International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 20-10-2025, Accepted: 19-11-2025, Published: 04-12-2025
Volume 10, Issue 4, 2025, Page No. 92-99

Recent advances in the use of polymers for bilayer tablet formulation and drug delivery

Deepika Gupta[2], Manju Pandey[1*], Neelkanth M Pujari[3]
[1] Institute of Pharmacy, Shri Ramswaroop Memorial University, Barabanki, Uttar Pradesh, India
[2] Maharishi School of Pharmaceutical Sciences, Maharishi University of Information Technology, Lucknow, Uttar Pradesh, India
[3] Department of Pharmacy, Dr. APJ Abdul Kalam Technical University, Lucknow, Uttar Pradesh, India

Abstract
Bilayer tablets represent an advanced oral drug-delivery platform designed to incorporate two active pharmaceutical ingredients (APIs) or two distinct release profiles in a single dosage form. Polymers play a fundamental role in the structural integrity, release modulation, stability, and biopharmaceutical performance of bilayer systems. Recent research has focused on polymer innovation, including novel synthetic and natural polymers, polymer blends, and smart or stimuli-responsive materials. Advances in molecular modeling, computational simulations, and polymer engineering have significantly improved polymer selection and optimization processes. Additionally, polymer-based strategies—such as controlled, delayed, targeted, mucoadhesive, and pH-responsive systems—offer enhanced drug-release precision and patient compliance. Despite their therapeutic advantages, bilayer tablets face formulation and manufacturing challenges, including layer separation, mechanical weakness, and stability issues. Emerging solutions, such as co-processed excipients, hot-melt extrusion, additive manufacturing, and advanced characterization techniques, continue to strengthen the reliability of polymer-based bilayer dosage forms. This review outlines recent progress in polymer science, formulation strategies, evaluation methods, and future opportunities for polymer-driven innovation in bilayer tablet technology.

Keywords: Bilayer tablets, polymers, controlled release, drug delivery, polymer optimization, stimuli-responsive polymers, mucoadhesive systems, formulation challenges

Introduction

Bilayer tablets are a type of pharmaceutical formulation that consists of two distinct layers, typically stacked on top of each other within a single tablet. Each layer is designed to have specific properties and functions, allowing for controlled drug delivery and enhanced therapeutic outcomes. The first layer, known as the immediate-release layer, releases the drug rapidly upon administration, providing an initial dose. The second layer, referred to as the sustained-release layer, releases the drug slowly and steadily over an extended period of time, maintaining therapeutic levels in the body.

The advantages of bilayer tablets in drug delivery are several-fold. Firstly, the biphasic release profile of bilayer tablets allows for optimized drug release kinetics, providing both an immediate and sustained drug release. This can be particularly beneficial for drugs that require rapid onset of action followed by a prolonged duration of therapeutic effect, such as in chronic conditions. Secondly, the use of bilayer tablets can help reduce dosing frequency, as the sustained-release layer can extend the drug's duration of action, resulting in improved patient compliance. Additionally, bilayer tablets can provide flexibility in dosing regimens, allowing for customized drug release profiles to match the specific therapeutic needs of a patient. Furthermore, bilayer tablets can also be used for combination therapy, where different drugs or doses can be incorporated into separate layers, enabling multiple drugs to be delivered simultaneously in a single tablet.

Several studies have highlighted the advantages of bilayer tablets in drug delivery. For example, bilayer tablets of metformin and glimepiride exhibited better glycemic control and reduced dosing frequency compared to conventional single-layer tablets. Another example like bilayer tablets of carvedilol showed sustained release and improved bioavailability compared to single-layer tablets.

Bilayer tablets are a promising approach in drug delivery, offering advantages such as optimized drug release kinetics, improved patient compliance, flexibility in dosing regimens, and potential for combination therapy. Further research and development in this area hold promise for the development of innovative and effective pharmaceutical formulations

Polymers are versatile materials that have found numerous applications in the field of pharmaceuticals, including drug delivery systems. One of the key areas where polymers play a critical role is in the formulation of bilayer tablets, which are tablets consisting of two distinct layers with different drug release profiles. Bilayer tablets offer advantages such as improved patient compliance, reduced dosing frequency, and enhanced therapeutic efficacy. Polymers are used in bilayer tablet formulations to achieve various functions, such as controlling drug release, providing structural integrity, improving stability, and enhancing drug bioavailability.

Importance of Polymers in Bilayer Tablet Formulation

1. **Drug Release Control:** Polymers are widely used in bilayer tablet formulations to control the release of drugs from different layers. The selection of appropriate polymers with specific properties, such as solubility, swelling, and erosion behavior, can be used to achieve different drug release profiles, such as immediate release, sustained release, or delayed release. For example, hydroxypropyl methylcellulose (HPMC).

2. **Structural Integrity:** Polymers are crucial in providing structural integrity to bilayer tablets. They act as binding agents, helping to hold the different layers together and preventing layer separation during manufacturing, packaging, and storage. Polymers such as polyvinylpyrrolidone (PVP) and polyvinyl alcohol (PVA) are commonly used as binders in bilayer tablets.

3. **Stability Enhancement:** Polymers play a significant role in enhancing the stability of bilayer tablets. They can protect the drug from degradation by providing a physical barrier against environmental factors such as moisture, light, and oxygen, which can adversely affect drug stability. Polymers with low permeability, such as ethyl cellulose, are often used as barrier coatings in bilayer tablets to protect the drug from environmental degradation and ensure its shelf-life stability.

4. **Drug Bioavailability:** Polymers can also impact the bioavailability of drugs in bilayer tablets. They can modify the drug's dissolution rate and improve its solubility, leading to enhanced drug absorption and bioavailability. Polymers such as cyclodextrins and solid dispersions are commonly used in bilayer tablets to improve drug solubility and bioavailability.

The objective of the review paper is to provide a comprehensive overview of recent advances in the use of polymers for bilayer tablet formulation and drug delivery. This includes summarizing the latest research findings, technological advancements, and applications of polymers in the development of bilayer tablets for drug delivery purposes. It also seeks to highlight the challenges and future prospects of polymer-based bilayer tablets in drug delivery, with a focus on novel strategies, innovative formulations, and emerging trends in this field.

Overview of Polymers for Bilayer Tablet Formulation

Polymers play a crucial role in the formulation of bilayer tablets, as they are used as excipients to provide structural integrity, control drug release, and improve overall performance. Some commonly used polymers for bilayer tablet formulation:

1. **Cellulose derivatives:** Cellulose derivatives such as hydroxypropyl methylcellulose (HPMC), hydroxyethyl cellulose (HEC), and methylcellulose (MC) are widely used in bilayer tablet formulations due to their excellent film-forming properties, good mechanical strength, and controlled drug release characteristics.

2. **Polyvinylpyrrolidone (PVP):** PVP is a water-soluble polymer that is commonly used in bilayer tablet formulations as a binder and disintegrant. It has good adhesive properties and can be used to improve the mechanical strength of the immediate-release layer.

3. **Polyethylene oxide (PEO):** PEO is a water-soluble polymer that is often used in bilayer tablet formulations as a matrix former in controlled-release layers. It forms a gel-like matrix when hydrated, which can control the release of the drug from the tablet.

4. **Ethyl cellulose (EC):** EC is a cellulose derivative that is commonly used in bilayer tablet formulations as a barrier coating material. It provides excellent moisture protection and is often used in the outer layer of the tablet to prevent drug degradation caused by moisture or oxygen.

5. **Polyvinyl alcohol (PVA):** PVA is a water-soluble polymer that is often used in bilayer tablet formulations as a binder and disintegrant. It has good film-forming properties and can be used to improve the mechanical strength of the immediate-release layer.

These are just some of the commonly used polymers in bilayer tablet formulations. Other polymers such as polyacrylates, polyvinyl acetate, and polyethylene glycol (PEG) are also used depending on the specific formulation requirements.

Polymers used in bilayer tablets need to possess specific characteristics to ensure the tablets are effective and meet the intended therapeutic goals. Here are some properties and characteristics of polymers that make them suitable for bilayer tablet:

1. **Controlled release:** Polymers with controlled release properties can regulate the release of active pharmaceutical ingredients (APIs) from the tablet, ensuring a sustained and controlled drug release profile. This can be important for drugs that require extended-release or targeted delivery to achieve optimal therapeutic effects [4]. See fig 1

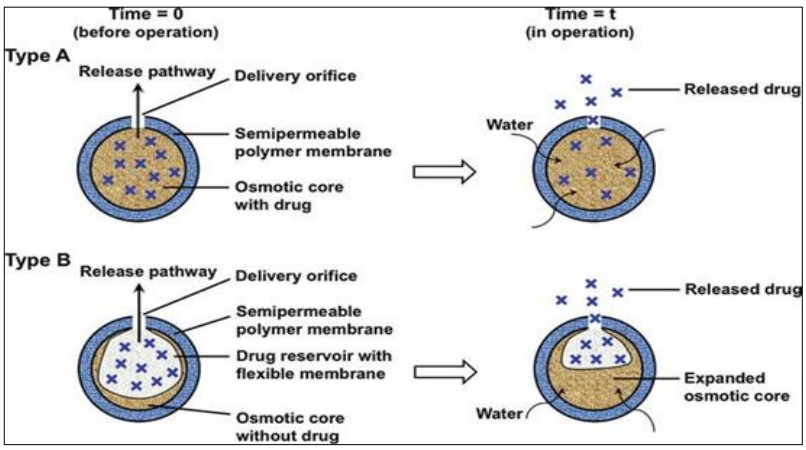

Fig 1: Different release pathway

2. **Compatibility with APIs:** Polymers used in bilayer tablets should be compatible with the APIs they are intended to encapsulate. Compatibility includes chemical stability, lack of interaction, and preservation of API efficacy during storage and use [5].

3. **Mechanical strength:** Polymers with sufficient mechanical strength are required to withstand the manufacturing process of tablet compression and handling during storage, transportation, and use without cracking or breaking [6].

4. **Film-forming ability:** Polymers that can form a uniform and stable film are often used as coating materials in bilayer tablets to provide protection, control drug release, and improve patient acceptability [7].

5. **Biocompatibility:** Polymers used in bilayer tablets should be biocompatible, meaning they do not cause adverse effects or toxicity in the body. Biocompatibility is particularly important for oral pharmaceuticals that are ingested by patients [8].

6. **Regulatory compliance:** Polymers used in bilayer tablets should comply with regulatory requirements for pharmaceuticals, such as those set forth by regulatory agencies such as the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA) [9].

It's important to note that the selection of polymers for bilayer tablets depends on the specific formulation and intended use, and should be based on thorough scientific evaluation and regulatory compliance.

Recent Advances in Polymer Selection and Optimization

Table 1: Summarized review on novel polymers or polymer combinations used in bilayer tablet formulation

Polymer(s) or Polymer Combination(s)	Specific Properties	Advantages	Disadvantages	References
Hydroxypropyl methylcellulose (HPMC) and Eudragit®	HPMC provides controlled release, Eudragit® provides pH-dependent release	▪ Dual release profiles possible ▪ pH-dependent release ▪ Enhanced stability ▪ Suitable for moisture-sensitive drugs	▪ Relatively high cost ▪ Limited availability of specific grades	[11]
Polyvinyl alcohol (PVA) and Polycaprolactone (PCL)	PVA provides immediate release, PCL provides sustained release	▪ Simple and cost-effective ▪ Tailored release profiles possible ▪ Enhanced drug stability	▪ PCL may have a slow degradation rate ▪ Potential for PCL crystallization	[12]
Chitosan and Alginate	Chitosan provides mucoadhesion, Alginate provides controlled release	▪ Mucoadhesive properties ▪ pH-dependent release ▪ Biocompatible and biodegradable	▪ Limited drug loading capacity ▪ Potential for batch-to-batch variability in chitosan properties	[13]
Eudragit® and Polyethylene oxide (PEO)	Eudragit® provides pH-dependent release, PEO provides controlled release	▪ pH-dependent release ▪ Enhanced drug stability ▪ Suitable for moisture-sensitive drugs	▪ Limited drug loading capacity ▪ PEO may affect tablet hardness	[14]
Hydroxypropyl cellulose (HPC) and Eudragit®	HPC provides immediate release, Eudragit® provides sustained release	▪ Tailored release profiles possible ▪ Enhanced drug stability ▪ Suitable for moisture-sensitive drugs	▪ Relatively high cost ▪ Limited availability of specific grades	[15]

Advanced techniques, such as molecular modeling and simulation, have become invaluable tools in the selection and optimization of polymers for bilayer tablets. These techniques enable researchers to gain insights into the molecular-level interactions and properties of polymers, which can guide the design and optimization of bilayer tablets with improved drug delivery performance [16].
Molecular modeling involves the use of computational methods to simulate the behavior of molecules and materials at the molecular level see fig 2. It allows researchers to predict the physical and chemical properties of polymers, such as their solubility, permeability, and mechanical strength, which are critical factors in the performance of bilayer tablets. Molecular modeling techniques, such as quantum mechanics (QM) and molecular dynamics (MD) simulations, have been widely used to study the behavior of polymers in various environments, including in the presence of drugs, excipients, and physiological fluids [17].

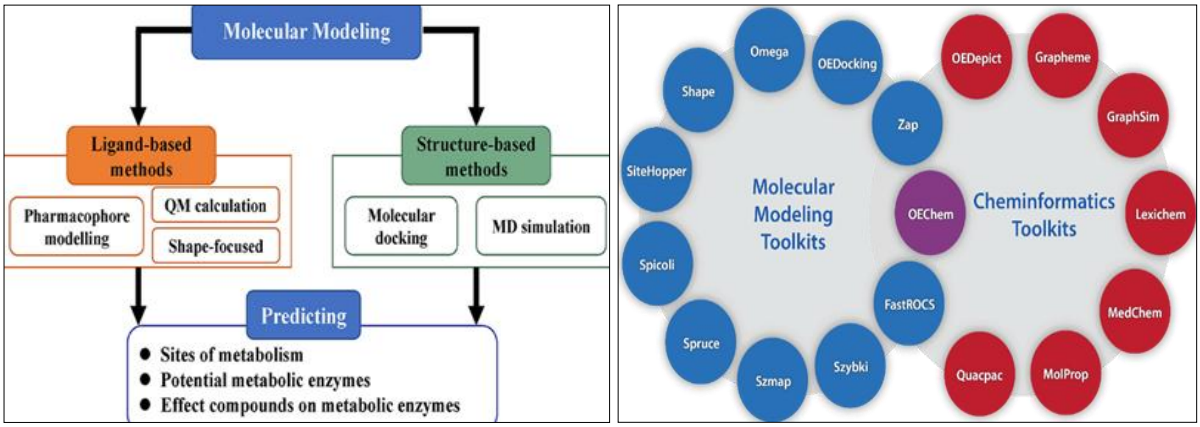

Fig 2: Molecular modelling by omputational method to design and optimization of bilayer tablets

For example, QM calculations can provide insights into the electronic and structural properties of polymers, such as their molecular orbitals, bond lengths, and bond angles. These properties can influence the interactions between polymers and drugs, as well as the mechanical properties of bilayer tablets. MD simulations, on the other hand, can provide information on the dynamic behavior and conformational changes of polymers in response to external stimuli, such as temperature, pressure, and pH. MD simulations can also be used to investigate the diffusion of drugs and excipients within polymers, which can impact the drug release behavior of bilayer tablets [18].

In addition to molecular modeling, advanced techniques such as coarse-grained simulations and free energy calculations can also be employed to study polymer behavior at larger length and time scales, respectively. Coarse-grained simulations simplify the molecular representation of polymers, allowing for the study of longer time scales and larger systems, while free energy calculations provide insights into the thermodynamics and kinetics of polymer-drug interactions [19].

The insights gained from molecular modeling and simulation can be used to guide the selection and optimization of polymers for bilayer tablets. For example, molecular modeling can help identify polymers with favorable drug-polymer interactions, such as hydrogen bonding, van der Waals interactions, and π-π stacking, which can enhance drug retention and release from bilayer tablets. MD simulations can provide information on the mechanical properties of polymers, such as their elasticity and plasticity, which can influence the mechanical stability and handling of bilayer tablets. Coarse-grained simulations can help optimize the formulation of bilayer tablets by predicting the optimal composition and thickness of polymer layers to achieve desired drug release profiles. Free energy calculations can be used to estimate the thermodynamic stability of polymer-drug complexes and predict the drug release kinetics from bilayer tablets [20].

Bilayer tablets consist of two distinct layers, typically a drug-containing layer and a drug-free layer, that are compressed together to form a single tablet. The properties of the polymers used in these layers significantly influence the drug release, stability, bioavailability, and overall performance of the bilayer tablets.

The importance of polymer selection and optimization in improving drug delivery performance of bilayer tablets

1. **Drug release control:** The polymer selection for the drug-containing layer in bilayer tablets determines the release rate of the drug, which is a critical parameter for achieving the desired therapeutic effect. Polymers with different physicochemical properties, such as solubility, permeability, and swelling behavior, can be chosen to achieve specific drug release profiles. For example, hydrophilic polymers like hydroxypropyl methylcellulose (HPMC) and polyethylene oxide (PEO) are commonly used to control the drug release from the matrix layer of bilayer tablets, as they can form a gel layer upon contact with water, thus retarding the drug release over time [21].

2. **Layer integrity and stability:** The polymer used in the drug-containing layer should be compatible with the drug and other excipients to maintain the layer integrity and stability during storage and transportation. Polymers with good mechanical strength, such as ethyl cellulose (EC) and polyvinyl alcohol (PVA), can be used to ensure the structural integrity of the drug-containing layer, preventing layer separation or delamination, which can affect the drug release performance [22].

3. **Drug protection:** Polymers used in the drug-containing layer can provide a protective barrier to the drug, shielding it from environmental factors such as moisture, light, and oxygen, which can degrade the drug and reduce its potency. Polymers with good barrier properties, such as polyvinyl chloride (PVC), polyvinylidene chloride (PVDC), and polyethylene terephthalate (PET), can be used in the drug-containing layer to ensure the stability of the drug during storage and transportation [23].

4. **Drug layer separation:** The polymer used in the drug-free layer of bilayer tablets should facilitate easy separation of the drug-containing layer during drug release. Polymers with low adhesion properties, such as magnesium stearate, talc, and colloidal silicon dioxide, are commonly used in the drug-free layer to prevent sticking between the two layers, ensuring proper drug release performance [24].

5. **Bioavailability enhancement:** Polymers used in bilayer tablets can also contribute to improving the bioavailability of poorly soluble drugs by enhancing their solubility, dissolution rate, and permeability. Polymers such as polyvinylpyrrolidone (PVP) and surfactants like sodium lauryl sulfate (SLS) can be used in the drug-containing layer to enhance drug dissolution and release, leading to improved bioavailability [25].

Table 2: Importance of polymer selection and optimization in improving drug delivery performance of bilayer tablets

Aspect	Importance	References
Polymer Selection	The choice of polymer in bilayer tablets can greatly impact drug release rates, bioavailability, stability, and patient compliance.	[26]
Polymer Compatibility	Optimal compatibility between the drug and polymer is crucial to prevent drug-polymer interactions, such as drug-polymer incompatibility or drug-polymer complex formation, which can affect drug release behavior and stability.	[27]
Polymer Properties	The physicochemical properties of the polymer, such as molecular weight, glass transition temperature, solubility, and swelling behavior, can impact drug release kinetics, mechanical strength, and stability of bilayer tablets.	[28]
Polymer Processing	The optimization of processing parameters, such as compression force, temperature, and dwell time, during bilayer tablet manufacturing can affect drug release, tablet hardness, and stability, and should be carefully considered in polymer selection and optimization.	[29]
Drug-Polymer Ratio	The ratio of drug to polymer in bilayer tablets can impact drug release kinetics, drug loading, and tablet	[30]

	properties. Optimization of this ratio is important to achieve desired drug delivery performance.	
Drug Release	Polymer selection and optimization can significantly impact drug release rates, leading to desired release profiles, sustained release, or targeted release for improved drug delivery performance.	[31]
Mechanical Strength	Appropriate polymer selection and optimization can enhance the mechanical strength of bilayer tablets, preventing physical damage during manufacturing, handling, and transport, and ensuring the tablets maintain their integrity for effective drug delivery.	[32]
Stability	Polymer selection and optimization can improve the stability of bilayer tablets by protecting the drug from degradation, moisture, and other environmental factors, thereby maintaining the drug's efficacy and shelf life.	[33]
Bioavailability	Appropriate polymer selection and optimization can enhance the bioavailability of drugs in bilayer tablets by improving their dissolution rates, solubility, and absorption, leading to increased therapeutic efficacy and patient compliance.	[34]
Drug Compatibility	Polymer selection and optimization are crucial in ensuring drug-polymer compatibility, preventing drug-polymer interactions that may result in drug degradation, reduced efficacy, or adverse effects, and ensuring safe and effective drug delivery.	[35]

Polymer-Based Strategies for Drug Delivery in Bilayer Tablets

Polymer-based strategies for drug delivery in bilayer tablets offer versatile approaches to achieve controlled release, delayed release, and targeted release of pharmaceutical compounds. These strategies involve the use of various polymers with specific properties to tailor the release kinetics and improve therapeutic outcomes.

1. Controlled Release

Its aim to provide a sustained and predictable release of the drug over an extended period. Several polymers have been employed to achieve controlled release in bilayer tablets, including:

a. Hydroxypropyl methylcellulose (HPMC): HPMC is a widely used hydrophilic polymer that forms a gel matrix upon hydration. It provides controlled drug release through diffusion and erosion mechanisms. The release rate can be modulated by varying the HPMC grade, viscosity, and concentration in the tablet formulation.

b. Eudragit® polymers: Eudragit® polymers, such as Eudragit® RS and Eudragit® RL, are pH-dependent polymers that exhibit different dissolution behaviors under acidic and alkaline conditions. These polymers can be used to formulate enteric-coated layers in bilayer tablets, providing controlled release in the desired region of the gastrointestinal tract [36].

2. Delayed Release

It is designed to release the drug at a specific time or location, such as in the intestine rather than the stomach. The following polymer-based strategies are commonly employed for delayed release:

a. Methacrylic acid copolymers: Such as Eudragit® L100 and Eudragit® S100, are pH-sensitive polymers that exhibit insolubility at low pH but dissolve rapidly at higher pH values. These polymers can be used to formulate delayed-release layers in bilayer tablets, ensuring drug release in the intestine [37].

b. Pectin: It is a natural polysaccharide derived from plants and can be used as a coating material for delayed release. Pectin gels in the presence of divalent cations, forming a barrier that delays drug release in the stomach but allows release in the intestine [38].

3. Targeted Release

Its aim to deliver the drug to a specific site or tissue, improving therapeutic efficacy and minimizing side effects. The following polymer-based strategies are employed for targeted release:

a. Polymeric nanoparticles: Such as poly (lactic-co-glycolic acid) (PLGA) nanoparticles, can encapsulate drugs and target specific tissues or cells. These nanoparticles can be incorporated into one of the bilayer tablet layers, allowing targeted drug delivery [39].

b. Chitosan: It is a natural cationic polysaccharide that exhibits mucoadhesive properties. It can be used to modify the surface of bilayer tablets, promoting targeted drug release in specific regions of the gastrointestinal tract [40].

Polymer-based drug delivery systems have gained significant attention in recent years due to their ability to improve the therapeutic efficacy, patient compliance, and targeted drug delivery. In this review, we will discuss the recent advances in three types of polymer-based drug delivery systems for bilayer tablets: stimuli-responsive polymers, pH-sensitive polymers, and mucoadhesive polymers.

1. Stimuli-Responsive Polymers

Stimuli-responsive polymers are designed to respond to specific stimuli in their surrounding environment, such as temperature, light, or pH, to release the drug in a controlled manner. They offer on-demand drug release, enabling targeted therapy and reducing side effects. Some notable examples include:

a. Thermoresponsive polymers: Thermoresponsive polymers, such as poly(N-isopropylacrylamide) (PNIPAAm), undergo a phase transition in response to temperature changes. These polymers can be incorporated into bilayer tablets to release the drug at a specific temperature, such as the body temperature [41].

b. Photoresponsive polymers: Photoresponsive polymers, like azobenzene-based polymers, can be triggered by specific wavelengths of light to undergo conformational changes, thereby releasing the drug. This controlled drug release mechanism has shown promise in targeted therapy [58].

2. pH-Sensitive Polymers

pH-sensitive polymers are designed to respond to changes in pH, such as those found in different regions of the gastrointestinal tract, for site-specific drug delivery. These

polymers can remain stable in one pH range and undergo swelling or dissolution in another pH range. Some examples of pH-sensitive polymers for bilayer tablets include:

a. **Methacrylic acid-based polymers:** Methacrylic acid-based polymers, such as Eudragit® series (e.g., Eudragit® S, L, and Eudragit® FS), are widely used in controlled drug release systems. These polymers remain intact in the acidic environment of the stomach and dissolve in the higher pH environment of the intestines, facilitating drug release [42].

b. **Chitosan-based polymers:** Chitosan is a natural polymer with pH-responsive properties. It can be used to form a pH-sensitive hydrogel layer in the bilayer tablet, enabling site-specific drug delivery to the colon, where the pH is relatively higher [43].

3. Mucoadhesive Polymers

Mucoadhesive polymers are designed to adhere to the mucosal surfaces, prolonging the residence time of the drug delivery system and enhancing drug absorption. They can improve the bioavailability of poorly absorbed drugs. Some notable mucoadhesive polymers for bilayer tablets include:

a. **Carbopol®:** Carbopol® is a commonly used mucoadhesive polymer that can form a gel-like structure upon hydration. It provides a prolonged release of drugs by adhering to the mucosal surfaces [44].

b. **Hyaluronic acid:** Hyaluronic acid is a naturally occurring mucoadhesive polymer that can be incorporated into bilayer tablets. It not only enhances mucoadhesion but also possesses anti-inflammatory properties, making it suitable for drug delivery in inflammatory conditions [45].

The use of polymers in bilayer tablet formulation offers unique advantages but also presents certain challenges related to compatibility, mechanical strength, and stability. Here are some of the key challenges associated with the use of polymers in bilayer tablet formulation, along with references for further reading:

Compatibility Issues

Drug-Polymer Compatibility: Certain drugs may exhibit incompatibilities with the polymers used in bilayer tablets, leading to issues such as drug degradation, reduced drug release, or altered drug stability. It is crucial to ensure compatibility between the drug and the polymer to maintain the desired therapeutic efficacy. Compatibility studies and selection of appropriate polymers are essential to address this challenge [46].

Polymer-Polymer Compatibility: In bilayer tablets, different polymers may be used in each layer. Compatibility between these polymers is crucial to prevent layer separation, interfacial interactions, or changes in drug release patterns. Careful consideration should be given to the selection of compatible polymer combinations to achieve a robust bilayer structure [51].

Mechanical Strength: Layer Adhesion and Cohesion: Achieving sufficient adhesion between the two layers of a bilayer tablet is crucial to maintain the integrity of the tablet during manufacturing, packaging, and handling. Insufficient adhesion can result in layer separation or tablet breakage. Proper selection of polymers, incorporation of adhesion-promoting excipients, and optimization of manufacturing processes are key considerations to enhance mechanical strength [47].

Compression Force Optimization: The compression force applied during the tablet manufacturing process can significantly impact the mechanical strength of bilayer tablets. Finding the right balance between compression force and polymer characteristics is essential to ensure tablet hardness, durability, and resistance to mechanical stress [48].

Stability

Moisture and Oxygen Barrier: Polymers used in bilayer tablets should possess adequate barrier properties against moisture and oxygen to prevent drug degradation and maintain stability throughout the product shelf life. Proper selection of moisture and oxygen barrier polymers or the incorporation of suitable coating technologies can help address stability challenges [49].

Photostability: Some drugs are sensitive to light exposure, which can lead to degradation. The choice of polymers with appropriate UV-blocking properties or the use of light-resistant packaging can help mitigate photostability issues in bilayer tablet formulations [50].

Conclusion

Polymers play a critical and multifaceted role in the development of bilayer tablets, enabling controlled, delayed, and targeted drug-release strategies. Recent advances in polymer innovation, molecular modeling, and drug-delivery technologies have significantly improved the design and performance of bilayer systems. Despite formulation and manufacturing challenges, innovative solutions such as co-processed excipients, hot-melt extrusion, and advanced evaluation methods have enhanced their reliability.

Future research should focus on smart polymer systems, personalized 3D-printed bilayer tablets, nanopolymer integrations, and predictive computational tools. The growing potential of polymers ensures that bilayer tablets will remain at the forefront of advanced oral drug-delivery technologies.

Acknowledgement

The authors sincerely express their gratitude to the Research and Consultancy Cell, SRMU, Barabanki, U.P., India; for their invaluable support and the provision of essential resources that facilitated the successful completion of this review study. Their unwavering assistance and encouragement are deeply appreciated.

References

1. Rekhi GS, Kildsig DO. Design and manufacture of pharmaceutical tablets. In: Lachman L, Lieberman HA, Kanig JL, editors. The Theory and Practice of Industrial Pharmacy. 3rd ed. Philadelphia, Lea and Febiger, 1986, 433–521.
2. Banker GS, Anderson NR. Tablets. In: Lachman L, Lieberman HA, Kanig JL, editors. The Theory and Practice of Industrial Pharmacy. 3rd ed. Philadelphia: Lea and Febiger, 1986, 293–345.

3. Rowe RC, Sheskey PJ, Quinn ME. Handbook of Pharmaceutical Excipients. 8th ed. London: Pharmaceutical Press, 2017.
4. Rathbone MJ, Hadgraft J, Roberts MS. Modified-release drug delivery technology. Boca Raton, CRC Press, 2016.
5. Brittain HG, editor. Polymorphism in pharmaceutical solids. Boca Raton: CRC Press, 2016.
6. Banker GS, Rhodes CT, editors. Modern pharmaceutics. Boca Raton, CRC Press, 2016.
7. Ghebre-Sellassie I, editor. Pharmaceutical film coatings and polymers. Boca Raton: CRC Press, 2017.
8. Ratner BD, Hoffman AS, Schoen FJ, Lemons JE. Biomaterials science an introduction to materials in medicine. San Diego: Academic Press, 2013.
9. United States Pharmacopeia National Formulary (USP–NF).
10. European Pharmacopoeia (Ph. Eur.).
11. Sharma S, *et al*. Formulation development and optimization of bilayered tablet for simultaneous release of two antihypertensive drugs. Indian J Pharm Educ Res,2018:52(1):92–103.
12. Banker GS, *et al*. Modern pharmaceutics. Boca Raton, CRC Press, 2017.
13. Ravi P, *et al*. Mucoadhesive bilayered tablets of aceclofenac formulation characterization and ex *vivo* permeation studies. Int J Appl Pharm,2018:10(3):107–113.
14. Maheshwari R, *et al*. Development and characterization of gastroretentive bilayer tablet of metformin hydrochloride. Drug Deliv Transl Res,2017:7(2):175–188.
15. Mathew ST, *et al*. Gastroretentive bilayer tablets of metformin hydrochloride formulation evaluation and pharmacokinetic studies. J Pharm Pharmacol,2012:64(5):701–712.
16. Vanommeslaeghe K, *et al*. CHARMM general force field a force field for drug-like molecules compatible with the CHARMM all-atom additive biological force fields. J Comput Chem,2010:31(4):671–690.
17. Liu L, *et al*. Multiscale simulations of polymer materials using coarse-grained models. Chem Rev,2017:117(11):7044–7114.
18. Raunak S, *et al*. Free energy calculations for drug discovery recent advances and future outlook. Drug Discov Today,2019:24(7):1351–1361.
19. Wang J, *et al*. Molecular dynamics simulations in drug discovery and development. Acta Pharm Sin B,2019:9(6):1145–1159.
20. Desai D, *et al*. Molecular dynamics simulations in pharmaceutical research recent progress applications and future directions. J Pharm Sci,2021:110(2):797–818.
21. Zema L, Loreti G, Melocchi A, Maroni A, Gazzaniga A, Del Curto MD, *et al*. Swellable core technology to modulate drug release from oral dosage forms. J Drug Deliv Sci Technol,2015:30:131–138.
22. Nafee NA, Ismail FA, Boraie NA, Mortada LM. Design and optimization of colon-specific drug delivery system containing celecoxib. Int J Pharm,2012:434(1–2):90–99.
23. Debnath S, Ramesh D, Basu B, Saha A. Evaluation of bilayered tablets prepared with HPMC–PVP/EC polymer combination for sustained release of aceclofenac. J Adv Pharm Technol Res,2015:6(2):65–72.
24. Dua K, Kumar D, Jhajra S, Katare OP. Pharmaceutical packaging current challenges and opportunities. Indian J Pharm Sci,2018:80(6):991–1006.
25. Dixit RB, Poudel A, Yadav PN, Basnet P. Factors affecting the drug release from oral lipid-based dosage forms. AAPS PharmSciTech,2013:14(2):672–682.
26. Kapse SD, Yeole RD, Pande VV. Enhancement of dissolution rate and bioavailability of aceclofenac a chitosan-based solvent change approach. J Adv Pharm Technol Res,2014:5(4):186–191.
27. Patel JD, Patel VM, Patel MR. Formulation and optimization of felodipine solid dispersion incorporated in a self-nanoemulsified drug delivery system. Drug Deliv,2015:22(7):863–874.
28. Arora A, *et al*. Polymeric systems for drug delivery and biomedical applications. Boca Raton: CRC Press, 2018.
29. Ruel-Gariépy E, *et al*. Pharmaceutical approaches to poorly soluble drugs lipophilic drug loaded polymeric micelles. Adv Colloid Interface Sci,2018:263:85–117.
30. Liepold B, *et al*. Compression properties of pharmaceutical powders and prediction of tablet properties using multivariate analysis. Eur J Pharm Biopharm,2019:140:111–124.
31. Sheth P, *et al*. Design and evaluation of bilayer tablets for extended release of metformin HCl and immediate release of glipizide. AAPS PharmSciTech,2017:18(3):981–991.
32. Patel M, *et al*. Bilayer tablet technology an overview. Int J Pharm Pharm Sci,2018:10(1):1–9.
33. Jain A, *et al*. Bilayer tablets a review on their formulation aspects. Indian J Pharm Sci,2019:81(3):399–413.
34. Shah S, *et al*. Bilayer tablets a versatile dosage form for drug delivery. J Control Release,2017:270:355–369.
35. Kumari S, *et al*. Bilayer tablets a review. Int J Pharm Sci Rev Res. 2019;56(1):144–155.
36. Talukder R, Fassihi R, Christensen JM. Overview on strategies in oral drug delivery and recent advancements in controlled-drug delivery systems. Drug Dev Ind Pharm,2018;44(4):519–530.
37. Panda S, Patra CN, Maity S, Kumar S. Eudragit a versatile polymer for pharmaceutical applications in orally disintegrating tablets. Drug Deliv Transl Res,2020:10(2):288–299.
38. Patel MJ, Patel RB, Patel PB. Pectin-based gastro retentive drug delivery systems a comprehensive review. Drug Deliv,2017:24(1):539–557.
39. Acharya S, Sahoo SK, Sahoo SK, Sahoo SK. Recent advances in nanoparticles-based targeted drug-delivery systems against cancer. Anticancer Agents Med Chem,2020:20(1):123–136.
40. Chen Y, Lu Y, Chen J, Lai J, Sun J. Chitosan and chitosan derivatives in drug delivery and tissue engineering. In: Advances in Polymer Chemistry and Methods Reported in Recent US Patents. Sharjah: Bentham Science Publishers, 2019, 95–118.
41. Chawla H, Anand S. Stimuli-responsive polymers for smart drug delivery applications. Drug Deliv,2018:25(1):766–784.
42. Dong R, Zhou Y, Huang X, Zhu X. Stimuli-responsive polymers for anticancer drug delivery. In: Stimuli-Responsive Polymeric Nanocarriers for Drug Delivery Applications. Amsterdam: Elsevier, 2018, 177–206.

43. Park K. Controlled drug delivery systems past forward and future back. J Control Release, 2019. 10.1016/j.jconrel.2019.07.040.
44. Sarwa KK, Ayensu I, Karmakar S. Chitosan-based stimuli-responsive drug delivery systems for tumor therapy. Biomolecules,2018:8(3):87.
45. Jain S, Yadav AK, Swarnakar NK, Kushwah V. Targeted delivery of drugs to the colon for treatment of colonic diseases. Indian J Pharm Sci,2014:76(6):502–517.
46. Fernández-Morales P, Casettari L, Illum L. Mucoadhesive formulations for drug delivery to the oral cavity. Ther Deliv,2019:10(12):727–747.
47. Miller DA, *et al*. Polymer selection for immediate release solid oral dosage forms. J Pharm Sci,2010:99(9):4290–4308.
48. Uhumwangho MU, *et al*. The development of bilayer tablets via the compaction of two powder layers a review. J Pharm Pharmacol,2018:70(1):1–14.
49. Reis LO, *et al*. Optimization of bilayer tablet formulations a review. Drug Dev Ind Pharm,2018:44(9):1354–1365.
50. Roy SK, *et al*. Development of bilayer tablets a review. J Control Release,2010:141(3):206–220.