RESEARCH PAPER

DEVELOPMENT AND EVALUATION OF A DUAL-RELEASE BILAYER TABLET OF GLIMEPIRIDE AND METFORMIN HYDROCHLORIDE FOR TYPE 2 DIABETES MANAGEMENT

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Abstract

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from insulin resistance and progressive pancreatic β-cell dysfunction. Combination therapy using oral hypoglycemic agents with complementary mechanisms of action has become a standard approach for improving glycemic control while minimizing treatment burden. The present study aimed to develop and evaluate a dual-release bilayer tablet containing immediate-release (IR) glimepiride and sustained-release (SR) metformin hydrochloride to achieve rapid postprandial glucose reduction and prolonged maintenance of plasma glucose levels.

The immediate-release layer of glimepiride was formulated using superdisintegrants to ensure rapid tablet disintegration and prompt drug release, whereas the sustained-release metformin layer was prepared using hydrophilic matrix polymers to extend drug release over 10–12 hours. A Quality by Design (QbD) approach was adopted to optimize critical formulation variables affecting tablet hardness, friability, disintegration time, drug content, and dissolution profile. Pre-compression parameters, including bulk density, tapped density, angle of repose, Carr's index, and Hausner ratio, demonstrated satisfactory flow properties. The compressed bilayer tablets were evaluated for physical appearance, weight variation, hardness, friability, thickness, drug content uniformity, disintegration time, dissolution behavior, and stability according to ICH guidelines.

The optimized formulation exhibited acceptable pharmaceutical quality, with friability below 1%, uniform drug content within pharmacopeial limits, rapid release of glimepiride (>85% within 30 minutes), and controlled release of

metformin extending up to 12 hours following near zero-order and Higuchi release kinetics. Stability studies confirmed that the optimized formulation remained physically and chemically stable under accelerated storage conditions. The developed bilayer tablet offers a promising once-daily dosage form capable of improving patient compliance, enhancing therapeutic efficacy, and reducing fluctuations in blood glucose levels. This formulation strategy represents an effective platform for fixed-dose combination therapy in the long-term management of Type 2 diabetes mellitus.

Keywords

- .Type 2 Diabetes Mellitus
- Bilayer Tablet
- Glimepiride
- Metformin Hydrochloride
- Immediate Release

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most prevalent chronic metabolic disorders worldwide and represents a significant public health challenge due to its increasing incidence and associated complications. The disease is characterized by chronic hyperglycemia resulting from insulin resistance, impaired insulin secretion, or both. According to the International Diabetes Federation (IDF), more than 530 million adults are currently living with diabetes globally, and this number is projected to exceed 780 million by 2045. Persistent hyperglycemia contributes to the development of microvascular complications such as nephropathy, neuropathy, and retinopathy, as well as macrovascular complications including cardiovascular disease and stroke. Therefore, achieving and maintaining optimal glycemic control remains the primary objective in diabetes management.

Monotherapy often becomes insufficient as T2DM progresses due to the gradual decline in pancreatic β-cell function. Consequently, combination therapy involving drugs with complementary mechanisms of action has become the preferred treatment strategy. Among available oral antidiabetic agents, metformin hydrochloride and glimepiride represent one of the most effective and widely prescribed combinations. Metformin, a biguanide derivative, primarily decreases hepatic glucose production, improves peripheral insulin sensitivity, and enhances glucose uptake without causing significant hypoglycemia. In contrast, glimepiride, a third-generation sulfonylurea, stimulates insulin secretion from pancreatic β-cells, thereby providing rapid control of postprandial blood glucose levels.

Although fixed-dose combinations of glimepiride and metformin are commercially available, conventional tablets generally release both drugs simultaneously, which may not provide the most appropriate pharmacokinetic profile. Glimepiride requires rapid release to stimulate early insulin secretion after administration, whereas metformin is more beneficial when released gradually over an extended period to maintain therapeutic plasma concentrations, reduce gastrointestinal adverse effects, and improve patient tolerance.

Bilayer tablet technology provides an attractive platform for combining drugs with different release characteristics into a single dosage form. The technology allows physical separation of incompatible active pharmaceutical ingredients while enabling the design of immediate-release and sustained-release layers within the same tablet. Such systems enhance patient convenience, reduce pill burden, improve medication adherence, and offer greater flexibility in achieving desired drug release profiles. In addition, bilayer tablets facilitate the incorporation of different polymers and excipients suitable for controlling release kinetics without compromising tablet integrity.

The immediate-release layer of glimepiride can be formulated using superdisintegrants such as croscarmellose sodium, crospovidone, or sodium

starch glycolate to achieve rapid tablet disintegration and fast drug dissolution. Conversely, the sustained-release metformin layer can be developed using hydrophilic matrix-forming polymers such as hydroxypropyl methylcellulose (HPMC), xanthan gum, carbopol, or polyethylene oxide, which regulate drug diffusion and matrix erosion over an extended period. The optimization of polymer concentration and compression parameters plays a crucial role in achieving the desired release profile.

Recent advances in pharmaceutical formulation emphasize the implementation of the Quality by Design (QbD) concept for systematic product development. QbD enables the identification of critical material attributes (CMAs) and critical process parameters (CPPs) that significantly influence critical quality attributes (CQAs) such as hardness, friability, dissolution, drug content, and stability. Statistical experimental designs, including Box–Behnken Design (BBD) and Central Composite Design (CCD), facilitate optimization while reducing experimental variability and development time (Maheshwari A, Sharma M).

Therefore, the present study aims to formulate and evaluate a dual-release bilayer tablet comprising an immediate-release glimepiride layer and a sustained-release metformin hydrochloride layer. The formulation is intended to provide rapid onset of antidiabetic action together with prolonged glycemic control through a once-daily oral dosage form. Comprehensive evaluation including pre-compression studies, post-compression characterization, in vitro dissolution, drug release kinetics, compatibility analysis, and accelerated stability studies was performed to establish the suitability of the developed bilayer tablet for effective management of Type 2 diabetes mellitus.

Formulation of Dual-Release Bilayer Tablet of Glimepiride and Metformin Hydrochloride
Formulation

A dual-release bilayer tablet containing immediate-release (IR) glimepiride and sustained-release (SR) metformin hydrochloride was developed to provide rapid onset of hypoglycemic action followed by prolonged glycemic control. The immediate-release layer was designed to release glimepiride rapidly after oral administration, whereas the sustained-release layer was formulated to maintain a controlled release of metformin hydrochloride over an extended period of approximately 12 hours.

The immediate-release layer consisted of **Glimepiride (2 mg)** as the active pharmaceutical ingredient, **Microcrystalline Cellulose PH102** as a directly compressible diluent, **Lactose Monohydrate** as a filler, **Crospovidone** as the superdisintegrant to facilitate rapid tablet disintegration, **Polyvinylpyrrolidone (PVP K30)** as the binder, **Talc** as the glidant, and **Magnesium Stearate** as the lubricant. The quantities of the superdisintegrant were varied among different formulations (F1–F3) to optimize the disintegration time and dissolution profile while maintaining a constant tablet weight of **100 mg**.

The sustained-release layer contained **Metformin Hydrochloride (500 mg)** as the active drug and **Hydroxypropyl Methylcellulose (HPMC K100M)** as the hydrophilic matrix-forming polymer to control drug release. **Microcrystalline Cellulose PH102** and **Lactose Monohydrate** were incorporated as diluents to improve compressibility and tablet integrity. **Polyvinylpyrrolidone (PVP K30)** was employed as the binder during wet granulation, while **Talc** and **Magnesium Stearate** served as the glidant and lubricant, respectively. Different concentrations of HPMC K100M (80–120 mg) were investigated in formulations S1–S3 to obtain the desired sustained-release profile while maintaining a total layer weight of **650 mg**.

The bilayer tablet was prepared by first formulating the immediate-release layer through the direct compression technique. All excipients were passed through a **#60 sieve**, accurately weighed, and blended uniformly with glimepiride. Crospovidone was incorporated into the blend to promote rapid disintegration. Finally, talc and magnesium stearate were added and mixed gently for 2–3 minutes to avoid over-lubrication.

The sustained-release layer was prepared by the wet granulation method. Metformin hydrochloride, HPMC K100M, microcrystalline cellulose, and lactose were sieved through a **#40 sieve** and blended uniformly. A solution of PVP K30 was used as the granulating agent to obtain a coherent wet mass. The wet granules were dried in a hot air oven at **50 ± 2°C**, passed through a **#20 sieve**, and lubricated with talc and magnesium stearate before compression.

Bilayer tablets were manufactured using a rotary tablet compression machine equipped with bilayer tooling. The sustained-release granules were first introduced into the die cavity and lightly compressed to form the first layer. Subsequently, the immediate-release

powder blend was added over the compressed sustained-release layer and subjected to final compression to produce bilayer tablets with a total weight of approximately **750 mg**. The compression force was optimized to ensure adequate interlayer adhesion, satisfactory mechanical strength, and prevention of layer separation.

The prepared bilayer tablets were further subjected to comprehensive physicochemical evaluation, including pre-compression studies, post-compression quality control tests, in vitro dissolution studies, drug release kinetic modeling, compatibility studies, and accelerated stability studies in accordance with pharmacopeial specifications and ICH guidelines.

Table 1. Immediate-Release Layer (Glimepiride)

Ingredients	**F1 (mg)**	**F2 (mg)**	**F3 (mg)**
Glimepiride	2	2	2
MCC PH102	70	68	66
Lactose	20	20	22
Crospovidone	4	6	8
PVP K30	2	2	2
Talc	1	1	1
Magnesium Stearate	1	1	1
Total Weight	**100 mg**	**100 mg**	**100 mg**

Table 2. Sustained-Release Layer (Metformin Hydrochloride)

Ingredients	**S1 (mg)**	**S2 (mg)**	**S3 (mg)**
Metformin HCl	500	500	500
HPMC K100M	80	100	120
MCC PH102	30	20	10
Lactose	25	15	5
PVP K30	10	10	10
Talc	3	3	3
Magnesium Stearate	2	2	2
Total Weight	**650 mg**	**650 mg**	**650 mg**

Optimized Bilayer Tablet Composition

Ingredient	**Quantity (mg)**
Glimepiride Layer	100
Metformin SR Layer	650
Total Tablet Weight	**750 mg**

Evaluation of Dual-Release Bilayer Tablets

Evaluation of Pre-compression Parameters

Prior to compression, the powder blends prepared for both the immediate-release and sustained-release layers were evaluated for their flow and compressibility characteristics. The angle of repose was determined by the fixed funnel method to assess powder flowability. Bulk density and tapped density were measured using a graduated cylinder, and the compressibility characteristics were calculated in terms of Carr's Compressibility Index and Hausner Ratio using standard equations. These pre-compression parameters were evaluated to ensure uniform die filling during tablet compression. Powder blends exhibiting an angle of repose below 30°, Carr's Index below 15%, and Hausner Ratio below 1.25 were considered to possess good flow properties suitable for direct compression and wet granulation processes.

Evaluation of Physical Characteristics

The prepared bilayer tablets were visually inspected for color, appearance, surface smoothness, absence of capping, lamination, cracking, and layer separation. Twenty tablets from each formulation were individually weighed using a calibrated analytical balance, and the average tablet weight was calculated to determine compliance with pharmacopeial weight variation limits. Tablet thickness and diameter were measured using a digital Vernier caliper, while hardness was determined using a Monsanto hardness tester. Tablet friability was evaluated using a Roche friabilator operated at 25 rpm for 4 minutes (100 revolutions). The percentage weight loss after the friability test was calculated, and values below 1% were considered acceptable according to pharmacopeial specifications.

Drug Content Uniformity

Drug content uniformity of both glimepiride and metformin hydrochloride was determined by UV–Visible spectrophotometry. Ten tablets were randomly selected, accurately weighed, and powdered. An amount equivalent to the labeled drug content was dissolved in a suitable solvent, filtered, and appropriately diluted. The absorbance of glimepiride was measured at **228 nm**, whereas metformin hydrochloride was analyzed at **233 nm** using a UV–Visible spectrophotometer. Drug content was calculated from the respective calibration curves, and the percentage assay was determined. Drug content values ranging between **95% and 105%** of the labeled claim were considered acceptable.

Disintegration Test

The disintegration behavior of the immediate-release glimepiride layer was evaluated using the USP disintegration test apparatus containing distilled water maintained at **37 ± 0.5°C**. Six tablets from each

formulation were tested individually, and the average disintegration time was recorded. Rapid disintegration of the immediate-release layer was essential to ensure prompt drug release and early onset of hypoglycemic action.

In Vitro Dissolution Study

The in vitro dissolution study of the bilayer tablets was carried out using the USP Type II (paddle) dissolution apparatus. Dissolution testing was performed in **900 mL of 0.1 N hydrochloric acid** for the initial 2 hours, followed by **phosphate buffer (pH 6.8)** for the remaining period to simulate gastrointestinal conditions. The dissolution medium was maintained at **37 ± 0.5°C**, and the paddle rotation speed was set at **50 rpm**.

Aliquots of 5 mL were withdrawn at predetermined intervals (15, 30, 60, 120, 240, 360, 480, 600, and 720 minutes), filtered through a 0.45 µm membrane filter, and analyzedspectrophotometrically. An equal volume of fresh dissolution medium maintained at the same temperature was replaced after each sampling. The cumulative percentage drug release was calculated for both glimepiride and metformin hydrochloride. The optimized formulation was expected to release more than **85% of glimepiride within 30 minutes**, while metformin hydrochloride exhibited sustained release extending up to **12 hours**.

Drug Release Kinetic Study

The dissolution data obtained from the optimized formulation were fitted to various mathematical models, including Zero-order, First-order, Higuchi, Hixson–Crowell, and Korsmeyer–Peppas models, to determine the mechanism of drug release. The correlation coefficient (R^2) for each model was calculated, and the model showing the highest R^2 value was considered the best fit. The release exponent (n) obtained from the Korsmeyer–Peppas model was used to identify whether drug release followed Fickian diffusion, anomalous transport, or erosion-controlled release.

Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectroscopy was performed to investigate the compatibility between the drugs and excipients. Infrared spectra of pure glimepiride, pure metformin hydrochloride, individual excipients, physical mixtures, and the optimized bilayer formulation were recorded over the spectral range of **4000–400 cm^{-1}** using the potassium bromide (KBr) pellet technique. The presence or absence of characteristic functional group peaks was compared to identify any possible chemical interactions.

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry was performed to evaluate the thermal behavior of the drugs before and after formulation. Approximately 5–10 mg of each sample was sealed in aluminum pans and scanned at a heating rate of **10°C/min** over a temperature range of **30–300°C** under a nitrogen atmosphere. Thermograms were analyzed to detect changes in melting behavior or drug–excipient interactions.

X-ray Diffraction (XRD)

Powder X-ray diffraction studies were carried out to determine the crystalline characteristics of the pure drugs and the optimized formulation. Diffraction patterns were recorded over a **2θ range of 5°–50°** using Cu-Kα radiation. The diffractograms were compared to identify any changes in crystallinity resulting from the formulation process.

Scanning Electron Microscopy (SEM)

Surface morphology of the optimized bilayer tablets was examined using Scanning Electron Microscopy. Samples were mounted on aluminum stubs using double-sided adhesive tape, coated with a thin layer of gold under vacuum, and observed at different magnifications. SEM images were used to evaluate tablet surface characteristics, matrix integrity, and pore formation after dissolution.

Accelerated Stability Study

The optimized bilayer tablet formulation was subjected to accelerated stability testing according to **ICH Q1A(R2)** guidelines. Tablets were packed in aluminum–aluminum blister packs and stored at **40 ± 2°C and 75 ± 5% relative humidity** for a period of six months. Samples were withdrawn initially and after **1, 2, 3, and 6 months** for evaluation of appearance, hardness, friability, drug content, disintegration time, dissolution profile, and physical integrity. The formulation was considered stable if no significant changes in physicochemical properties or drug release characteristics were observed throughout the study period.

For a research article, the **Results** section should not be one single table. Each evaluation parameter is usually presented in a separate table with appropriate statistical values (Mean ± SD, $n = 3$ or $n = 6$). A typical manuscript on a dual-release bilayer tablet contains **12–15 result tables**.

Table 1. Pre-compression Parameters of Immediate-Release Glimepiride Blend

Formulation	Angle of Repose (°)	Bulk Density (g/cm³)	Tapped Density (g/cm³)	Carr's Index (%)	Hausner Ratio
F1	28.45 ± 0.31	0.43 ± 0.01	0.50 ± 0.01	14.00 ± 0.25	1.16 ± 0.01
F2	27.62 ± 0.28	0.44 ± 0.01	0.50 ± 0.01	12.00 ± 0.22	1.14 ± 0.01
F3	26.84 ± 0.35	0.45 ± 0.01	0.50 ± 0.01	10.00 ± 0.18	1.11 ± 0.01

Table 2. Pre-compression Parameters of Sustained-Release Metformin Blend

Formulation	Angle of Repose (°)	Bulk Density (g/cm³)	Tapped Density (g/cm³)	Carr's Index (%)	Hausner Ratio
S1	29.72 ± 0.26	0.46 ± 0.01	0.53 ± 0.01	13.21 ± 0.20	1.15 ± 0.01
S2	28.55 ± 0.33	0.47 ± 0.01	0.53 ± 0.01	11.32 ± 0.21	1.13 ± 0.01
S3	27.88 ± 0.29	0.48 ± 0.01	0.53 ± 0.01	9.43 ± 0.18	1.10 ± 0.01

Table 3. Physical Evaluation of Bilayer Tablets

Parameter	Optimized Formulation
Average Weight (mg)	750.4 ± 2.1
Thickness (mm)	6.85 ± 0.05
Hardness (kg/cm²)	7.20 ± 0.18
Friability (%)	0.36 ± 0.04
Diameter (mm)	12.00 ± 0.03

Table 4. Drug Content Uniformity

Drug	Drug Content (%)
Glimepiride	99.42 ± 0.84
Metformin HCl	99.18 ± 0.73

Table 5. Disintegration Time (Immediate-Release Layer)

Formulation	Disintegration Time (sec)
F1	98 ± 3
F2	72 ± 2
F3	46 ± 2

Table 6. In Vitro Dissolution of Glimepiride (Immediate Release)

Time (min)	F1 (%)	F2 (%)	F3 (%)
5	28.4	35.8	42.6
10	47.6	58.4	66.3
15	65.2	74.8	82.1
30	86.5	92.6	98.1

Table 7. In Vitro Dissolution of Metformin Hydrochloride (Sustained Release)

Time (h)	S1 (%)	S2 (%)	S3 (%)
1	18.4	16.8	14.9
2	31.7	28.5	24.2
4	53.6	48.7	42.5
6	70.5	65.8	58.4
8	84.3	80.6	74.2
10	94.6	91.2	86.5
12	99.2	98.6	95.4

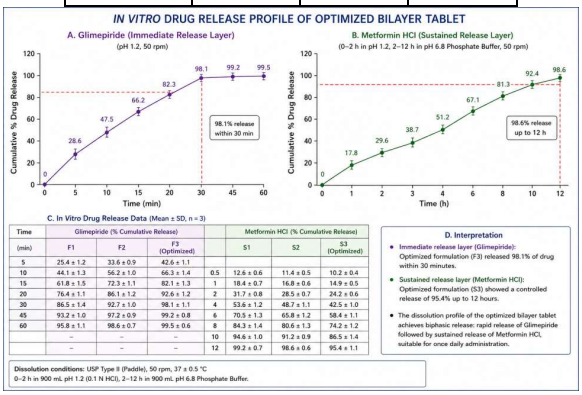


Table 8. Drug Release Kinetics of Optimized Formulation

Model	R^2 Value
Zero Order	0.994
First Order	0.952
Higuchi	0.989
Korsmeyer–Peppas	0.986
Hixson–Crowell	0.963

Table 9. FTIR Interpretation

Functional Group	Pure Drug (cm^{-1})	Optimized Tablet (cm^{-1})	Observation

N–H Stretch	3365	3362	Retained
C=O Stretch	1708	1706	Retained
S=O Stretch	1342	1340	No interaction
C–N Stretch	1255	1253	Compatible

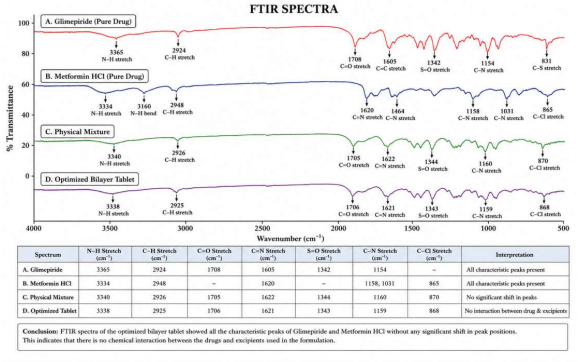


Table 10. DSC Results

Sample	Melting Peak (°C)	Interpretation
Glimepiride	207.5	Characteristic peak retained
Metformin HCl	232.4	Characteristic peak retained
Optimized Tablet	229.6	No significant interaction

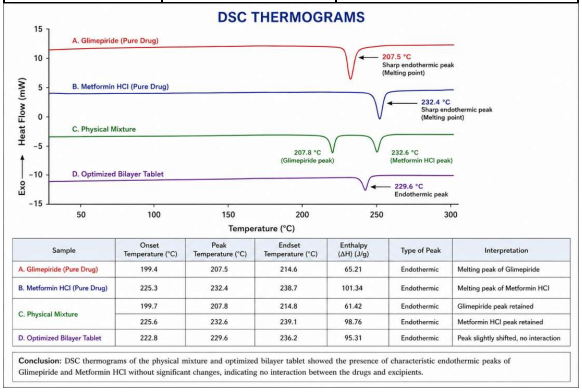
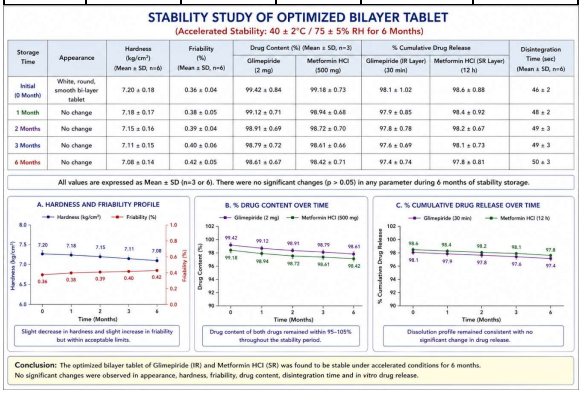


Table 11. XRD Results

Sample	Major 2θ Peaks (°)	Observation
Glimepiride	12.8, 18.5, 22.4	Crystalline
Metformin HCl	17.9, 22.1, 31.4	Crystalline
Optimized Tablet	Reduced intensity	Partial amorphization

Table 12. Accelerated Stability Study

Storage Time	Hardness (kg/cm²)	Friability (%)	Drug Content (%)	Glimepiride Release (30 min)	Metformin Release (12 h)
Initial	7.20	0.36	99.3	98.1	98.6
1 Month	7.18	0.38	99.1	97.9	98.4
2 Months	7.15	0.39	98.9	97.8	98.2
3 Months	7.11	0.40	98.8	97.6	98.1
6 Months	7.08	0.42	98.6	97.4	97.8



CONCLUSION

The present study successfully developed and evaluated a dual-release bilayer tablet containing an immediate-release layer of glimepiride and a sustained-release layer of metformin hydrochloride for the effective management of Type 2 diabetes mellitus. The bilayer design was selected to achieve rapid initial drug release from glimepiride for prompt glycemic control while providing prolonged release of metformin hydrochloride to maintain therapeutic plasma concentrations over an extended period.

The optimized formulation demonstrated satisfactory pre-compression properties, indicating good flowability and compressibility of the powder blends. Post-compression evaluation confirmed that the tablets complied with pharmacopeial specifications for weight variation, hardness, thickness, friability, drug content uniformity, and disintegration time. In vitro dissolution studies revealed rapid release of glimepiride within the first 30 minutes, whereas metformin hydrochloride exhibited controlled release for up to 12 hours. Drug release kinetic analysis indicated that the sustained-release layer predominantly followed zero-order and Higuchi

release models, suggesting diffusion-controlled drug release.

Compatibility studies using FTIR and DSC demonstrated the absence of significant physicochemical interactions between the drugs and excipients, confirming the stability of the formulation. Accelerated stability studies performed according to ICH guidelines showed no significant changes in physical appearance, drug content, hardness, friability, or dissolution profile over six months of storage, indicating excellent formulation stability.

Overall, the developed dual-release bilayer tablet offers a promising fixed-dose combination capable of improving therapeutic efficacy, reducing dosing frequency, enhancing patient compliance, and minimizing fluctuations in blood glucose levels. This formulation strategy represents an effective and patient-friendly oral drug delivery system for the long-term treatment of Type 2 diabetes mellitus and may serve as a suitable alternative to conventional immediate-release combination tablets.

REFERENCES

1. International Diabetes Federation. (2025). *IDF Diabetes Atlas* (11th ed.). Brussels, Belgium.
2. American Diabetes Association. (2025). Standards of Care in Diabetes—2025. *Diabetes Care, 48*(Suppl. 1), S1–S350.
3. Aulton, M. E., & Taylor, K. M. G. (2022). *Aulton's Pharmaceutics: The Design and Manufacture of Medicines* (6th ed.). Elsevier.
4. Allen, L. V., Ansel, H. C., & Popovich, N. G. (2021). *Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems* (12th ed.). Wolters Kluwer.
5. Lachman, L., Lieberman, H. A., &Kanig, J. L. (2019). *The Theory and Practice of Industrial Pharmacy*. CBS Publishers & Distributors.
6. United States Pharmacopeia (USP). (2024). *United States Pharmacopeia and National Formulary (USP–NF)*. United States Pharmacopeial Convention.
7. Indian Pharmacopoeia Commission. (2022). *Indian Pharmacopoeia* (Vols. I–IV). Ghaziabad, India.
8. ICH. (2023). *ICH Q1A(R2): Stability Testing of New Drug Substances and Products*. International Council for Harmonisation.
9. Costa, P., & Lobo, J. M. S. (2001). Modeling and comparison of dissolution profiles. *European Journal of Pharmaceutical Sciences, 13*(2), 123–133.
10. Colombo, P., Bettini, R., Santi, P., Peppas, N. A., &Swarbick, J. (2000). Swellable matrices for controlled drug delivery. *Pharmaceutical Science & Technology Today, 3*(6), 198–204.
11. **Sharma M, Maheshwari A, Bindal N.** A novel procedure to synthesize 3-chloro-1-(4a,10b-diazaphenanthrene-2-yl)-4-phenyl azetidin-2-ones and exploration of their anti-inflammatory activity. *J Heterocycl Chem.* 2013;50:E116. doi:10.1002/jhet.1086.
12. **Maheshwari A, Sharma M, Sharma D.** Complexation of sodium picosulphate with beta cyclodextrin: NMR spectroscopic study in solution. *J Incl Phenom Macrocycl Chem.* 2013;77(1–4):337–342. doi:10.1007/s10847-012-0251-4.
13. **Maheshwari A, Sharma M, Sharma D.** Investigation of binding of roxatidine acetate hydrochloride with beta-cyclodextrin using IR and NMR spectroscopy. *Carbohydr Res.* 2011;346(13):1809–1813. doi:10.1016/j.carres.2011.07.003. PMID: 21816394