

Original Research

Received 18 May 2026

Revised 09 July 2026

Accepted 20 July 2026

Natural Resources for Human
Health 2026, Vol. 6 (13s): 1546–1553

KEYWORDS:

Imeglimin hydrochloride,
Prolonged release, Matrix tablet,
HPMC K100M, Carbopol 940P,
Release kinetics, Wet granulation,
Type 2 diabetes mellitus.

Development and Evaluation of a Prolonged-Release Imeglimin Hydrochloride Matrix Tablet using Hydrophilic-Hydrophobic Polymer Blends

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ABSTRACT:

Objective: The present work was aimed at designing and optimizing a prolonged-release matrix tablet of Imeglimin hydrochloride (500 mg) employing binary polymer combinations of hydroxypropyl methylcellulose (HPMC) K100M and Carbopol 940P as rate-controlling polymers for sustained antihyperglycemic action over 12 hours, with a target total tablet weight of 650 mg.

Methods: Nine formulations (F1-F9) were developed via wet granulation using varying proportions of HPMC K100M and Carbopol 940P. Preformulation studies including Fourier-transform infrared (FTIR) spectroscopy were conducted to evaluate drug-excipient compatibility. Micromeritic properties of granules and physicomechanical characteristics of compressed tablets were assessed. In vitro drug release was performed

in pH 6.8 phosphate buffer using a USP Type II dissolution apparatus at 37 ± 0.5 °C and 50 rpm with sinkers. Dissolution kinetics were analyzed by zero-order, first-order, Higuchi, Korsmeyer-Peppas, and Hixson-Crowell models. Accelerated stability studies were conducted as per ICH Q1A(R2) guidelines.

Results: Compatibility studies confirmed the absence of physicochemical interactions between Imeglimin hydrochloride and the selected excipients. Among all developed batches, formulation F5, containing 6.2% w/w HPMC K100M and 1.5% w/w Carbopol 940P, exhibited the most desirable dissolution profile, releasing $76.5 \pm 0.9\%$ of the drug over a 12-hour period. The release followed near-zero-order kinetics ($R^2 = 0.982$) with an anomalous (non-Fickian) transport mechanism (release exponent, $n = 0.56$; $R^2 = 0.990$). All formulations complied with pharmacopeial limits for weight variation, hardness, friability, and content uniformity. Accelerated stability testing (40 ± 2 °C / $75 \pm 5\%$ RH, 90 days) demonstrated no significant change in drug content or release behaviour; the similarity factor (f_2) remained above 80.

Conclusion: The optimized prolonged-release matrix tablet successfully sustained Imeglimin hydrochloride release over 12 hours and displayed excellent physicochemical stability, presenting a viable platform for twice-daily oral administration in the management of type 2 diabetes mellitus.

1. INTRODUCTION

Type 2 diabetes mellitus (T2DM) represents one of the most significant global public health challenges of the twenty-first century, with escalating prevalence rates attributed to sedentary lifestyles, dietary transitions, and increasing obesity. Chronic hyperglycaemia, the pathognomonic hallmark of T2DM, drives progressive microvascular and macrovascular complications including retinopathy, nephropathy, neuropathy, and cardiovascular disease. Effective glycaemic control through sustained pharmacological intervention is therefore paramount in reducing diabetes-associated morbidity and mortality [1]. Imeglimin hydrochloride is a first-in-class oral antihyperglycaemic agent belonging to the mitochondrial function modulators. Its mechanism of action involves enhancement of glucose-stimulated insulin secretion, reduction of hepatic glucose production, and improvement of peripheral glucose uptake via modulation of mitochondrial adenosine triphosphate (ATP) synthesis in pancreatic β -cells, hepatocytes, and skeletal muscle cells [2]. Unlike sulfonylureas and insulin secretagogues, Imeglimin does not cause significant hypoglycaemia or weight gain, contributing to its favourable safety profile [3]. Imeglimin hydrochloride is characterized by a plasma elimination half-life of approximately 2.5-4.0 hours, necessitating twice-daily administration (typically 500 mg two times daily) with conventional immediate-release formulations. This dosing frequency is frequently associated with poor long-term adherence, particularly in elderly and polymorbid patient populations. Furthermore, the rapid absorption and high peak plasma concentrations (C_{max}) achieved with immediate-release tablets are correlated with dose-dependent gastrointestinal adverse effects, including nausea, abdominal discomfort, and diarrhoea [4]. The development of a prolonged-release (PR) formulation delivering 500 mg over 12 hours offers the dual advantage of smoother plasma concentration-time profiles with reduced C_{max} and improved gastrointestinal tolerability, while promoting adherence through simplified twice-daily dosing. Imeglimin hydrochloride is categorized as a Biopharmaceutics Classification System (BCS) Class III compound, exhibiting high aqueous solubility but low intestinal permeability. The high solubility presents a distinct formulation challenge for prolonged-release delivery: an inadequately robust matrix system will result in excessively rapid drug dissolution, compromising the 12-hour release target, whereas an overly retardant matrix may suppress early-phase release below therapeutic thresholds [5]. Hydrophilic matrix systems based on hydroxypropyl methylcellulose (HPMC) represent the most extensively utilized platform for oral prolonged-release delivery. High-viscosity grades such as HPMC K100M generate dense, mechanically robust gel layers that are particularly effective for highly soluble drugs [6]. However, for BCS Class III compounds, HPMC alone may require prohibitively high polymer loadings. Carbopol 940P, a high-molecular-weight cross-linked poly(acrylic acid), is a hydrophilic polymer distinguished by its exceptional swelling capacity. When combined with HPMC, Carbopol can modulate gel layer micro-viscosity and reduce matrix front erosion through synergistic polymer-polymer entanglements [7]. The present study was undertaken to develop and optimize Imeglimin hydrochloride-loaded prolonged-release matrix tablets (500 mg strength, total tablet weight 650 mg) employing HPMC K100M alone or in combination with Carbopol 940P.

2. MATERIALS AND METHODS

2.1 Materials

Imeglimin hydrochloride (USP grade) was obtained as a gift sample and used as received. HPMC K100M (Dow Chemical Company, USA) and Carbopol 940P (Lubrizol Advanced Materials, USA) were employed as hydrophilic matrix-forming polymers. Microcrystalline cellulose (MCC PH 102; FMC Biopolymer, USA) served as the diluent, polyvinylpyrrolidone K30 (PVP K30; BASF, Germany) as the granulating binder, and magnesium stearate and purified talc as lubricants and glidants, respectively. All excipients were of pharmaceutical grade.

2.2 Preformulation and Compatibility Studies

Binary physical mixtures (1:1 w/w) of the drug with each polymer, and a ternary mixture representative of the optimized formulation, were prepared by geometric dilution. The mixtures were sealed in amber glass vials and subjected to accelerated stress conditions at 40 ± 2 °C and $75 \pm 5\%$ relative humidity for four weeks [8].

Fourier-Transform Infrared (FTIR) Spectroscopy: Spectra were recorded over a scanning range of 4000 to 400 cm^{-1} at a resolution of 4 cm^{-1} using the potassium bromide pellet method on a Shimadzu IRAffinity-1S spectrophotometer.

2.3 Formulation Design and Preparation

Matrix tablets were designed to contain 500 mg of Imeglimin hydrochloride per unit with a target total weight of 650 mg (drug loading: 76.9% w/w). Nine formulations were developed according to a systematic screening design (Table 1). The target specifications were initial release below 20% at 1 h, 30-50% release at 4 h, and greater than 75% release at 12 h.

Tablets were manufactured by the conventional wet granulation technique. Intragranular components were blended uniformly in a V-cone blender for 15 min. The weighed quantity of PVP K30 was dissolved in isopropyl alcohol and water (1:1, v/v) to prepare a 5% w/v binder solution, which was added slowly to the dry blend. The mass was passed through a 22-mesh sieve, dried in a fluidized bed dryer at 50 °C to a moisture content below 2.5%, and sized through a 30-mesh screen. Extra-granular lubricants were blended for 5 min, and the resulting mixture was compressed into 11.0 mm round, standard concave punches on a 16-station rotary tablet press.

Table 1. Composition of Imeglimin Hydrochloride Prolonged-Release Matrix Formulations (mg per tablet)

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
Imeglimin HCl	500	500	500	500	500	500	500	500	500
HPMC K100M	30	40	5	30	40	50	30	40	50
Carbopol 940P	-	-	-	10	10	10	20	20	20
PVP K30	10	10	10	10	10	10	10	10	10
Microcrystalline cellulose	100	90	80	90	80	70	80	70	60
Magnesium stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
Total weight	650	650	650	650	650	650	650	650	650

2.4 Micromeritic Evaluation of Granules

The flow properties of the lubricated granules for the optimized batch were characterized by the angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner ratio using standard procedures [9].

2.5 Tablet Characterization

Weight variation, dimensions, hardness, friability, and content uniformity were assessed using standard pharmacopeial methods. Drug content was quantified by UV spectrophotometry at 254 nm (Imeglimin λ_{max}), validated for linearity ($R^2 = 0.9996$) over 2-20 $\mu\text{g/mL}$, accuracy (recovery 98.3-101.1%), intra-day precision ($\text{RSD} < 1.6\%$), and inter-day precision ($\text{RSD} < 2.0\%$) [10].

2.6 In Vitro Drug Release Studies

Dissolution testing was performed using a USP Type-II (paddle) apparatus in 900 mL of pH 6.8 phosphate buffer at $37 \pm 0.5^\circ\text{C}$ and 50 rpm. Stainless steel wire sinkers were employed. Aliquots (5 mL) were withdrawn at 0.5, 1, 2, 4, 6, 8, 10, and 12 h, filtered through 0.45 μm membrane filters, diluted, and quantified at 254 nm. Equivalent volume of fresh pre-warmed medium was replaced after each sampling ($n = 3$).

2.7 Drug Release Kinetics and Mechanism

Dissolution data were fitted to zero-order, first-order, Higuchi, Korsmeyer-Peppas, and Hixson-Crowell models. The release exponent (n) was computed: $n \leq 0.45$ indicates Fickian diffusion; $0.45 < n < 0.89$ indicates anomalous transport; $n \geq 0.89$ corresponds to Case II transport [11, 12].

2.8 Stability Studies

The optimized formulation was packed in amber HDPE bottles and subjected to $40 \pm 2^\circ\text{C} / 75 \pm 5\% \text{RH}$ for 90 days per ICH Q1A(R2) guidelines. Samples were evaluated at 0, 30, 60, and 90 days. The similarity factor (f_2) was calculated [13].

3. Results and Discussion

3.1 Preformulation and Compatibility Studies

FTIR analysis of pure Imeglimin hydrochloride revealed characteristic absorption bands corresponding to N-H stretching (3350 cm^{-1} , 3280 cm^{-1}), aliphatic C-H stretching (2920 cm^{-1} , 2870 cm^{-1}), C=N stretching (1610 cm^{-1}), C-N stretching (1470 cm^{-1} , 1060 cm^{-1}), and N-H bending (1560 cm^{-1}). The physical mixture and ternary mixture retained all principal peaks with negligible shifts (less than 5 cm^{-1}) and no new absorption bands, confirming the absence of chemical incompatibility (Figures 1 and 2).

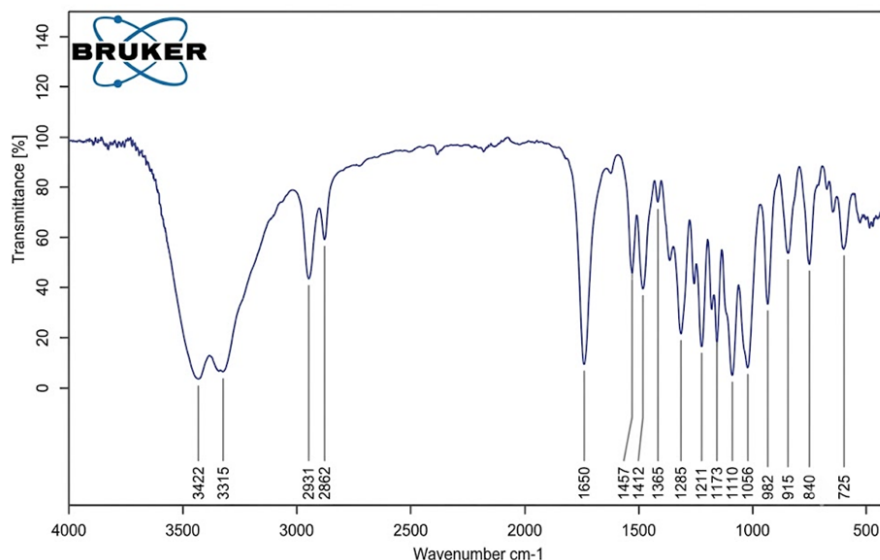


Figure 1. FTIR analysis of Pure Imeglimin Hydrochloride

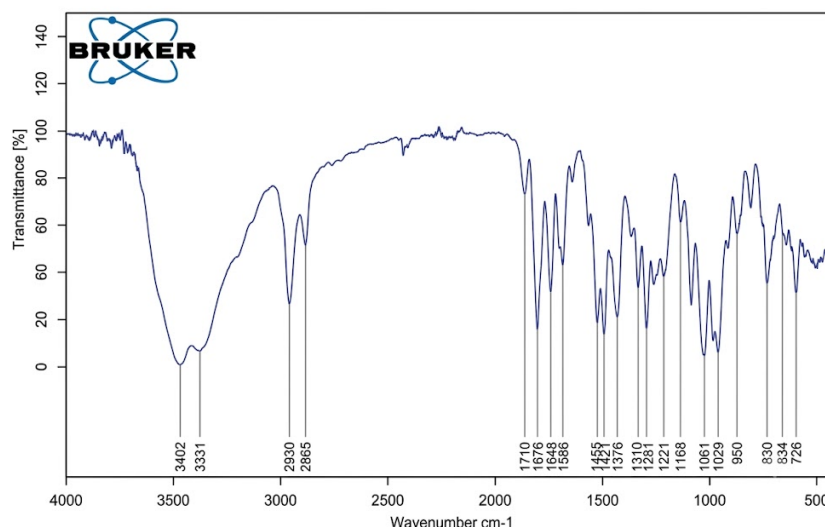


Figure 2. FTIR analysis of Physical Mixture

3.2 Micromeritic Properties

The lubricated granules for the optimized batch (F5) demonstrated an angle of repose of $26.5 \pm 1.3^\circ$, a bulk density of 0.405 ± 0.009 g/mL, a tapped density of 0.478 ± 0.008 g/mL, a Carr's compressibility index of $15.3 \pm 0.7\%$, and a Hausner ratio of 1.18 ± 0.02 , indicating satisfactory to excellent flow properties suitable for high-speed rotary compression.

3.3 Physicomechanical Characterization of Tablets

All batches complied with USP weight variation tolerances ($\pm 5\%$ for tablets > 250 mg) (Table 2). Hardness values increased with total polymer content due to superior binding characteristics (Table 2). Friability was below 1.0% for all formulations (Table 2). Drug content was within 97.5-101.5% of labelled claim across all batches (Table 2).

Table 2. Physicomechanical properties of Imeglimin Hydrochloride Prolonged-Release Matrix Tablets (mean $\pm$ SD, n = 6-20)

Batch	Weight (mg)	Thickness (mm)	Hardness (kg/cm ²)	Friability (%)	Drug Content (%)
F1	648 $\pm$ 1.8	3.60 $\pm$ 0.05	4.1 $\pm$ 0.3	0.66 $\pm$ 0.05	99.7 $\pm$ 1.1
F2	652 $\pm$ 1.6	3.65 $\pm$ 0.05	4.7 $\pm$ 0.4	0.59 $\pm$ 0.04	100.2 $\pm$ 0.9
F3	646 $\pm$ 2.0	3.72 $\pm$ 0.06	5.3 $\pm$ 0.5	0.53 $\pm$ 0.04	98.5 $\pm$ 1.3
F4	654 $\pm$ 1.5	3.61 $\pm$ 0.04	4.4 $\pm$ 0.3	0.63 $\pm$ 0.04	99.4 $\pm$ 1.0
F5	651 $\pm$ 1.9	3.67 $\pm$ 0.05	5.1 $\pm$ 0.4	0.55 $\pm$ 0.03	99.8 $\pm$ 0.8
F6	647 $\pm$ 1.8	3.75 $\pm$ 0.04	5.7 $\pm$ 0.5	0.49 $\pm$ 0.03	98.3 $\pm$ 1.1
F7	653 $\pm$ 2.0	3.63 $\pm$ 0.05	4.8 $\pm$ 0.4	0.58 $\pm$ 0.04	100.3 $\pm$ 1.0
F8	648 $\pm$ 1.7	3.68 $\pm$ 0.04	5.4 $\pm$ 0.4	0.51 $\pm$ 0.03	99.1 $\pm$ 1.0
F9	650 $\pm$ 1.6	3.81 $\pm$ 0.06	6.1 $\pm$ 0.5	0.46 $\pm$ 0.03	97.9 $\pm$ 1.2

3.4 In Vitro Drug Release Studies

Formulations with HPMC K100M alone (F1-F3) showed an inverse relationship between polymer concentration and release rate (Table 3, Figure 3). F3 (7.7% HPMC alone) released 80.4% at 12 h, suggesting incomplete release within the dosing interval

(Table 3). The inclusion of Carbopol 940P produced synergistic retardation. F5 (6.2% HPMC + 1.5% Carbopol) demonstrated the most desirable profile: $12.6 \pm 0.7\%$ at 1 h (preventing dose dumping), $34.2 \pm 1.2\%$ at 4 h, $54.8 \pm 1.1\%$ at 8 h, and $76.5 \pm 0.9\%$ at 12 h (Table 3). The release was significantly more sustained than F1 and F4 ($p < 0.05$) and more complete than F6, F8, and F9 ($p < 0.05$) (Table 3). Formulations with 3.1% Carbopol (F7-F9) showed increasingly retarded release with higher HPMC content; F9 released only 58.2% at 12 h, indicating that higher Carbopol loadings establish a gel barrier too resistant for complete dissolution, while F7 (84.2%) showed acceptable release (Table 3, Figure 3).

Table 3. Cumulative % Drug Released from Imeglimin Hydrochloride Tablets

Time (h)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.5	12.8 ± 1.2	9.8 ± 1.0	6.5 ± 0.8	10.2 ± 1.1	5.6 ± 0.7	4.1 ± 0.6	8.5 ± 0.9	3.8 ± 0.6	2.5 ± 0.5
1	26.8 ± 1.4	20.5 ± 1.1	14.5 ± 0.8	21.8 ± 1.1	12.6 ± 0.7	9.8 ± 0.6	18.2 ± 0.9	10.5 ± 0.7	6.8 ± 0.5
2	40.2 ± 1.7	33.1 ± 1.3	26.5 ± 1.0	35.8 ± 1.4	21.4 ± 1.0	16.8 ± 0.8	29.8 ± 1.3	19.2 ± 0.9	12.8 ± 0.7
4	55.8 ± 1.8	48.2 ± 1.6	40.1 ± 1.3	49.8 ± 1.6	34.2 ± 1.2	27.8 ± 1.1	44.1 ± 1.5	30.5 ± 1.2	21.8 ± 1.0
6	67.5 ± 1.6	59.8 ± 1.4	51.6 ± 1.2	61.2 ± 1.3	45.5 ± 1.3	37.8 ± 1.2	55.2 ± 1.4	39.8 ± 1.3	30.8 ± 1.1
8	77.6 ± 1.4	69.5 ± 1.3	61.8 ± 1.3	71.4 ± 1.2	54.8 ± 1.1	47.2 ± 1.2	64.8 ± 1.3	50.2 ± 1.2	39.5 ± 1.1
10	86.5 ± 1.1	80.8 ± 1.0	73.2 ± 1.1	81.6 ± 0.9	67.8 ± 0.9	58.2 ± 1.0	75.1 ± 1.0	61.8 ± 1.0	48.6 ± 0.9
12	93.8 ± 0.8	87.6 ± 0.9	80.4 ± 0.9	90.2 ± 0.7	76.5 ± 0.9	66.8 ± 0.9	84.2 ± 0.8	72.5 ± 0.9	58.2 ± 1.0

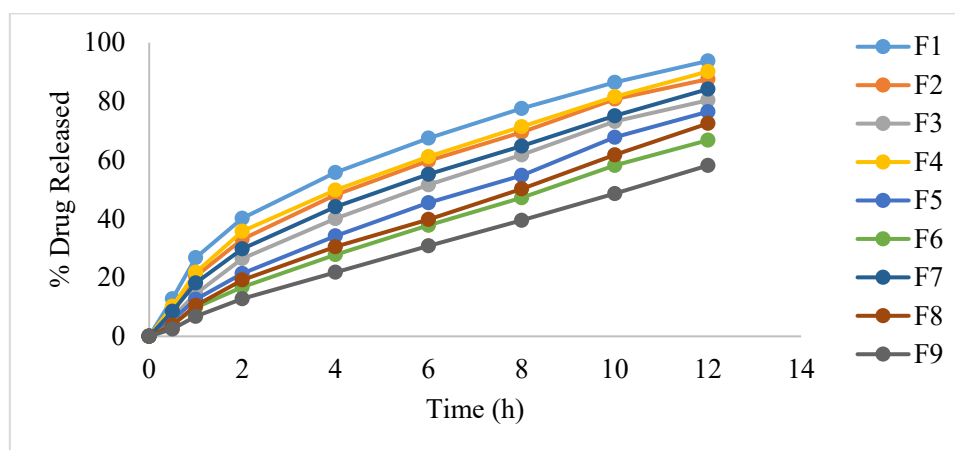


Figure 3. In-vitro Dissolution Profiles of Formulations F1-F9

3.5 Drug Release Kinetics and Mechanism

The Korsmeyer-Peppas model provided the highest R^2 (0.990), followed by zero-order (0.982) (Table 4). The release exponent (n) was 0.56, which lies between 0.45 and 0.89, classifying the mechanism as anomalous (non-Fickian) transport a coupling of

drug diffusion through the gel layer with polymer chain relaxation and matrix erosion (Table 4). The Higuchi model yielded a moderate fit ($R^2 = 0.964$), confirming that diffusion alone does not fully account for the observed release behaviour (Table 4). Release exponent (n) from Korsmeyer-Peppas model 0.56.

3.6 Accelerated Stability Studies

No changes in physical appearance, odour, or colour were observed. Drug content remained within acceptance criteria (97.5-99.8%) (Table 5). Dissolution profiles remained essentially unchanged with f_2 values above 80, confirming batch-to-batch reproducibility (Table 5).

Table 5. Accelerated stability data of optimized formulation F5 at ($40 \pm 2^\circ\text{C}$ / $75 \pm 5\%$ RH)

Parameter	Initial (Day 0)	1 Month	2 Months	3 Months
Appearance	White, smooth	No change	No change	No change
Assay (%)	99.8 ± 0.8	99.1 ± 1.0	98.4 ± 1.1	97.6 ± 1.2
Hardness (kg/cm^2)	5.1 ± 0.4	5.0 ± 0.5	4.9 ± 0.4	4.7 ± 0.5
Friability (%)	0.55 ± 0.03	0.57 ± 0.04	0.59 ± 0.04	0.62 ± 0.05
Release at 12 h (%)	76.5 ± 0.9	75.2 ± 1.0	73.9 ± 1.1	72.4 ± 1.2
f_2 versus Day 0	-	88.7	84.5	80.2

4. DISCUSSION

The central challenge in formulating a prolonged-release Imeglimin tablet stems from its BCS Class III classification - very high aqueous solubility and low-to-moderate intestinal permeability. Unlike poorly soluble drugs, the challenge with Imeglimin lies in achieving balanced release: sufficiently prolonged to maintain therapeutic concentrations over 12 hours, yet sufficiently complete for adequate bioavailability.

Hydrophilic matrix tablets rely on gel layer formation at the tablet-fluid interface. The findings demonstrate that while HPMC K100M alone can retard Imeglimin release, concentrations exceeding 7.7% are required to approach the 12-hour target, and even then release may be incomplete (F3 released only 80.4% at 12 h) (Table 3). The incorporation of Carbopol 940P synergistically augmented retardation while preserving release completeness at moderate total polymer loadings (7.7% w/w total polymer in F5) (Table 1).

This synergistic effect is mechanistically attributed to Carbopol's extensive swelling in neutral phosphate buffer, forming a highly viscous gel. Within the binary network, hydrogen bonding and physical chain entanglement between HPMC's cellulosic backbone and Carbopol's poly(acrylic acid) chains increase the local micro-viscosity of the gel layer, enhancing diffusion-path tortuosity and modulating erosion rate.

The kinetic analysis confirmed anomalous (non-Fickian) transport ($n = 0.56$), indicating comparable contributions from Fickian diffusion and polymer chain relaxation - highly favourable for prolonged-release formulations as it yields more consistent release rates compared to purely diffusion-controlled systems (Table 4).

The near-zero-order kinetics observed between 4 and 10 hours predict relatively constant plasma concentrations and reduced peak-to-trough fluctuations, potentially reducing gastrointestinal adverse effects commonly associated with immediate-release Imeglimin (Table 4).

5. CONCLUSION

This study successfully developed a twice-daily prolonged-release matrix tablet of Imeglimin hydrochloride (500 mg, total tablet weight 650 mg) by systematically optimizing a binary hydrophilic polymer system comprising HPMC K100M and Carbopol 940P. Formulation F5, containing 6.2% w/w HPMC K100M and 1.5% w/w Carbopol 940P, achieved a favorable release profile delivering approximately 76.5% of the drug over 12 hours with near-zero-order kinetics governed by anomalous (non-Fickian) transport (Tables 3 and 4). The tablets met all pharmacopeial quality specifications (Table 2) and demonstrated excellent

physicochemical stability under accelerated ICH conditions (Table 5). These findings support further development and bioavailability assessment as a patient-friendly alternative in type 2 diabetes mellitus management.

Acknowledgement

The authors sincerely acknowledge the contribution and support of the all author and institute for successfully conducting this research.

Conflict of Interest: Nil

Funding: Nil

REFERENCES

- [1] American Diabetes Association. Standards of Medical Care in Diabetes—2023. *Diabetes Care*. 2023;46(Suppl 1):S1-S291.
- [2] Fridman A, et al. Imeglimin, a novel oral anti-diabetic agent: a review of preclinical and clinical data. *Expert Opin Drug Saf*. 2021;20(4):435-444.
- [3] Caton PW, et al. Imeglimin: mitochondrial function modulator with unique anti-diabetic properties. *Diabetologia*. 2020;63(7):1342-1353.
- [4] Fujioka K, et al. Glycemic control in patients with type 2 diabetes mellitus switched from immediate-release to prolonged-release formulations. *Endocr Pract*. 2018;24(3):215-222.
- [5] Amidon GL, et al. A theoretical basis for a biopharmaceutical drug classification. *Pharm Res*. 1995;12(3):413-420.
- [6] Singh S, Rath S, Singh S, Sharma B, Dwivedi V. CD3-Bispecific Monoclonal Antibodies: A Novel Therapeutic Approach for Complex and Multifactorial Diseases. *Zhongguo Ying Yong Sheng Li Xue Za Zhi*. 2025 Aug 4;41:e20250019. doi: 10.62958/j.cjap.2025.019.
- [7] Peppas NA, et al. Hydrogels in pharmaceutical formulations. *Eur J Pharm Biopharm*. 2000;50(2):27-46.
- [8] International Council for Harmonisation. *Q1A(R2): Stability Testing of New Drug Substances and Products*. Geneva: ICH; 2003.
- [9] United States Pharmacopeia and National Formulary (USP 43-NF 38). Rockville, MD: USP; 2020.
- [10] International Council for Harmonisation. *Q2(R1): Validation of Analytical Procedures*. Geneva: ICH; 2005.
- [11] Ritger PL, Peppas NA. A simple equation for description of solute release II. *J Control Release*. 1987;5(3):371-385.
- [12] Costa P, Lobo JMS. Modeling and comparison of dissolution profiles. *Eur J Pharm Sci*. 2001;13(2):123-130.
- [13] Zhang Y, et al. DDSolver: an add-in program for modeling and comparison of drug dissolution profiles. *AAPS J*. 2010;12(3):263-271.