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Review Article

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A Holistic Review on Applications of Different Grades of Polyethylene oxide in Pharmaceutical Formulation Development

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ABSTRACT

Polyethylene oxide (PEO) is a multifaceted polymer with extensive applications in pharmaceutical product development. This review highlights its significant roles in various drug delivery systems. In hydrogels, PEO's hydrophilicity and gel-forming capabilities enhance drug stability and controlled release. Osmotic pumps benefit from PEO's ability to regulate osmotic pressure and drug solubility, ensuring precise and consistent drug delivery. PEO's mucoadhesive properties improve drug retention and bioavailability in mucoadhesive drug delivery systems, providing sustained therapeutic effects. In gastro-retentive drug delivery systems, PEO prolongs gastric residence time, enhancing the bioavailability of drugs absorbed primarily in the stomach. Finally, PEO's thermoplastic properties make it an essential component in hot melt extrusion processes, facilitating the formation of homogenous drug-polymer matrices and improving the solubility of poorly water-soluble drugs. Overall, PEO's versatility and effectiveness across these applications underscore its critical role in advancing pharmaceutical formulations and optimizing therapeutic outcomes.

Key Words: Hydrogel, Osmotic DDS, Mucoadhesive DDS, Gastro-retentive DDS, Hot-melt extrusion process and polyox

INTRODUCTION

Polyethylene oxide (PEO), a synthetic polymer composed of repeating ethylene oxide units, has found widespread applications in the pharmaceutical industry due to its unique properties. These properties, such as biocompatibility, non-toxicity, water solubility, and ability to form various structures, make PEO an ideal material for a wide range of pharmaceutical formulations. The degree of polymerization (DP) of PEO plays a crucial role in determining its physical and chemical properties, and consequently, its suitability for different pharmaceutical applications. Different grades of PEO, classified based on their molecular weight or DP, exhibit distinct characteristics that influence their performance in various formulations.

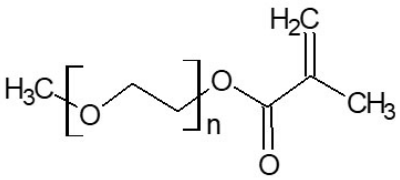

Figure 1: Chemical Structure of Polyethylene oxide.

A long chain poly (ethylene oxide), POLYOX™ is available in a wide range of molecular weights making it an excellent choice for a formulator trying to tailor a specific end viscosity. Because of its wide-ranging compatibility, it is readily used in a variety of applications. It imparts lubricity [1], binding [2], water retention [3], thickening [4] and film formulation.[5] POLYOX™ stands out from other water-soluble thickeners due to its unique properties, including high wet tack, suitability for use in thermoplastics, and its ability to impart a silky feel to final products. This polymer enhances the lubricity of end products, resulting in a silky texture that becomes tacky when wet while maintaining low tack when dry, A single grade is capable of performing in various formulations, effectively reducing turbulent friction and drag. It efficiently separates fines from aqueous systems and forms highly water-retentive gels. Acting as a useful binder, it burns off cleanly during firing, providing superior adhesive grab without leaving any residual stickiness. Ideal for ionically conductive polymer electrolytes, it is versatile enough to function in certain solvent blends and can be extruded, injection-molded, or cast. Additionally, it creates flexible films that are resistant to oil and greases, while also reducing splattering and controlling drift and misting when sprayed. It is available in various grades as shown in Table 1.

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Table 1: Properties of Different grades of Polyethylene glycol

Polyox Grades	Avg. Molecular Weight (g/mol)	Viscosity (cP, 2% aq. sol., 25°C)	Typical Applications
WSR N-10	1,00,000.	12 to 50	Binder, suspension, emulsion.
WSR N-12K	1,000,000	400 to 800	Multifunctional Thickener, Binder, Stabilizer, and Dispersant in Cleaners and Detergents.
WSR N-60	2,000,000	60,000	Thickening, suspension
WSR N-80	4,000,000	80,000	Thickening, suspension, emulsion stabilization
WSR N-100	6,000,000	100,000	Thickening, rheology control, water-soluble films
WSR N-200	10,000,000	200,000	Thickening, suspension, emulsion stabilization, drag reduction
WSR 205	600,000	4500-8800	effective thickener, binder and film former which can be used in many applications such as adhesives, coatings and cleaning solutions
WSR-N-300	15,000,000	300,000	Thickening, rheology control, water-soluble films, adhesives
WSR N-301	15,000,000	300,000	Thickening, rheology control, water-soluble films, adhesives
WSR 308	8,000,000	10,000 to 15,000	Multifunctional Thickener, Binder, Stabilizer, and Dispersant in Cleaners and Detergents
WSR N-750	30,000,000	750,000	Thickening, rheology modification
WSR 1105	900,000	8,800–17,600	Thickening, binding and controlled release
WSR coagulant	5,000,000	5,500 to 7,500	Thickening, Binding and controlled release
WSR N3000	400,000	2,250 to 4,500	thickener, binder, film former, lubricant, and wet tacking agent
WSR N3000 LS	400,000	2,250 to 4,500	POLYOX™ WSR N3000 LS has the same characteristics as POLYOX™ WSR N3000, except LS version has a low silicon dioxide level of less than 1.5 WT%.
WSR 301 Fine Powder	4,000,000	1,650 to 5,500 cP	Lubricant, foam stabilizer, water retention aid, binder, thickener

This review article aims to provide a comprehensive overview of the pharmaceutical applications of different grades of PEO. We will discuss the properties of PEO and how they are influenced by its molecular weight, and explore the diverse applications of PEO in drug delivery, biomaterials, and other pharmaceutical areas. By understanding the relationship between PEO's molecular weight and its applications, we can understand its versatility and potential for future advancements in the pharmaceutical industry.

Relationship between Molecular Weight and Properties of PEO

The molecular weight of polyethylene oxide (PEO) significantly influences its physical and chemical properties, which in turn determine its suitability for various pharmaceutical applications. Low molecular weight PEO exhibits high solubility, low viscosity, and rapid drug release. As molecular weight increases, PEO becomes less soluble, more viscous, and forms thicker, more rigid films. High molecular weight PEO is often used in applications requiring sustained drug release, tissue engineering, and medical devices due to its mechanical strength and biocompatibility. Intermediate molecular weight PEO offers a balance between the properties of low and high molecular weight PEO, making it suitable for a wide range of applications. Understanding the relationship between molecular weight and PEO's properties is essential for selecting the appropriate grade for specific pharmaceutical formulations (Table 2).

Table 2: Classification of PEO based on their Molecular Weights and Properties

Property	Low Molecular Weight PEO (< 1,00,000)	Intermediate Molecular Weight PEO (1,00,000 to 10,00,000)	High Molecular Weight PEO (> 10,00,000)
Solubility	Readily soluble in water and most organic solvents	Generally soluble in water and organic solvents	Less soluble in water and organic solvents, especially at higher concentrations
Viscosity	Low viscosity solutions	Moderate viscosity solutions	High viscosity solutions

Table 2: *(Continued)*

Property	Low Molecular Weight PEO (< 1,00,000)	Intermediate Molecular Weight PEO (1,00,000 to 10,00,000)	High Molecular Weight PEO (> 10,00,000)
Film Formation	Forms thin, flexible films	Forms films with intermediate properties between low and high molecular weight	Forms thicker, more rigid films
Biocompatibility	Generally considered biocompatible	Generally considered biocompatible	May exhibit increased biocompatibility or biodegradability depending on specific applications and modifications
Drug Release	May enhance drug release rates	Can provide moderate drug release	Can provide sustained drug release
Biomaterials	Used in coatings, hydrogels, and drug delivery systems	Used in various biomaterial applications	Often used in tissue engineering and medical devices
Excipients	Used as a plasticizer, surfactant, and solubilizer	Used in various excipient applications	Employed as a binder, thickener, and tablet coating agent

Pharmaceutical Applications of PEO

There are many applications of PEO in drug delivery and pharmaceutical formulation development. However, in the current an extensive review is done on the following applications of PEO as hydrogel, osmotic drug delivery, mucoadhesive drug delivery system, gastro-retentive drug delivery system and hot melt extrusion.

PEO as Hydrogel

The different grades of PEO have been reported in the formulation development of gel for different drugs. Polyethylene oxide (PEO) is a versatile polymer widely utilized in the pharmaceutical industry, particularly in the formulation of gels. Its high molecular weight and hydrophilic nature make it an excellent candidate for creating gels with desirable properties such as high viscosity, stability, and controlled drug release. PEO's ability to form a gel upon hydration and its significant swelling capacity enhance its application in various drug delivery systems. Additionally, PEO's compatibility with other polymers allows for the customization of gel formulations to meet specific therapeutic need. PEO has been used in the formulation development of gels, hydrogels, liposomes, polymeric nanoparticles and micelles.

Stringer IL et al., 1996 [6] attempted crosslinking of PEO using gamma radiation for three different grades of PEO vis-a vis PEO (35,000, 9,00,000 & 50,00,000 Mw) at various concentration levels. They reported that partitioning of model drug i.e., theophylline decreased with increase in molecular weight concentration of PEO. Transport of solute was not affected by the cross-linking. Bergstrand N et al., 2004 [7] worked to improve the stability of DOPE liposomes. They reported that use of PEO triblock copolymer by co-polymerization method improved the stability of liposomes due to the presence of PEO segment length in liposomes. Crcareveska M.S et al., 2013 [8] conducted research on improving the loading of irinotecan HCl in to nanoparticles. These nanoparticles were prepared by precipitation method. Kanjickal et al., 2008 [9] investigated the methods of sterilization on the properties of PEO gels. They reported that method of sterilization had on significant impact on swelling of PEO based hydrogels where as hydrogen peroxide sterilization increased the degree of swelling. The summary of literature on applications PEO as hydrogel are presented in Table 3.

Table 3: Literature on PEO as Hydrogel

Drug	Objective	Formulation	Method	PEO	Results	References
Theophylline	development of an experimental method for the preparation of PEO gels.	Gel	Cross linking of PEO using Gamma radiation	PEO 35000 PEO 900000 PEO 5000000	Partition coefficients decreased with increasing concentration of PEO.	6
Hydrophilic markers	stability of dioleoylphosphatidylethanolamine (DOPE) liposomes	Liposome	copolymerization	PEO triblock copolymer	PEO segment lengths protected liposomes	7

Table 3: *(Continued)*

Drug	Objective	Formulation	Method	PEO	Results	References
Irinotecan HCl	To improve incorporation of hydrophilic drug	LGA/PEO–PPO–PEO blended nanoparticles	Nano-precipitation method	PEO–PPO–PEO	Prolonged circulation time for nanoparticles	[8]
Cyclosporin A Rhodamine B	To study the effect of sterilization on poly(ethylene glycol)	Hydrogel	Effect of sterilization methods	PEO 2250 PEO 800	Ethylene oxide and gamma sterilization reduced swelling. Hydrogen peroxide sterilization led to increase in swelling.	[9]
Fentanyl	to investigate the feasibility of PEO–PPO–PEO copolymer gel	Gel Polymeric micelle	Cold method	PEO–PPO–PEO copolymer	Prolonging percutaneous input into the systemic circulation in the rabbit.	[10]

PEO in osmotic pumps

Polyethylene oxide (PEO) has emerged as a crucial component in the development of advanced drug delivery systems, particularly osmotic pumps. Its unique properties, including biocompatibility, non-toxicity, and ease of processing, make it an ideal candidate for various pharmaceutical applications. By incorporating PEO into osmotic pump formulations, researchers can fine-tune drug release profiles, enhance drug stability, and improve overall system performance. This review will delve into the specific roles of PEO in osmotic pump design, focusing on its impact on membrane permeability, drug release kinetics, and overall system efficacy.

Emara LH et al., 2012 [11] prepared osmotic pump tablet of Diclofenac Na for zero order drug delivery. It was prepared by non-aqueous wet granulation method using two grades of PEO (mw 3,00,000) and PEO (mw 9,00,000). They reported inversely proportional relationship between molecular weight of PEO and release of Dicofenac Na. The selected osmotic tablet formulation exhibited zero order drug delivery. Wu C et al., 2014 [12] designed push pull osmotic pump by using PEO (mw 1,00,000) and PEO (mw 60,00,000) as suspending and expanding agent respectively. The push pull osmotic pump was loaded with mesopores silica nanoparticles of felodipine. The research findings suggest improvement in bioavailability and reduction in fluctuation in plasma drug concentrations. Li Y et al., 2019 [13] attempted to develop double layered osmotic pump tablets for actrait using two grades of PEO i.e. PEO N 80, PEO WSR 303. The results indicated better therapeutic effects in the treatment of rheumatoid arthritis. Kumar P et al., 2009 [14] embarked on the development of elementary osmotic pump for tramadol HCl by using PEO (mw 3,00,000). The osmotic pump tablet was prepared by direct compression method followed by subsequent coating the formulation exhibited zero order drug release with swelling controlled release mechanism. The summary of literature in role of PEO in osmotic drug delivery system is presented in Table 4.

Table 4: Literature review on role of PEO in Osmotic DDS

Drug	Objective	Formulation	Method	PEO	Results	References
Diclofenac Sodium (DS)	zero-order deliver	Osmotic pump tablet	Non aqueous wet granulation	PEO 3,00,000 And 9,00,000	Release rate of DS decreased as PEO molecular weight increased.	[11]
felodipine	to improve drug dissolution	push–pull osmotic pump	Direct compression followed by coating	PEO (Mw 100,000) and PEO (Mw 6,000,000)	Mesoporous silica nanoparticles effectively increased the bioavailability and reduced fluctuations in its plasma concentration.	[12]
Actarit	Improved drug delivery	double-layered osmotic pump tablets	Granulation, compression and then coating	PEON80 PEOWSR303	designed actarit osmotic pump tablets can be applied for rheumatoid arthritis	[13]
Tramadol HCl	To achieve zero order DD	Elementary osmotic pump	Direct compression followed by coating	PEO300000	Drug release was inversely proportional to the level of swellable polymer (PEO)	[14]
Topiramate	Extended release	controlled release push-pull osmotic pump (PPOP) tablets	Double compression method	Polyethylene oxides (PEO) with a wide range of molecular weight	drug plasma levels with lower fluctuations could also be achieved	[15]

PEO as Mucoadhesive

Polyethylene oxide (PEO) plays a crucial role in the development of mucoadhesive drug delivery systems due to its unique physicochemical properties. As a hydrophilic polymer, PEO enhances the retention time of the delivery system on mucosa tissues, leading to a more controlled and sustained release of the active ingredient. Its film-forming ability, combined with its mucoadhesive properties, ensures that the drug remains at the site of application for an extended period, improving therapeutic efficacy. Additionally, PEO's versatility allows it to be used in various formulations, including buccal films, ocular inserts, and osmotic tablets. This makes it an invaluable component in designing advanced drug delivery systems aimed at optimizing drug release profiles and patient compliance.

Site M.B et al., 2020 [16] initiated a study on the development of mucoadhesive chitosan based nanofibers by electrospinning technique for a placebo mucoadhesive formulation. PEO of mw 900 KDa played a significant role in swelling nanofibers with significant mucoadhesive properties. Park J.S et al., 2002 [17] has undertaken the challenges of improved delivery of plasmid DNA through intra-nasal administration. The intranasal gel was prepared by using PEO and Poloxane. The results suggest improved rate and extent of absorption with mucoadhesion. Salehi S et al., 2011 [18] engaged in a research investigation on formulation of buccal films of Rizatropin benzoate (RB) by solvent optimum drug release and mucoadhesion. The summary of literature on role of PEG in development of mucoadhesive DDS are presented in Table 5.

Table 5: Literature review on role of PEO in Mucoadhesive and Gastro-retentive DDS

Drug/polymers	Objective	Formulation	Method	PEO	Results	References
Placebo	To overcome challenges associated with sub-lingual delivery	Mucoadhesive chitosan-based electrospun nanofibers for sub-lingual administration.	Electrospinning	PEO (Mw ~900 kDa)	The swelling of the nanofibers and dehydration of the mucosal tissue upon contact were found to be highly significant for mucoadhesion.	[16]
Plasmid DNA	To improve intranasal absoption of plasmid DNA	Intranasal	Continuous agitation	PEO, Polyox WSR-1105	rate and extent of nasal absorption could be controlled by choice of mucoadhesive polymers and their contents	[17]
Rizatriptan benzoate (RB)	To achieve control release	Buccal films	Solvent casting method	PEO	potential approach to achieve optimum drug release	[18]
poly(2-hydroxyethyl methacrylate) (PHEMA)	To increase the mucoadhesive capacity of PHEMA	PHEMA microparticles were loaded with linear PEO chains	suspension polymerization of HEMA monomer	PEO 1000 PEO 100000	Microparticles loaded with PEO 1000 showed nearly doubled mucoadhesive property.	[19]
NaCMC Polyacrylic acid (PAA), medium viscosity sodium alginate	To explore the possibility of using polymer blends for the preparation of nanofibres that offer substantial mucoadhesive capabilities.	Nanofibers with mucoadhesion	Continues agitation followed by pressurized gyration	PEO 200000 NaCMC Polyacrylic acid (PAA), medium viscosity sodium alginate	Blend containing carboxymethylcellulose and PEO consistently demonstrated the best prospect of mucoadhesion.	[20]
Methylene blue and phenylazoaniline	to formulate a slow dissolving bioadhesive matrix using PEO	Compacts	Direct compression method	Polyox WSR 301, polyox WSR co-agulant, and polyox WSR 303	PEO in combination with PVP yields a non- disintegrating bioadhesive tablet	[21]

Table 5: ***(Continued)***

Drug/polymers	Objective	Formulation	Method	PEO	Results	References
Diltiazem HCl	To evaluate the potential of PEO as a sole polymer for the controlled release gastric retention	Trilayer floating tablet	compression	PEO 20 L, PEO 40 L PEO 70 L	one can achieve complete zero-order release from a tri-layered tablet of a single grade of PEO	[22]
Allopurinol	to develop gastroretentive dosage form (GRDF) for allopurinol (ALP)	gastroretentive dosage form	Direct compression	polyoxyethylene oxide WSR 303 and sodium carboxymethyl cellulose	desired gastroretentive performance and drug release properties for ALP.	[23]
Alfuzosin HCl	Zero order delivery	Gastroretentive matrix	Direct compression	PEO	Exhibited enhanced bioavailability	[24]
Metformin HCl	Retention of dosage form in stomach	Tablets	Wet granulation method	Polyox WSR 301	tablets were able to float in less than 4 min and remained floating for more than 24 h	[25]

PEO as Gastro-retentive

Polyethylene oxide (PEO) is pivotal in the development of gastro-retentive drug delivery systems owing to its high molecular weight and hydrophilic nature. This polymer enhances the gastric residence time of the drug delivery system by forming a gel-like matrix in the acidic environment of the stomach, which prolongs the release of the active ingredient. The mucoadhesive properties of PEO ensure that the system adheres to the gastric mucosa, thereby improving the bioavailability of the drug. Additionally, PEO's swelling and erosion characteristics can be fine-tuned to achieve the desired release profile, making it a versatile component in gastro retentive formulations. The use of PEO in these systems not only improves patient compliance by reducing dosing frequency but also enhances therapeutic outcomes by maintaining consistent drug levels in the bloodstream.

Mahalingam R et al., 2009 [21] developed gastro-retentive bioadhesive matrix tablets of phenylazoaniline using three different grades of polyox such as WSR 301, WSR coagulant and WSR 303. The bioadhesive tablets were prepared by direct compression method. The combination of PEO and PVP yielded a non-disintegrating type bioadhesive tablet with increased retention time and sustain release. Raut Desai S et al., 2014 [22] formulated trilayered floating tablets of highly water soluble drug i.e., Diltiazem HCL using PEO as a sole polymer to achieve Zero order controlled release with gastric retention. Drug release was slower from high molecular weight PEO and the floating lag time of 3 to 4 min was attributed to the optimum amount of Sodium Bicarbonate. Sharma O.P.et al., 2015 [23] developed gastro-retentive dosage form of allopurinol using combined approach of mucoadhesion and floating system. They reported that appropriate combination of PEO and NaCMC exhibited desirable gastro-retentive properties like quicker buoyancy and longer duration of floating and higher mucoadhesive force. Liu a et al., 2008 [24] reported zero order delivery of Alfuzosin HCl from gastro-retentive layered matrix tablets. The summarized literature on role of PEG in development of gastro-retentive DDS is presented in Table 5.

PEO in Hot melt extrusion

Polyethylene oxide (PEO) is integral to the hot melt extrusion (HME) process due to its excellent thermoplastic properties. As a high molecular weight polymer, PEO facilitates the formation of a stable melt that can be processed at relatively low temperatures, preserving the integrity of heat-sensitive drugs. Its ability to form a homogeneous matrix ensures uniform drug distribution, which is crucial for consistent drug release profiles. Additionally, PEO's hydrophilic nature aids in enhancing the solubility and bioavailability of poorly water-soluble drugs when processed via HME. The versatility of PEO in adjusting the mechanical properties of the extrudate allows for the development of a wide range of dosage forms, including films, pellets, and implants. Its use in HME not only improves the manufacturability of pharmaceutical products but also enhances their therapeutic efficacy and patient compliance.

Cantin O et al., 2016 [26] studies about effect of molecular weight of PEO on the release of theophylline as hot melt extrude. The extrudes were prepared by fusion method. The theophylline release rate substantially decreased with increase in the molecular weight from 100 KDa to 600 KDa. But a further increase to 7000 KDa only led to a slight ad-

ditional decrease in release of Theophylline. Crowley M Metal., et al, 2002 [27] explored the thermal stability Chlorpheniramine maleate SR tablets prepared by using PEO as matrixing agents. HOT melt extrusion approach was found to be suitable for PEO based SR tablets. They reported that stability of PEO exhibited increased degradation when stored above its melting point. PEO also showed oxidative degradation when stored below its melting point due to permeation of oxygen in the amorphous region of polymer. Catin O et al., 2021 [28] examined the importance of type of drug and loading for PEO based hot melt extrudes. They performed the experiment by taking 3 model drugs i.e., theophylline, Ibuprofen and metroprolol tartarate. They reported that molecular weight of PEO and solubility of drug played a significant role. In case of highly water soluble drug , Metroprolol tartarate the drug release increased with increase in drug loading irrespective of molecular weight of PEO. This can be attributed to increased porosity effect. In case of sparingly water-soluble drugs like Theophilline and Ibuprofen, limited drug solubility effects played a pivotal role. The summarized literature on role of PEO in hot melt extrusion process is presented in Table 6.

Table 6: Literature review on role of PEO in Hot Melt Extrusion

Drug	Objective	Formulation	Method	PEO	Results	References
Theophylline, ibuprofen or metoprolol tartrate	To study PEO hot melt extrudates for controlled drug delivery: Importance of the type of drug and loading	Matrix tablets	Hot melt extrusion	Polyox WSR N-750, Polyox WSR N-12K, Polyox WSR-303	relative release rates always increased with increasing drug loading	[28]
chlorpheniramine maleate	To study the thermal stability of polyethylene oxide (PEO) in sustained release tablets	Sustain release tablets	Hot melt extrusion	PEO 10 L	thermal stability of PEO was dependent on both the storage temperature and the molecular weight of the polymer	[27]
Theophylline	To study the effects of changes in the molecular weight of PEO on theophylline release	Extrudes	Fusion	Polyox WSR N-10, 80, 750. Polyox WSR-60,105,205,301, 303. Polyox WSR Coagulant	The theophylline release rate decreased with increase in the PEO molecular weight from 100 kDa to 600 kDa, but a further increase to 7,000 kDa only led to a slight additional decrease in the drug release rate.	[26]
guaifenesin and ketoprofen	To investigate thermal properties of the hot-melt extruded films were investigated	Films	Hot melt extrusion	Polyethylene oxide (Polyox WSR-N80, molecular weight 200,000)	The percent elongation decreased with increasing GFN concentrations and significantly increased with increasing levels of KTP.	[29]
nifedipine	To investigate Poly(ethylene oxide) (PEO) as a drug carrier in hot-melt extrusion	extrudes	Hot melt (Twin screw extrusion)	(POLYOX® WSR N-80) 2L Da	Such a drug/ PEO solid dispersion system can potentially be used for solubility enhancement of poorly soluble compounds.	[30]

CONCLUSION

Polyethylene oxide (PEO) has proven to be a remarkably versatile polymer in pharmaceutical product development, with significant applications across various drug delivery systems. Its hydrophilic properties and excellent gel-forming capabilities make PEO an ideal candidate for hydrogel formulations, enhancing drug stability and controlled release. In osmotic pumps, PEO contributes to the precise regulation of drug release by ensuring consistent osmotic pressure and drug solubility. The mucoadhesive properties of PEO improve the retention and bioavailability of drugs in mucoadhesive drug delivery systems, ensuring sustained therapeutic effects. Furthermore, in gastro-retentive drug delivery systems, PEO prolongs gastric residence time, enhancing the bioavailability of drugs that are primarily absorbed in the stomach. Finally, its thermoplastic characteristics make PEO a crucial component in hot melt extrusion processes, facilitating the formation of homogenous drug-polymer matrices and improving the solubility of poorly water-soluble drugs. Overall, PEO's multifaceted applications underscore its critical role in advancing pharmaceutical formulations and improving patient outcomes.

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Authors' Contribution

Dinesh Kumar Das collected the literature information and prepared the tables.

Anjan Kumar conceptualized the topic, designed the structure of manuscript and corrected the manuscript.

Ch. Niranjan Patra contributed in reference collection and English editing.

REFERENCES

1. Hussain G, Al-Ghamdi K. PEO coating as lubrication means for SPIF of titanium sheet: characteristics and performance. Mater Res Innov 2014; 18 (2): 727-733.
2. Kim M, Vala M, Ertsgaard CT, Oh SH, Lodge TP, Bates J, et al. Surface plasmon resonance study of the binding of PEO–PPO–PEO triblock copolymer and PEO homopolymer to supported lipid bilayers. Langmuir 2018; 34 (23): 6703-6712.
3. Khan K, Hanif MB, Xin H, Hussain A, Ali HG, Fu B, et al. PEO-Based Solid Composite Polymer Electrolyte for High Capacity Retention All-Solid-State Lithium Metal Battery. Small. 2024; 20 (4): 57-72.
4. Rivero D, Gouveia LM, Müller AJ, Saez AE. Shear-thickening behavior of high molecular weight poly (ethylene oxide) solutions. Rheologica Acta 2012; 51: 13-20.
5. Ahmed HT, Abdullah OG. Preparation and composition optimization of PEO: MC polymer blend films to enhance electrical conductivity. Polymers. 2019, 11 (5), 853.
6. Stringer JL, Peppas NA. Diffusion of small molecular weight drugs in radiation-crosslinked poly (ethylene oxide) hydrogels. Journal of Controlled Release (JCR). 1996; 42 (2): 195-202.
7. Bergstrand N, Edwards K. Effects of poly (ethylene oxide)–poly (propylene oxide)–poly (ethylene oxide) triblock copolymers on structure and stability of liposomal dioleoylphosphatidylethanolamine. J Colloid and Interface Sci. 2004; 276 (2): 400-407.
8. Crcarevska MS, Geskovski N, Calis S, Dimchevska S, Kuzmanovska S, Petrusevski G, et al. Definition of formulation design space, *in vitro* bioactivity and *in vivo* biodistribution for hydrophilic drug loaded PLGA/PEO–PPO–PEO nanoparticles using OFAT experiments. Eur J Pharm Sci. 2013; 49 (1): 65-80.
9. Kanjickal D, Lopina S, Evancho-Chapman MM, Schmidt S, Donovan D. Effects of sterilization on poly (ethylene glycol) hydrogels. J Biomed Mater Res Part A: An Official Journal of The Society for Biomaterials, The Japanese Society for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials. 2008; 87 (3): 608-617.
10. Liaw J, Lin YC. Evaluation of poly (ethylene oxide)–poly (propylene oxide)–poly (ethylene oxide)(PEO–PPO–PEO) gels as a release vehicle for percutaneous fentanyl. Journal of Controlled Release (JCR). 2000; 68 (2): 273-282.
11. Emara LH, Taha NF, Badr RM, Mursi NM. Development of an osmotic pump system for controlled delivery of diclofenac sodium. Drug Discoveries & Therapeutics. 2012; 6 (5): 269-277.
12. Wu C, Zhao Z, Zhao Y, Hao Y, Liu Y, Liu C. Preparation of a push–pull osmotic pump of felodipine solubilized by mesoporous silica nanoparticles with a core–shell structure. Inter J Pharm. 2014; 475 (1-2); 298-305.
13. Li Y, Pan H, Duan H, Chen J, Zhu Z, Fan J, et al. Double-layered osmotic pump controlled release tablets of actarit: *In vitro* and *in vivo* evaluation. Asian J Pharm Sci. 2019; 14 (3); 340-348.
14. Kumar P, Singh S, Mishra B. Development and evaluation of elementary osmotic pump of highly water-soluble drug: tramadol hydrochloride. Curr Drug Deliv. 2009; 6 (1): 130-139.
15. Lin W, Li Y, Shi Q, Liao X, Zeng Y, Tian W, et al. Preparation and evaluation of bilayer-core osmotic pump tablets contained topiramate. Plos One. 2022; 17 (2): e0264457.
16. Stie MB, Gätke JR, Wan F, Chronakis IS, Jacobsen J, Nielsen HM. Swelling of mucoadhesive electrospun chitosan/polyethylene oxide nanofibers facilitates adhesion to the sublingual mucosa. Carbohydrate polymers. 2020; 242: 116-128.
17. Park JS, Oh YK, Yoon H, Kim JM, Kim CK. In situ gelling and mucoadhesive polymer vehicles for controlled intranasal delivery of plasmid DNA. Journal of Biomedical Materials Research: An Official Journal of The Society for Biomaterials and The Japanese Society for Biomaterials. 2002; 59 (1): 144-151.
18. Salehi S, Boddohi S. New formulation and approach for mucoadhesive buccal film of rizatriptan benzoate. Progress in biomaterials. 2017; 6: 175-187.
19. De Ascentiis A, Degrazia JL, Bowman CN, Colombo P, Peppas NA. Mucoadhesion of poly (2-hydroxyethyl methacrylate) is improved when linear poly (ethylene oxide) chains are added to the polymer network. Journal of controlled release (JCR). 1995;

33 (1): 197-201.
20. Brako F, Raimi-Abraham B, Mahalingam S, Craig DQ, Edirisinghe M. Making nanofibres of mucoadhesive polymer blends for vaginal therapies. European Polymer Journal. 2015; 70: 186-196.
21. Mahalingam R, Jasti B, Birudaraj R, Stefanidis D, Killion R. Alfredson T. et al. Evaluation of polyethylene oxide compacts as gastroretentive delivery systems. AAPS PharmSciTech. 2009; 10: 98-103.
22. Raut DS, Rohera BD. Formulation, *in vitro* evaluation and study of variables on tri-layered gastro-retentive delivery system of diltiazem HCl. Drug development and industrial pharmacy. 2014; 40 (3): 380-389.
23. Sharma OP, Shah MV, Parikh DC, Mehta TA. Formulation optimization of gastroretentive drug delivery system for allopurinol using experimental design. Expert Opinion on Drug Delivery. 2015; 12 (4): 513-524.
24. Liu Q, Fassihi R. Zero-order delivery of a highly soluble, low dose drug alfuzosin hydrochloride via gastro-retentive system. Inter J Pharm. 2008; 348 (1-2): 27-34.
25. Senjoti FG, Jaffri JM, Mandal UK. In Fabrication and optimization of gastro retentive drug delivery system with HPMC and polyethylene oxide (PEO) matrix, International Conference on Pharmaceutical Sciences and Biomedical and Chemical Engineering. Kuantan, Malaysia: Kulliyyah of Pharmacy International Islamic University Malaysia (IIUM). 2014; pp 113-7.
26. Cantin O, Siepmann F, Danede F, Willart J, Karrout Y, Siepmann J. PEO hot melt extrudates for controlled drug delivery: Importance of the molecular weight. Journal of Drug Delivery Science and Technology. 2016; 36:; 130-140.
27. Crowley MM, Zhang F, Koleng JJ, McGinity JW. Stability of polyethylene oxide in matrix tablets prepared by hot-melt extrusion. Biomaterials. 2002; 23 (21): 4241-4248.
28. Cantin O, Siepmann F, Willart JF, Danede F, Siepmann J, Karrout Y. PEO hot melt extrudates for controlled drug delivery: Importance of the type of drug and loading. J Drug Deliv SciTechnol. 2021; 61: 102-238.
29. Crowley M M, Fredersdorf A, Schroeder B, Kucera S, Prodduturi S, Repka M A, et al. The influence of guaifenesin and ketoprofen on the properties of hot-melt extruded polyethylene oxide films. Eur J Pharm Sci. 2004; 22 (5): 409-418.
30. Li L, AbuBaker O, Shao Z J. Characterization of poly (ethylene oxide) as a drug carrier in hot-melt extrusion. Drug development and industrial pharmacy. 2006;32 (8): 991-1002.