hydroxy ethyl methyl cellulose (HEMC), Sodium carboxy methyl cellulose
Poly-esters	Poly (lactic) and related copolymers, Poly (ε-caprolactone), polyglycolide
Polysac charides	Chitosan, Carragenan, Tragacanth, Acacia, Poly(allginic acid), xanthum gum
Misce-llaneous Poly-mers	Gelatin, polyanhydrides, polyethyleneglycols, poyethyene oxides

The polymer can also be classified as biodegradable and non-biodegradable polymers. The polymer classification as per the chemical nature with examples has been given in Table 1.

POLYMERS USED IN DRUG DELIVERY:

Poly lactic-co-glycolic acid:

In past two decades poly lactic-co-glycolic acid (PLGA) has been used among the most attractive polymeric candidate to fabricate devices for drug delivery and tissue engineering applications [8]. The mechanism of drug delivery from the dosage form has been shown in Fig 1, 2 and 3.

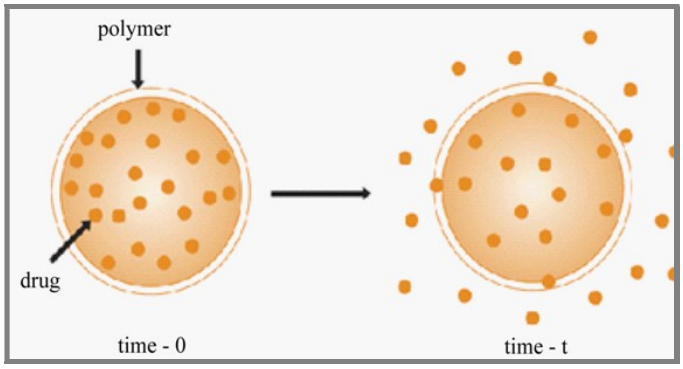

Fig 1. Diffusion based drug delivery system.

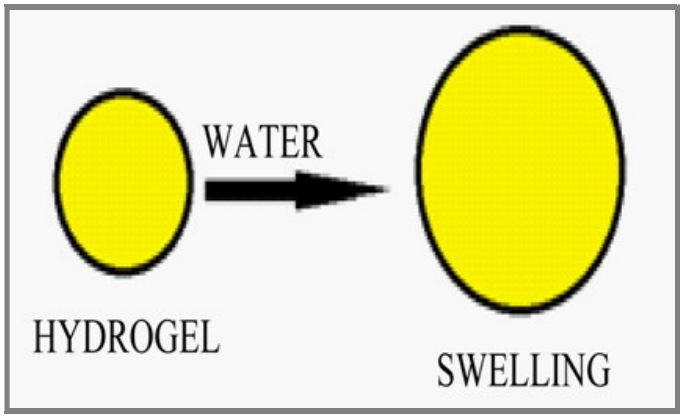

Fig 2. Hydrogel based drug delivery system.

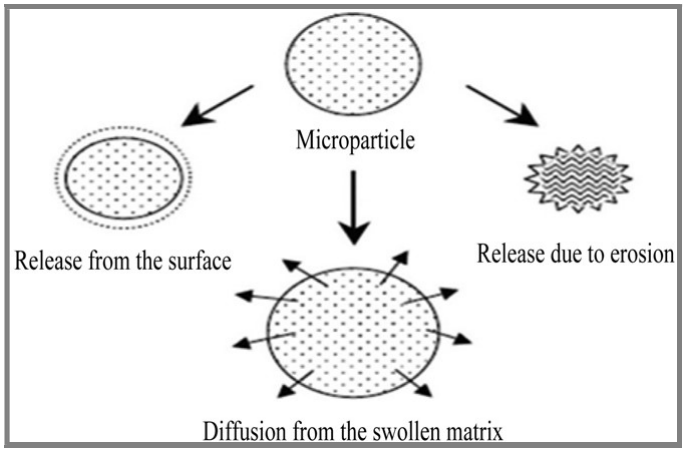

Fig 3. Various drug release mechanisms from polymeric dosage form.

PHARMACEUTICAL APPLICATIONS:

Plastics and Rubbers:[9]

- Polyurethane Transdermal patch backing, blood pump, artificial heart, and vascular grafts [10].
- Polyisobutylene Pressure sensitive adhesives for transdermal delivery.
- Polycyanoacrylate Biodegradable tissue adhesives in surgery, a drug carrier in nano- and microparticles., chewing gum, Blood bag, and tubing [11].

- Polyethylene Transdermal patch backing for drug in adhesive design, wrap, packaging, containers, hard contact lenses, Soft contact lenses.

Starch-Based Polymers:

- Starch Glidant, a diluent in tablets and capsules, a disintegrant in tablets and capsules and a tablet binder [12].

Hydrocolloids:

- Alginic acid Oral and topical pharmaceutical products, Carrageenan Modified release, viscosifier [13].

Water-Insoluble Biodegradable Polymers:

- (Lactide-co-glycolide) polymers Microparticle-nanoparticle for protein delivery [14].

NOVEL DRUG DELIVERY SYSTEMS:

Novel drug delivery systems include micelles, dendrimers, liposomes, polymeric nanoparticles, cell hosts, microcapsules and lipoproteins. The ongoing growth in polymer based encapsulations. It enhances bioavailability. Role of polymers in drug delivery will grow steeply in future to handle various unsolved issues [15,16].

COMPREHENSIVENESS STUDY:

The polymers used in film coating are to find out the polymers that are more effective than available polymers [17,18]. Another scope is that it do not show the changes in the properties of tablets like dissolution rate, disintegration, wait sustain release, action and pharmacokinetic and pharmacodynamic properties of drug formulation [19].

The properties that will enhances the quality to be use more Pharmaceutically are low abrasion, smooth surface, good flow behavior, masking of taste and smell, good protection against light, air and moisture, impervious separating layers in the case of multilayer composition, systematic release of active ingredients, retardation, delayed dissolving and low hygroscopicity, visual attractiveness [20].

POLYMERIC PLANT-DERIVED EXCIPIENTS IN DRUG DELIVERY SYSTEM:

Cellulose:

Plant cell wall consists mainly of cellulose, hemicelluloses and pectin. The cellulose derived polymers (Fig 4) are used as pharmaceutically that is filler in tablets [23].

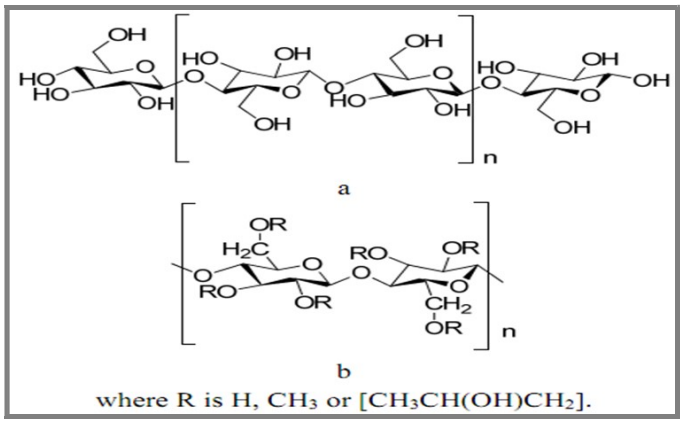

Fig 4. Chemical structure of (a) powdered cellulose or microcrystalline cellulose (b) hydroxyl propyl methyl cellulose.

Pectin:

Pectin (Fig 5) is obtained from apples and has proven that investigated as excipients in many different types of dosage forms such as film coating of colon-specific drug delivery systems when mixed with ethyl cellulose, microparticulate delivery systems for ophthalmic preparations and matrix type transdermal patches [21].

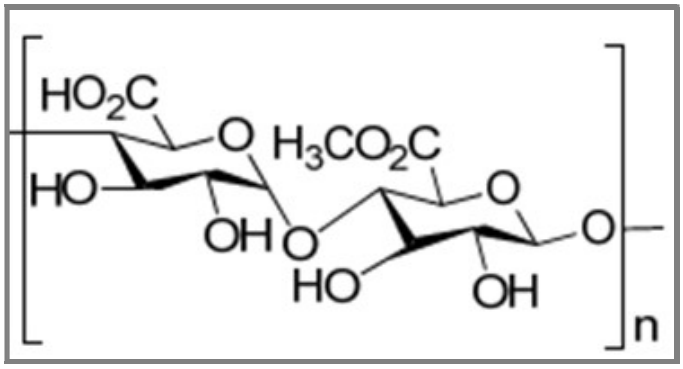

Fig 5. The chemical structure of pectin.

Alginates:

Alginates (Fig 6) has been proved from the research study that it is used as stabilizers in emulsions, suspending agents, tablet binders and tablet disintegrates [25]. The gelling properties of alginate's guluronic residues with polyvalent ions such as calcium or aluminium allow cross-linking with subsequent formation of gels that can be employed to prepare matrices, films, beads and pellets [22].

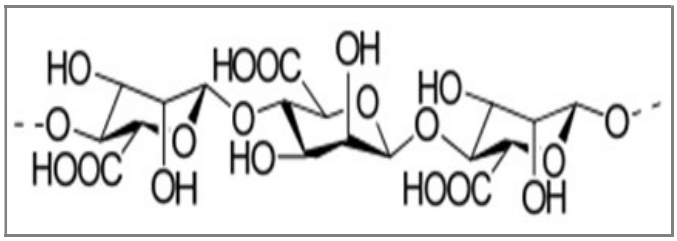

Fig 6. The chemical structure of alginates.

Guar gum:

Guar gum (Fig 7) is inexpensive and flexible carrier for oral extended release drug delivery [23]. Guar gum is particularly useful for colon delivery because it can be vulgarize by specific enzymes in this region of the gastrointestinal tract.

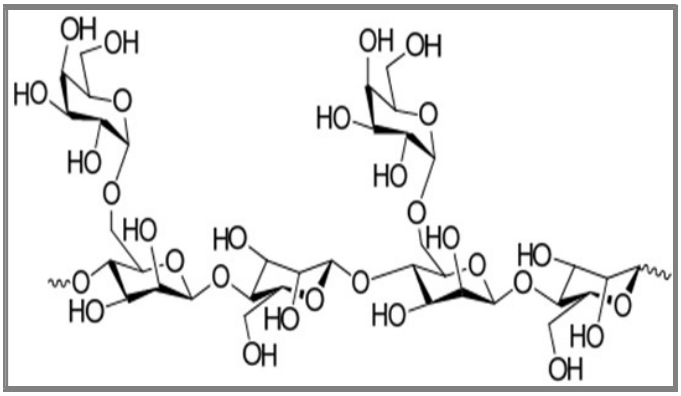

Fig 7. The chemical structure of guar gum.

EUDRAGIT POLYMER IN TARGETED DRUG DELIVERY:

The eudragit is the esters of acrylic and methacrylic acid. Eudragit polymers are available in a broad range of change physical forms (Aqueous dispersions, organic solutions, granules and powders) [24].

Types of Eudragit polymers:

***Poly(meth)acrylates (Soluble)*:**

They are soluble in digestive fluids by the salt formation. The examples of Eudragit of this category are eudragit L, S, FS and E polymers. These polymers with acidic or alkaline groups enable pH-dependent release of the active ingredient [25-27]. This type of eudragit polymers are used a simple taste masking through gastric resistance and this polymer used to control drug release in all sections of the intestine.

***Poly(meth)acrylates (Insoluble)*:**

These are insoluble but permeable in digestive fluids. The example of this type of eudragit polymers are Eudragit RL and RS, which carry alkaline groups and Eudragit NE polymers which carry neutral groups. These polymers enable controlled time release of the active ingredient by pH-independent swelling [28,29]. This type of eudragit polymers are used in delayed and sustained drug release formulations.

Advantages of Eudragit polymers:

The Eudragit offers valuable advantages for enteric coatings. In addition to this the Eudragit polymer offers several merits that are PH-dependent drug release, protection of actives substances from gastric fluid, protection of gastric mucosa from aggressive actives, increases drug effectiveness, offers good storage stability and enable gastrointestinal and colon targeting of drug [30,31].

CONCLUSION:

The use of polymer is an ancient approach in Pharmaceutical applications. The polymers play a challenging role in designing novel formulations. Varieties of novel polymers have been developed. Still more research has to be done for development of more advanced polymers economically with greater advantages. The use of acrylic polymers holds a good platform in formulation field. Such a polymer has to be developed which shall be enable the drug to target the cancer cell *in vivo* manner.

ACKNOWLEDGEMENT:

The Authors wish to thanks the Principal and Management of the Chhatrapati Shivaji College of Pharmacy, Deori Maharashtra for providing Library and Internet facility for the compilation of this review study

REFERENCES:

1. Park Y, Sugimoto M, Watrin A, Chiquet M, Hunziker EB. BMP-2 Induces The Expression of Chondrocyte-Specific Genes In Bovine Synovium-Derived Progenitor Cells Cultured In Three-Dimensional Alginate Hydrogel. Osteoarthr Cartilage, 2005; 13(6): 527-536.
2. Tabata Y, Ikada Y. Protein Release from Gelatin Matrices. Adv Drug Del Rev, 1998; 31: 287-301.
3. Rakesh Tiwle, *et al*. Crack The Hard Nut Known As Wall Nut (Akhroat) - A Review. World J Pharm Res, 2016; 5(4): 2023-2041.
4. George M, Abraham T. Polyionic Hydrocolloids for the Intestinal Delivery of Protein Drugs: Alginate and Chitosan - A Review. J Control Rel, 2006; 114: 1-14.
5. Langer R. Synthesis and Characterization of Degradable Polyanhydrides. Macromolecule, 1995; 28: 2148-2193.
6. Illum L. Chitosan and Its use as Pharmaceutical Excipient. Pharm Res, 1998; 15: 1326-1331.
7. Knapczyk J. Excipient Ability of Chitosan for Direct Tableting. Int J Pharm, 1993; 89: 1-7.
8. Bondurant S, Ernster V, Herdman R. Silicone Toxicology. In: Bondurant S, Ernster V, Herdman R, Editors. Safety of Silicone Breast Implants. Washington: The National Academic Press; 2000. pp. 80-113.

9. Caputo A, Castaldello A, Brocca-Cofano E, Voltan R, Bortolazzi F, Altavilla G, *et al*. Induction of Humoral and Enhanced Cellular Immune Responses by Novel Core-Shell Nanosphere - and Microsphere-based Vaccine Formulations following systemic and Mucosal Administration. Vaccine, 2009; 27(27): 3605-3615.
10. Sanghi DK, Tiwle R. Formulation and Characterization of Diltiazem Hydrochloride matrix granules and Its possible evaluation. World J Pharmacy Pharm Sci, 2013; 2(6): 5309-5320.
11. Park JH, Allen MG, Prausnitz MR. Biodegradable Polymers Microneedles: Fabrication, Mechanics and Transdermal Drug Delivery. J Control Rel, 2005; 104: 51-66.
12. Vilar G, Tulla-Puche J, Albericio F. Polymers and Drug Delivery Systems. Curr Drug Del, 2012; 9: 367-394.
13. Mahajan A, Aggarwal G. Smart Polymers: Innovations in Novel Drug Delivery. Int J Drug Dev Res, 2011; 3: 16-30.
14. Edman P, Artursson P, Laakso T, Sjoholm I. Polymers. In: Illum L, Davis SS, editors. Controlled Drug Delivery. Bristol: Wright; 1981.
15. Cho JW, Woo KS, Chun BC, Park JS. Ultraviolet Reflective and Mechanical Properties of Polyethylene Mulching Films. Eur Polym J, 2001; 37: 1227-1232.
16. Rosen HB, Kohn J, Leong K, Langer R. Fabrication Technology. In: Controlled Release Systems. Boca Raton: CRC Press, 1986.
17. Beneke CE, Viljoen AM, Hamman JH. Polymeric Plant-Derived Excipients in Drug Delivery. Molecules, 2009; 14(7): 2602-2620.
18. Chhetri HP, Thapa P. An Overview on Gastroretentive Drug Delivery System. Infection, 2014; 5: 12-18.
19. Gomber C, Parihar S. Envisioning The Role of Renewable Energy Sources for a Sustainable future. Int J Environ Eng Manag, 2013; 4: 25-32.
20. Illum L, Jabbal-Gill I, Hinchcliffe M, Fisher AN, Davis MSS. Chitosan as a Novel Nasal Delivery System for Vaccines. Adv Drug Del Rev, 2001; 51: 81-96.
21. Klock G, Pfeffermann A, Ryser C, Grohn P, Kuttler B, Hahn HJ, *et al*. Biocompatibility of Mannuronic Acid-Rich Alginates. Biomaterials, 1997; 18: 707-713.
22. Augst AD, Kong HJ, Mooney DJ. Alginate Hydrogels as Biomaterials. Macromol Biosci, 2006: 6(8): 623-633.
23. Tiwle R, *et al*. A Noval Transdermal Drug Delivery System and Its Possible evaluation: A Review. World J Drug Discovery Therapeut, 2013; 1(3): 57-65.
24. Borchard G. Chitosans for Gene Delivery. Adv Drug Deliv Rev, 2001; 52: 145-150.
25. Chourasis MK, Jain SK. Polysaccharides for Colon Targeted Drug Delivery. Drug Del, 2004; 11: 129-148.
26. Tiwle R, *et al*. Effect of pH $AlCl_3$ solution on Drug Entrapment Efficiency of IPN Beads. Int J Chem Pharm Sci, 2014; 2(6): 898-901
27. Olson J. The History of Cancer: An Annotated Bibliography. New York: Greewood Press; 1989.
28. Papac R. Origins of cancer therapy. Yale J Biol Med, 2001; 74: 391-398.
29. Pallavi P, Ganesh CK, Jayashree K, Manjunath GV. Unfurling the Rationale use of Platelet Transfusion in Dengue Fever. Indian J Hematol Blood Transfus, 2011; 27(2): 70-74.
30. Mahapatra AK, *et al*. Dissolution rate enhancement and solid state characterization of Ritonavir - PEG 4000 solid dispersions. J Pharm Adv Res, 2019; 2(9): 650-656.
31. Parija S, *et al*. Polymers for Colon Targeted Drug Delivery: A Review. J Pharm Adv Res, 2019; 2(7): 568-576.

Conflict of Interest: None
Source of Funding: Nil
Paper Citation: Agrawal T*, Lade U, Tiwle T. Application of Polymers in Pharmaceutical Formulation – A concise review. J Pharm Adv Res, 2019; 2(10): 691-695.