International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 1055-1061 www.ijprajournal.com ISSN: 2456-4494

Polymeric Excipients in Pharmaceutical Formulations: A Comprehensive Review

C.Arun, Arya Krishna, Banupriya, C. Bhuvaneshwari, C. Povindhar, P. Adithi*

Department of Pharmaceutics, The Oxford College of Pharmacy, Bangalore, Karnataka 560068, India

Date of Submission: 01-08-2024 Date of Acceptance: 10-08-2024

ABSTRACT

Pharmaceutical polymers serve as the core components in the formulation of pharmaceuticals in conventional and novel drug delivery system. This comprehensive overview includes the classification of distinct polymers based on either synthetic or natural origin, where polymers play a crucial role in pharmaceutical applications such as manufacturing, packaging and healthcare due to their versatile properties like durability, flexibility and conductivity. Their application span from binding agents in tablet formulations to controlling viscosity, liquid flow and certainly their uses in suspensions and emulsions. The current review article signifies different polymers that have been employed as primary agents to regulate the release rate of drugs from the formulations according to their implementations and the development of polymers in various dosage forms that includes tablets and capsules.

Keywords: Polymer, drug delivery system, emulsion, suspension, tablet, capsules.

I. INTRODUCTION

Polymer comes from the Greek word poly, meaning "many," and mere, meaning "parts." These materials belong to a broad class that are composed of numerous small molecules called monomers that are joined to form lengthy chains known as macromolecules. They are significantly used as pharmaceutical dosage forms in drug delivery systems [1]. Different types of polymeric excipients are showcased, highlighting their unique functions in different drug delivery systems. Various polymers have the potential to enhance solubility, bio-degradability, viscosity, pH of dependency, advanced coatings, inhibition of crystallization and mucoadhesion. The modification of the drug release rate can be effectively achieved through the application of a polymer coating on oral pharmaceutical dosage forms [2].

Polymers are also used as a carrier medium in various pharmaceutical preparations. The primary objective of polymeric drug carriers is to deliver drugs to a specific site of action in the body, either by entrapping drug-activated windows molecules or chemically binding them [1,3]. In the domain of polymer science, Henri Braconnot arose as a pioneer in the field of subsidiary cellulose compounds during the year 1811 [4]. This weighty work can be thought of as one of the earliest critical commitments to the discipline. Consequently, in the last option part of the nineteenth century, the approach of vulcanization reformed the sturdiness of normal polymer elastic. This is undeniably a huge achievement as it presented the idea of semi-manufactured polymers to a more extensive crowd, subsequently preparing for additional progressions in the field [5].

Excipients

Excipients, whether of natural or synthetic origin, constitute the majority of components in pharmaceutical formulations. Synthetic additives have become prevalent in contemporary pharmaceutical dosage forms, with lipids, carbohydrates, and proteins representing natural polymeric materials [5]. Polymers are frequently utilized as excipients in the pharmaceutical sector, where they help formulate dosage forms that are solid, liquid, or semi-solid. They perform various tasks as disintegrants, viscosity improvers, binders, matrix binders, release modifiers, film formers, thickeners, stabilizers, emulsifiers, muco-adhesives and suspending agents. They are used in particular in the production of solid monolithic matrix systems, implants, films, beads, micro particles, nanoparticles, inhalable and injectable systems as well as viscous liquid formulations. Polysaccharides and their derivatives form a category of polymers extensively employed in pharmaceutical formulations. In many instances, their inclusion significantly influences the mechanism and speed of drug release from the

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 1055-1061 www.ijprajournal.com ISSN: 2456-4494

dosage form [6]. The increasing significance and utilization of polymers in the pharmaceutical industry can be attributed not only to their biodegradability and low toxicity, making them cost-effective and abundantly available compared to synthetic counterparts but also to the renewable nature of natural resources. When cultivated or harvested sustainably, these resources offer a consistent supply of raw materials [7].

Classification of polymers

Polymers can be classified in various ways, including by their chemical structure, source, molecular forces and polymerisation.

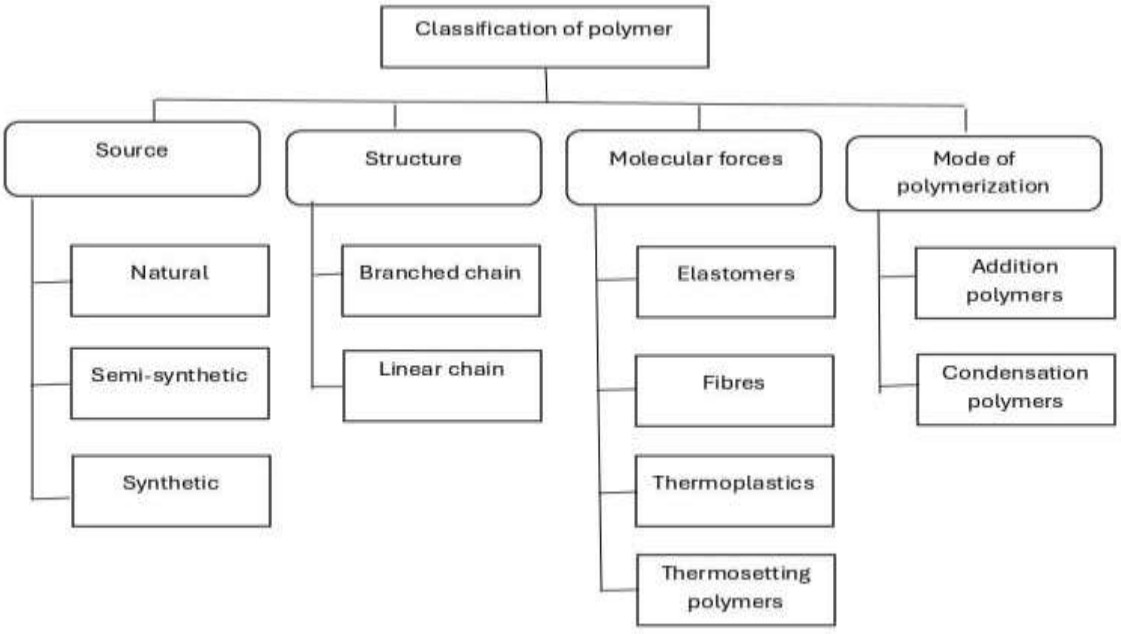

Fig 1: Classification of polymers.

Polymers involved in various pharmaceutical formulations Polymers in solid formulation:

The most prevalent and convenient method of drug administration is through the oral intake of solid dosage forms such as tablets and capsules. When formulating solid oral dosage forms for challenging molecules, polymeric pharmaceutical excipients allow for the concealment of undesirable physicochemical properties. As a result, this alteration in pharmacokinetic profiles contributes to enhancing the therapeutic effect [8].

Exploring the diverse roles of polymers as agents in liquid dosage formulations.

- TABLETS
- CAPSULES

Tablets

For numerous years, polymers have served as excipients in traditional immediate-release oral forms. They assist in manufacturing or shield the drug from degradation during storage. Polymers play a crucial role in sustaining release. Polymers play a role in crafting sustained release tablets, where these products offer advantages such as decreased dosing frequency and enhanced control of the therapeutic window for sustained release products. Polymers are commonly used in the formulation of sustained-release (SR) tablets [9]. Tablets, though mainly composed of non-polymeric excipients like sugars and polyols by weight, often benefit from unique functionalities offered by polymer blends in certain cases. Hydrogel-forming polymers are commonly employed in the production of matrix tablets, where the drug release takes place through a combination of diffusion within the matrix and gel

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 1055-1061 www.ijprajournal.com ISSN: 2456-4494

erosion. Advance modifiedrelease drug delivery tablets involves exploring diverse techniques like matrix systems, film coating, multi-layering, and osmotic controlled release systems [10]. Microcrystalline cellulose is frequently employed as a substitute for carbohydrates in tablet formulations containing highly potent low- dose drugs. Starch and cellulose, serving as disintegrants, induce tablet swelling upon water contact, causing it to "burst." This enhances drug dissolution by increasing the exposed surface area, improving formulation dissolution characteristics. Polymers such as polyvinyl-pyrrolidone and hydroxyl-propyl-methylcellulose (HPMC) are used as binders, allowing, prior to the actual pressing process, the production of granules that enhance the flow and compaction qualities of tablet formulations [1,9,10].

Capsules

Capsules offer a versatile solution in the world of pharmaceuticals, addressing various challenges like taste masking and improving drug absorption. Indeed, the versatility of polymeric excipients allows them to play a dual role in both capsule fills and intermediate release tablets[11]. Gelatin held a monopoly as the sole choice for forming the shells of both hard and soft capsules for many years, whether in hard or soft shells, remains a common and effective choice in pharmaceutical formulations. For quite some time, gelatin was the primary choice for the shell material in both hard (two-piece) and soft (one-piece) capsules. However, the recent development and acceptance of HPMC provide an alternative for crafting hard (twopiece) capsule [11].

Film coating:

Film coating is the application of a thin polymeric layer onto tablets, capsules, or pellets, replacing traditional sugar coating. Widely adopted by pharmaceutical companies for solid dosage forms, this process involves depositing a thin film onto the dosage form [12]. Its objectives are twofold:

1. Functional Protection: The primary goal is to create a functional protective barrier on the substrate's outer surface.
2. Aesthetic Appeal: Additionally, film coating aims to improve the appearance of the dosage form, offering a more pleasing aesthetic [13].

Components of film coating material

- Polymers
- Plasticizers
- Additives

Polymers:

Transitioning from sugar coating to film coating brought about a shift to polymers such as methylcellulose, hydroxyl propyl methylcellulose (HPMC), and ethyl cellulose. While higher viscosity HPMC grades enhance film tensile strength, they often result in poor adhesion to the tablet core, making film peeling common. Dissolving HPMC in water presents challenges due to high solution viscosity, water being a less effective solvent than organic solvents, and poor material wetting, leading to suboptimal film properties. The choice of polymer systems is crucial for aqueous coating success. Opting for lower-viscosity polymers increases solid content, reducing water needs and enhancing coating speed. Other polymers like sodium carboxymethyl cellulose, polyvinyl alcohol, polyvinyl pyrrolidone, sodium alginate, and polyethylene glycol, either individually or in combination, are also employed in aqueous film coating formulations [14].

Plasticizers:

It is a vital component in coating formulations, offer a wide selection including phthalate esters, stearates, phosphate esters, citrates, sebacate, adipate, oleate, oils, glycols and glycerol [15]. Key considerations are:

- **Water Solubility:** Hydrophobic plasticizers pose challenges in solution preparation, impacting disintegration and dissolution profiles.
- **Water Vapour Transmission:**Higher plasticizer concentrations increase water vapour permeability through the film.
- **Concentrations:** Elevated plasticizer levels reduce modulus of elasticity (desired) but also decrease film tensile strength. Adhesion generally improves with higher concentrations.
- **Glossiness:** Excessive plasticizer concentrations may lead to tablet surface oiliness while improving gloss in the finished product.
- **Volatility:** Aqueous coating with less volatile water requires higher drying capacity; more volatile Optimizing plasticizers like propylene glycol may be lost during the process [16].

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 1055-1061 www.ijprajournal.com ISSN: 2456-4494

Additives:
Film coating formulations requires careful consideration of additive properties. Various components play crucial roles:

- **Colorants:** Water-soluble dyes, commonly used in sugar coating, may lead to visible colour differences among tablets due to variations in dye concentration, film thickness, and residual moisture content.
- **Opacity:** The film's opacity is influenced by differences in refractive index between polymers and components like lake colours, resulting in poor opacity.
- **Anti-tacking Agent:** Talc, a common anti-tacking agent, can settle and impact the coating suspension if used in higher concentrations. It is also a poor opacifier, yielding translucent films.
- **Flavours:** Aqueous film coating, requiring higher drying capacity, can alter flavour characteristics. Volatile matters in flavours may interact with other coating components, necessitating a balanced approach in formulation development [17].

Polymers in Liquid Formulations:

Polymers have been successfully employed in the formulations of liquid dosage forms, particularly in the implementation of modified release drug delivery systems. In most of the liquid formulations, water insoluble polymers like PVA, CMC are commonly utilized. These polymers, chosen for their water resistance, are employed in applications for extended release.
Exploring the diverse roles of polymers as agents in liquid dosage formulations.

- EMULSIONS
- GELS
- SUSPENSIONS

Emulsions:

Surfactants, also known as emulsifiers, are used to stabilize emulsions by decreasing surface tension, which lowers the interfacial tension between the water and oil phases. Furthermore, they provide a shielding layer on the dispersed phase droplets, making them reject one another. Emulsions are frequently stabilized through the addition of polymeric thickeners, which increase the continuous phase's viscosity. This contributes to the dispersion of the droplet suspension. Generally speaking, polymer thickeners are employed to stabilize emulsions by making the continuous phase more viscous, which aids in keeping the dispersed droplets suspended [18].

Gels:

Particles suspended in the dispersing medium create a three-dimensional structure of interlacing particles or solvated macromolecules that limits mobility within the dispersing medium, forming a gel. When hydrated, these gelling agents experience significant crosslinking or association, leading to a notable increase viscosity [19].

Suspensions:

Insoluble particles, called suspending agents, are distributed in the carrier liquid to slow the rate of sedimentation. These active ingredients help maintain the stability of the formulation. They form films around suspended particles, reducing the attraction between particles, act as thickeners and increase the viscosity of the solution [19].

Applications of polymers in pharmaceuticals:

POLYMERS	DOSAGE FORM	APPLICATIONS	REFERENCES
Polyvinyl chloride	Solid form dosage	Oxygen bags, blood bags, catheters	[20]
Polyurethane	Liquid form dosage	Tissue engineering, prostheses, surgical drapes	[21]
Poly lactic acid	Liquid form dosage	Controlled drug release, artificial ligaments,	[22]
Polyethylene Glycol	Liquid form dosage	Suppository bases, dispersing agents, biosensors	[23]
Polypropylene	Solid form dosage	Hospital disposables, implants	[24]

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 1055-1061 www.ijprajournal.com ISSN: 2456-4494

Polyethylene oxide	Solid form dosage	Muco-adhesives, rheology control agent, thickeners	[25]
Poly acrylic acid	Solid form dosage	Anticancer drug delivery, biocompatibility, improves stability,	[26]
Polytetrafluoroethylene	Solid form dosage	Vascular prostheses, coatings,	[27]
Polysulfone	Solid form dosage	Dialysis device, biocompatibility, oxygenator	[28]
Polyvinyl pyrrolidone	Liquid form dosage	Tissue engineering, stabilizer, binders	[29]
Polycarbonate	Liquid form dosage	Blood reservoirs, haemodialysis, blood filters	[30]
Poly acrylonitrile	Solid form dosage	Wound dressing, dialysis devices,	[31]
Polyglycolic acid	Solid form dosage	Drug carrier, adhesives, tissue engineering,	[32]
Polyvinyl alcohol	Solid form dosage	Lubricant, swelling property, oxygen mask, blister packaging	[33]

Table 2: Applications of polymers used in pharmaceuticals.

II. CONCLUSION

Based on the above review procured, several natural and semi-synthetic polymers are actively researched for their role as excipients in sustained release drug delivery to adaptable carriers. Beyond sustained-release formulations and for diverse administration routes, polymers contribute to increased bioavailability, reduced side effects, and improved patient compliance. Ultimately, polymers will play significant role in the pharmacy of the future and particularly in the area of drug delivery.

REFERENCE:

[1]. Vicky V. Mody, Introduction to Polymeric Drug Delivery, Internet Journal of Medical Update, 5(2):2010 July;1- 2.
[2]. Omanathanu Pillai, Ramesh, Polymers in drug delivery, Current Opinion in chemical biology, Vol 5, issue 4, 2001,447- 451.
[3]. Clochard M, Dinand E, Rankin S, Simic S, Brocchini S, New Strategies for polymer development in pharmaceutical Science- a short review, J Pharm Pharmacol
[4]. Bari, H.A.A., E. Suali and Z. Hassan, 2008. "Glycolic acid ethoxylate lauryl ether
[5]. performance as drag reducing agent in aqueous media flow in pipelines"
[6]. 5.Hoffman, A.S., Hydrogels for biomedical applications, Adv. Drug Delivery Rev.54, 2002, 3–12
[7]. 6.Whitehead, L., Floating dosage forms: an in- vivo study demonstrating prolonged gastric retention, J. Controlled Release, 55, 1998, 3.
[8]. Timmermans, J. and Moes, A.J., How well do floating dosage forms float? Int. J. Pharm., 62, 1990, 207
[9]. Debotton N, Dahan A. Applications of polymers as pharmaceutical excipients in solid oral dosage forms. Medicinal research reviews. 2017 Jan;37(1):52-97.
[10]. Park, K. and Robinson, J.R., Bioadhesive polymers as platforms for oral- controlled drug delivery: method to study bioadhesion, Int. J. Pharm., 19, 1984, 107.
[11]. Longer, M.A., Ch'ng, H.S., and Robinson, J.R., Bioadhesive polymers as platforms for oral controlled drug delivery III: oral delivery of chlorothiazide using a bioadhesive polymer, J. Pharm. Sci., 74(4), 1985, 406.
[12]. Deepak Sen et al, Int. Journal of Pharmaceutical Sciences and Medicine (IJPSM), Vol.4 Issue. 10, October- 2019, pg. 1-15

[13]. Shah, H.P.; Prajapati, S.T. Quality by design based development and optimization of novel gastro retentive floating osmotic capsules of clopidogrel bisulfate. J. Pharm. Investig. 2019, 49, 295–311
[14]. Knop K., Kleinebudde P. PAT-tools for process control in pharmaceutical film coating applications. Int. J. Pharm. 2013;457:527–536
[15]. DR.P.H. Sharma, S.N.Kalasare, R.A.Kamble, Review on Polymers Used For Film Coating, Asian Journal of Pharmaceutical Technology & Innovation, 01 (02); 2013;0116.
[16]. A. Harper, Modern Plastics Handbook, Published by McGraw-Hill, 2000; 2.1-2.88.
[17]. Snejdrova, M. Dittrich, Pharmaceutical used plasticizers, Recent Advances in Plasticizers, 2012; 45-68
[18]. Bruce Muller 24b - Colorants for Thermoplastic Polymers,Editor(s): Myer Kutz,In Plastics Design Library,Applied Plastics Engineering Handbook,William Andrew Publishing,2011.
[19]. Encyclopedia of polymers and thickeners. Cosm Toil 2002; 117(12):61–120.
[20]. Fox C. Sticks and gels – patent and literature update. Cosm Toil 1987;102(10):33–63.
[21]. Grosu, Elena & Ficai, Anton & Râpă, Maria & Zaharia, Catalin & Chifiriuc, Mariana & Ulinici, S. & Jecu, L.. (2015). Plastified polyvinyl chloride for antimicrobial medical device applications. Journal of Optoelectronics and Advanced Materials. 17. 11391145.
[22]. Akindoyo, John & Beg, Mohammad Dalour & Ghazali, Suriati & Islam, Muhammad & Jeyaratnam, Nitthiyah & A. R., Yuvaraj. (2016). Polyurethane types, synthesis and applications-a review. RSC Adv.. 6. 114453-114482. 10.1039/C6RA14525F.
[23]. Vlachopoulos, Antonios & Karlioti, Georgia & Balla, Evangelia & Daniilidis, Vasilis & Kalamas, Theocharis & Stefanidou, Myrika & Bikiaris, Nikolaos & Christodoulou,
[24]. Evi & Koumentakou, Ioanna & Karavas, Evangelos & Bikiaris, Dimitrios. (2022). Poly (Lactic Acid)-Based Microparticles for Drug Delivery Applications: An Overview of Recent Advances. Pharmaceutics. 14. 359. 10.3390/pharmaceutics14020359.
[25]. Hutanu, Daniela. (2014). Recent Applications of Polyethylene Glycols (PEGs) and PEG Derivatives. Modern Chemistry & Applications. 02. 10.4172/2329-6798.1000132.
[26]. Hossain, Md & Shahid, Md Abdus & Mahmud, Nadim & Habib, Ahasan & Rana, Masud & Khan, Shadman & Hossain, Md. (2024). Research and application of polypropylene: a review. Discover Nano. 19. 10.1186/s11671-023-03952-z.
[27]. Rane, Manish & Parmar, Jayesh & Tiwari, Sandip & Rajabi-Siahboomi, Ali. (2013). Application of Polyethylene OXide in Hydrophilic Matrix Tablets. Pharma Times. 45. 41-48.
[28]. Basuni, Moneer & Zahran, Magdy. (2016). Poly Acrylic Acid: Synthesis, aqueous Properties and their Applications as scale Inhibitor. KGK rubberpoint.
[29]. Mustafa NS, Omer MA, Garlnabi ME, Ismail HA, Ch CH. Reviewing of general polymer types, properties and application in medical field. Int J Sci Res (IJSR). 2016;5(8):212e221.
[30]. Lin, Bingxian & Liu, Kaiming & Qiu, Yunren. (2021). Preparation of modified polysulfone material decorated by sulfonated citric chitosan for haemodialysis and its haemocompatibility. Royal Society Open Science. 8. 210462. 10.1098/rsos.210462.
[31]. Teodorescu, Mirela & Bercea, Maria. (2015). Poly(vinylpyrrolidone) – A Versatile Polymer for Biomedical and Beyond Medical Applications. Polymer-Plastics Technology and Engineering. 54. 923–943. 10.1080/03602559.2014.979506.
[32]. Raj, Prudhvi & Kumar, Ravi. (2021). A Brief Review: Study on Mechanical Properties of Polycarbonate with Different Nanofiller Materials. 10.1007/978-981-15-6267-9_34.
[33]. Sadrearhami, Zahra & Morshed, Mohammad & Varshosaz, Jaleh. (2015). Production and Evaluation of Polyblend of Agar and Polyacrylonitrile Nanofibers for in vitro Release of Methotrexate in Cancer Therapy. Fibers and Polymers. 16. 254-262.
[34]. 10.1007/s12221-015-0254-z.

[35]. Abd Alsaheb, Ramzi A & Aladdin, Azzam & Othman, Nor & Malek, Roslinda Abd & Leng, Ong & Aziz, R. & El Enshasy, Hesham. (2015). Recent applications of polylactic acid in pharmaceutical and medical industries. Journal of Chemical and Pharmaceutical Research. 2015. 51-63.

[36]. Gajra, Balaram & Pandya, Saurabh & Vidyasagar, Gali & Rabari, Haribhai & Dedania, Ronak & Rao, Srinivasa. (2011). Poly vinyl alcohol Hydrogel and its Pharmaceutical and Biomedical Applications: A Review. International Journal of Pharmaceutical Research. 4. 20-26