RESEARCH PAPER

Development and Evaluation of Glimepiride Transdermal Patches for Sustained Drug Delivery

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Background: Long-term management of Type 2 diabetes mellitus often relies on oral hypoglycaemic agents such as glimepiride; however, conventional administration is associated with variable bioavailability, first-pass metabolism, and fluctuations in plasma drug levels. These limitations can affect therapeutic outcomes and patient adherence. **Objective:** The present study was undertaken to develop and evaluate a membrane-moderated transdermal drug delivery system of glimepiride capable of providing controlled and sustained drug release. **Methods:** Transdermal patches were fabricated using a solvent casting technique with HPMC K100M and Eudragit RLPO as rate-controlling polymers. The formulations were subjected to pre-formulation studies, drug–polymer compatibility analysis using DSC and FTIR, and evaluation of physicochemical and mechanical properties. In-vitro drug release studies and stability testing under ICH conditions were also performed. R**esults:** The prepared patches exhibited uniform thickness, satisfactory mechanical strength, and consistent drug content. Compatibility studies confirmed the stability of glimepiride within the polymeric system. In-vitro release profiles demonstrated sustained drug release over 24 hours, with the optimized formulation achieving near-complete release while maintaining controlled kinetics. Stability studies indicated no significant changes in physicochemical properties or drug release behaviour over the study period. **Conclusion:** The developed transdermal system effectively provided controlled delivery of glimepiride and demonstrated adequate stability and performance characteristics. This approach offers a promising alternative to oral therapy by supporting sustained drug release and potentially improving therapeutic consistency in the management of Type 2 diabetes mellitus.

Keywords: Glimepiride, transdermal drug delivery system, HPMC K100M, Eudragit RLPO, sustained release, diabetes mellitus

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INTRODUCTION

Diabetes mellitus is a complex metabolic disorder characterized by chronic hyperglycaemia resulting from impaired insulin secretion, insulin resistance, or both[1]. The global incidence of Type 2 diabetes mellitus (T2DM) has risen steadily, making it one of the leading causes of morbidity and mortality worldwide[2]. Persistent elevation of blood glucose levels is closely

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associated with the development of long-term complications such as cardiovascular disease, neuropathy, nephropathy, and retinopathy, highlighting the need for effective and sustained glycaemic control[3].

Among the pharmacological agents used in the management of T2DM, sulfonylureas continue to play a significant role due to their insulin secretagogue activity. Glimepiride, a third-generation sulfonylurea, is widely prescribed because of its potency and comparatively improved safety profile. It lowers blood glucose levels by stimulating insulin release from pancreatic β-cells and enhancing peripheral glucose utilization[4],[5]. Despite these advantages, conventional oral administration of glimepiride presents several drawbacks, including extensive hepatic first-pass metabolism, variability in absorption, and the potential for hypoglycaemic episodes[6]. In addition, fluctuations in plasma drug concentration and gastrointestinal side effects can reduce therapeutic consistency and patient compliance during prolonged treatment[3].

To overcome these limitations, alternative drug delivery strategies have been explored, among which transdermal drug delivery systems (TDDS) have gained considerable attention. Transdermal delivery offers multiple benefits, including bypassing hepatic first-pass metabolism, maintaining steady plasma drug levels, minimizing dosing frequency, and improving patient adherence[7]. Furthermore, it reduces gastrointestinal irritation and enables controlled and sustained drug release, which is particularly advantageous in the management of chronic diseases such as diabetes[8].

The success of a transdermal system depends largely on both the physicochemical properties of the drug and the design of the polymeric matrix. Drugs suitable for transdermal delivery generally possess low molecular weight, moderate lipophilicity, and high potency[7]. Glimepiride fulfils these criteria, as it exhibits a molecular weight below 500 Da, moderate lipophilicity, and effectiveness at low doses, making it a promising candidate for transdermal administration[9],[13]. However, achieving a controlled and reproducible release profile requires the careful selection of polymers with complementary properties.

Hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC K100M) are known to form hydrated gel layers upon contact with moisture, facilitating drug diffusion and sustained release[10]. In contrast, hydrophobic polymers like Eudragit RLPO provide structural strength and regulate permeability due to the presence of quaternary ammonium groups[11]. The combination of these polymers enables the development of a balanced delivery system capable of modulating drug release while maintaining mechanical integrity.

Recent advancements in transdermal systems have demonstrated that polymer-based matrices can effectively control drug release and improve therapeutic performance[15]. Membrane-moderated systems, in particular, offer an additional level of control by incorporating rate-controlling barriers that regulate drug diffusion and reduce the likelihood of dose dumping[26],[27]. Such systems are especially valuable for drugs like glimepiride, where maintaining consistent plasma concentrations is critical for avoiding hypoglycaemic events.
In this context, the present study focuses on the design, development, and evaluation of a membrane-moderated transdermal drug delivery system of glimepiride using a combination of HPMC K100M and Eudragit RLPO. The objective is to achieve controlled and sustained drug release, minimize fluctuations in plasma drug levels, and enhance patient compliance in the long-term management of Type 2 diabetes mellitus.

2. METHODOLOGY

2.1. Materials

Glimepiride was obtained as a gift sample from a pharmaceutical manufacturer. Hydroxypropyl methylcellulose (HPMC K100M) and Eudragit RLPO were used as rate-controlling polymers. Organic solvents such as methanol, acetone, chloroform, and dichloromethane were employed for film preparation. Glycerine was used as a plasticizer to enhance flexibility. All other reagents used in the study were of analytical grade.

2.2. Pre-formulation Studies

Initial characterization of glimepiride was carried out to confirm its suitability for transdermal formulation. Physical properties such as appearance and odour were assessed by visual inspection. The melting point was determined using the capillary method to evaluate purity and crystalline nature.

Solubility was examined in various solvents, including distilled water, phosphate buffer (pH 7.4), and selected organic solvents, to identify suitable media for formulation and analysis. The partition coefficient was determined using an n-octanol and phosphate buffer system to assess lipophilicity and predict skin permeation behaviour.

2.3. Analytical Method Development

A UV spectrophotometric method was developed for the quantitative estimation of glimepiride. A standard stock solution was prepared in phosphate buffer (pH 7.4), followed by serial dilution to obtain working concentrations. Absorbance was measured at 228 nm,

and a calibration curve was constructed to establish linearity within the selected concentration range. The method was validated for precision and reproducibility prior to use in further studies.

2.4. Drug–Excipient Compatibility Studies

Compatibility between glimepiride and selected polymers was evaluated using Differential Scanning Calorimetry (DSC) and Fourier Transform Infrared (FTIR) spectroscopy.

For DSC analysis, accurately weighed samples were sealed in aluminium pans and heated under a controlled nitrogen atmosphere. Thermal transitions, including melting behaviour, were recorded to detect any potential interactions.

FTIR analysis was performed using the KBr pellet method. Spectra were recorded over an appropriate wavelength range, and characteristic peaks were analyzed to identify possible chemical interactions between the drug and excipients.

2.5. Preparation of Transdermal Patches

Transdermal patches were prepared using the solvent casting technique. Required quantities of HPMC K100M and Eudragit RLPO were dissolved separately in suitable organic solvents to form homogeneous solutions. Glimepiride was dissolved in a compatible solvent and incorporated into the polymer mixture with continuous stirring to ensure uniform dispersion.

A predetermined amount of glycerine was added as a plasticizer to improve film flexibility. The resulting solution was sonicated to remove entrapped air bubbles and then cast onto a flat surface using a Petri dish. The solvent was allowed to evaporate under controlled conditions to form uniform films. The dried films were carefully removed and cut into patches of defined size, then stored in a desiccator until further evaluation.

2.6. Evaluation of Transdermal Patches

The prepared patches were subjected to a series of physicochemical and mechanical evaluations.

- **Physical appearance:** Assessed for uniformity, smoothness, and absence of defects.
- **Thickness and weight variation:** Measured to ensure uniformity of the films.
- **Folding endurance:** Determined by repeatedly folding the patch at the same point until breakage.
- **Tensile strength and elongation:** Evaluated to assess mechanical integrity.
- **Moisture content and uptake:** Measured to understand stability and hygroscopic behaviour.
- **Drug content uniformity:** Determined by dissolving the patch and analyzing spectrophotometrically.
- **Surface pH:** Evaluated to ensure compatibility with skin.
- **Water vapour transmission rate (WVTR):** Measured to assess permeability characteristics.

2.7. *In-vitro* Drug Release Studies

Drug release studies were performed using a paddle-over-disc apparatus. The patches were placed in contact with phosphate buffer (pH 7.4) maintained at skin temperature conditions. Samples were withdrawn at predetermined intervals and analyzed spectrophotometrically. The cumulative amount of drug released was calculated and plotted against time.

2.8. Release Kinetic Analysis

The release data obtained from in-vitro studies were fitted to different kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. This analysis was performed to determine the mechanism governing drug release from the transdermal system.

2.9. Stability Studies

The optimized formulation was subjected to stability testing under controlled environmental conditions in accordance with ICH guidelines. Samples were stored at specified temperature and humidity conditions and evaluated at regular intervals for physical appearance, drug content, and release characteristics to assess formulation stability over time.

3. RESULTS AND DISCUSSION

3.1. Physicochemical Properties of Glimepiride

Glimepiride was obtained as a white to off-white crystalline powder with no detectable odour. The melting point was observed within the range of 207–209 °C, which closely corresponds to reported values, confirming the purity and crystalline nature of the drug. The drug exhibited negligible solubility in water but showed good solubility in organic solvents such as methanol, ethanol, chloroform, and acetone. The partition coefficient was found to be approximately 2.9, indicating moderate lipophilicity favourable for transdermal permeation.

Table 1. Physicochemical characterization of glimepiride including melting point, solubility, and partition coefficient confirming its suitability for transdermal delivery.

Parameter	Observed Value	Interpretation
Appearance	White to off-white crystalline powder	Pure drug
Odor	Odorless	Acceptable
Melting Point (°C)	207–209	Confirms purity
Solubility (Water)	Practically insoluble	Poor aqueous solubility
Solubility (Organic solvents)	Soluble	Suitable for formulation
Partition Coefficient (log P)	2.9 ± 0.1	Favorable for TDDS

Pre-formulation Findings

Glimepiride showed:

- Crystalline nature (melting point 207–209°C)
- Poor aqueous solubility
- Moderate lipophilicity

These properties support its suitability for TDDS[8,13].

3.2 Compatibility Studies

Table 2. Drug–excipient compatibility data (DSC parameters) of glimepiride and polymer mixture indicating absence of interaction and preservation of drug stability.

Sample	Onset Temp (°C)	Peak Temp (°C)	End Temp (°C)	Enthalpy (ΔH, J/g)	Interpretation
Pure Glimepiride	197.12	199.20	201.26	−63.82	Crystalline nature
Drug + Polymers	196.71	198.44	200.11	295.85	No interaction

DSC and FTIR results confirmed:

- No chemical interaction
- Stability of drug within polymer matrix

Similar compatibility outcomes have been reported in polymeric delivery systems[14].

3.3 Physicochemical Evaluation

Table 3. Mechanical properties of transdermal patches (thickness, folding endurance, tensile strength, and % elongation) demonstrating structural integrity and flexibility.

Formulation	Thickness (mm)	Folding Endurance	Tensile Strength (kg/cm²)	% Elongation
F1	0.313 ± 0.002	184 ± 2	0.38 ± 0.02	24.6 ± 1.2
F2	0.326 ± 0.002	197 ± 1	0.42 ± 0.02	28.3 ± 1.0
F3	0.340 ± 0.002	212 ± 1	0.47 ± 0.01	32.9 ± 1.1
F4	0.356 ± 0.002	229 ± 2	0.52 ± 0.02	37.4 ± 1.3
F5	0.369 ± 0.002	246 ± 1	0.58 ± 0.02	41.2 ± 1.5

Table 4. Drug content uniformity and surface pH of glimepiride patches confirming homogeneous drug distribution and skin compatibility.

Formulation	Drug Content (%)	Surface pH
F1	99.4 ± 0.6	6.4 ± 0.2
F2	99.1 ± 0.7	6.5 ± 0.2
F3	98.8 ± 0.6	6.6 ± 0.1
F4	98.5 ± 0.5	6.8 ± 0.1
F5	98.2 ± 0.6	6.9 ± 0.1

Table 5. Water vapour transmission rate (WVTR) and moisture characteristics of patches indicating controlled permeability and stability.

Formulation	Moisture Content (%)	Moisture Uptake (%)	WVTR (g/cm²/24 h)
F1	1.11 ± 0.08	1.33 ± 0.09	2.18 ± 0.09
F2	1.27 ± 0.07	1.58 ± 0.08	2.36 ± 0.08
F3	1.40 ± 0.06	1.71 ± 0.07	2.58 ± 0.07
F4	1.52 ± 0.05	1.91 ± 0.06	2.79 ± 0.06
F5	1.63 ± 0.06	2.10 ± 0.08	3.02 ± 0.08

All formulations demonstrated:

- Uniform thickness (0.31–0.36 mm)
- High folding endurance (>180 folds)

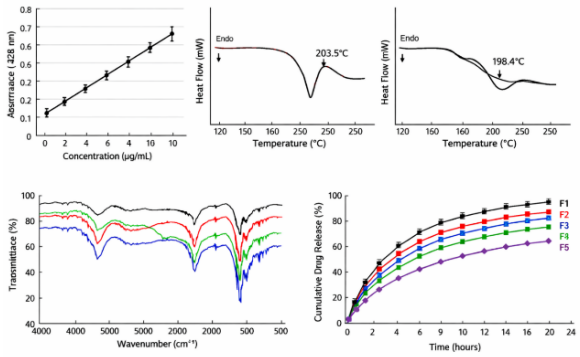
- Drug content within acceptable limits

Mechanical strength improved with increased polymer concentration, consistent with literature findings[15].

3.4 In-vitro Drug Release

Table 6. In-vitro cumulative drug release (%) of formulations (F1–F5) over 24 hours highlighting sustained release behaviour.

Time (h)	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	12.6 ± 0.8	10.8 ± 0.6	9.4 ± 0.7	8.1 ± 0.5	7.2 ± 0.6
2	21.9 ± 1.1	19.6 ± 0.9	17.3 ± 0.8	15.2 ± 0.7	13.8 ± 0.8
4	35.8 ± 1.2	32.4 ± 1.0	29.7 ± 0.9	26.5 ± 0.8	24.1 ± 0.9
6	48.7 ± 1.0	44.9 ± 1.1	41.6 ± 1.0	38.2 ± 0.9	35.6 ± 1.0
8	61.5 ± 1.3	57.2 ± 1.2	53.8 ± 1.1	50.4 ± 1.0	47.1 ± 1.1
12	78.9 ± 1.4	73.6 ± 1.3	69.2 ± 1.2	64.7 ± 1.1	60.8 ± 1.2
16	88.6 ± 1.2	83.1 ± 1.1	78.5 ± 1.0	73.4 ± 1.0	69.7 ± 1.1
20	93.4 ± 1.0	88.9 ± 1.0	84.2 ± 0.9	79.6 ± 0.9	75.8 ± 1.0
24	96.8 ± 0.9	92.4 ± 0.8	88.1 ± 0.8	83.5 ± 0.8	79.6 ± 0.9



All formulations showed sustained release over 24 hours.

- F1: 96.8% release
- F5: 79.6% release

Drug release decreased with increasing polymer concentration due to increased diffusional resistance[17].

Release followed:

- Higuchi model (diffusion-controlled)
- Korsmeyer–Peppas mechanism

These findings agree with established TDDS behavior[26].

3.5 Stability Studies

Table 7. Stability study results of optimized formulation (F1) under accelerated conditions showing retention of physicochemical properties and drug release profile.

Parameter	Initial	30 Days	60 Days	90 Days
Physical Appearance	Smooth	No change	No change	No change
Folding Endurance	184 ± 2	182 ± 2	181 ± 3	180 ± 3
Drug Content (%)	99.4 ± 0.6	99.1 ± 0.7	98.8 ± 0.6	98.5 ± 0.7
Drug Release at 24 h (%)	96.8 ± 0.9	96.2 ± 1.0	95.7 ± 1.1	95.1 ± 1.2

The optimized formulation remained stable for 90 days with:

- Minimal drug degradation
- Consistent release profile

This confirms formulation robustness for long-term use[22].

Figure 2. DSC Thermogram of pure Glimepiride and drug–polymer mixture confirming compatibility and absence of thermal interaction.

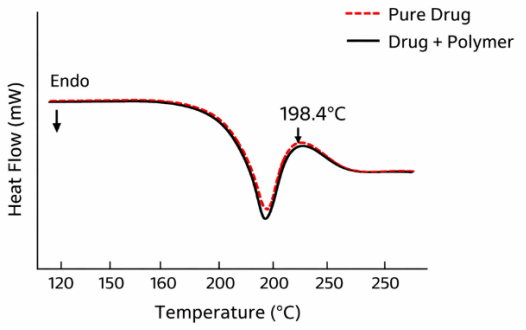


Figure 3. FTIR Spectra of Glimepiride and polymeric formulations showing retention of characteristic functional groups without chemical interaction.

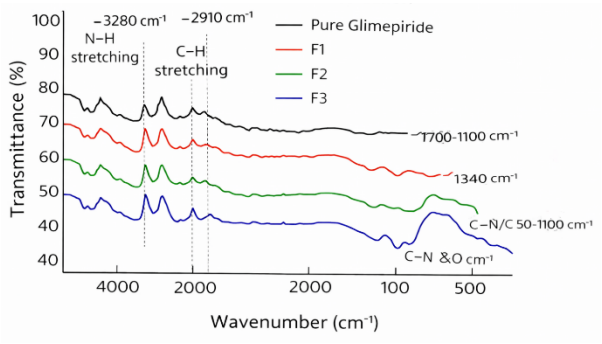


Figure 4. Comparative in-vitro drug release profiles of formulations F1–F5 illustrating sustained release and effect of polymer composition.

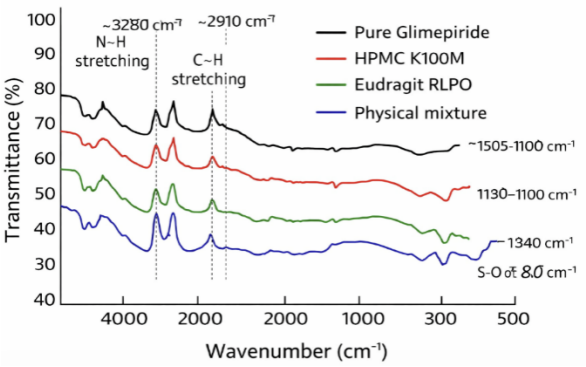
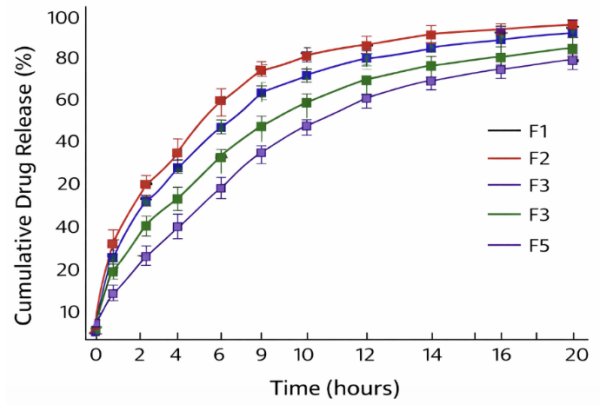


Figure 5. Drug release kinetic plots (Higuchi/Korsmeyer–Peppas) indicating diffusion-controlled release mechanism.



4.DISCUSSION

The present investigation demonstrates the successful development of a membrane-moderated transdermal drug delivery system of glimepiride with desirable physicochemical and release characteristics. The selection of glimepiride was guided by its moderate lipophilicity, low dose requirement, and short biological half-life, which collectively favor sustained transdermal delivery. The pre-formulation data summarized in **Table 1** confirmed that the drug possesses suitable physicochemical attributes, including adequate partition coefficient and solubility in organic solvents, facilitating its incorporation into polymeric matrices and subsequent permeation across the skin barrier.

Drug-excipient compatibility is a critical determinant of formulation stability. The thermal analysis presented in **Table 2** and **Figure 2** revealed that the characteristic melting endotherm of glimepiride remained largely unaltered in the presence of HPMC K100M and Eudragit RLPO, indicating the absence of significant interactions. This observation was further corroborated by FTIR spectral analysis (**Figure 3**), where all functional group peaks of the drug were retained without the appearance of new peaks or disappearance of existing ones. Such findings suggest that the drug remains chemically stable within the polymeric network, which is essential for maintaining therapeutic efficacy during storage and application.

Mechanical properties play a vital role in determining the practical applicability of transdermal patches. The results summarized in **Table 3** demonstrate that all formulations exhibited uniform thickness, adequate tensile strength, and high folding endurance, reflecting good film-forming ability and flexibility. The gradual improvement in mechanical strength with increasing polymer concentration can be attributed to enhanced intermolecular interactions within the polymer matrix. These findings are consistent with earlier reports where hydrophilic–hydrophobic polymer combinations contributed to improved mechanical integrity and durability of transdermal systems[15].

Uniform drug distribution and skin compatibility are essential for consistent therapeutic performance. The data presented in **Table 4** indicate that drug content across all formulations remained within acceptable limits, confirming homogeneous dispersion of glimepiride within the matrix. Additionally, the surface pH values were close to physiological skin pH, suggesting that the developed patches are unlikely to cause irritation upon application.

Moisture handling characteristics significantly influence both stability and performance of transdermal systems. As shown in **Table 5**, the formulations exhibited moderate moisture uptake and controlled water vapour transmission rates. The increase in WVTR with higher polymer content may be attributed to the hydrophilic nature of HPMC, which facilitates water diffusion through the matrix. At the same time, the presence of Eudragit RLPO contributes to controlled permeability due to its quaternary ammonium groups. This balance between hydrophilicity and hydrophobicity is crucial in maintaining optimal hydration at the skin interface without compromising structural integrity.

The in-vitro drug release profiles (**Table 6**, **Figure 4**) clearly demonstrate that all formulations provided sustained release of glimepiride over a 24-hour period. The initial phase of release can be attributed to rapid hydration and swelling of HPMC, followed by a controlled diffusion phase governed by the polymeric network. Among the formulations, F1 exhibited the highest cumulative drug release, indicating an optimal balance between polymer concentration and matrix porosity. In contrast, formulations with higher polymer content showed slower release rates, likely due to increased diffusional path length and matrix density.

To further elucidate the mechanism of drug release, kinetic modeling was performed, as illustrated in **Figure 5**. The release profiles predominantly followed Higuchi kinetics, indicating diffusion-controlled release, while Korsmeyer–Peppas analysis suggested a combination of diffusion and polymer relaxation mechanisms. These findings are in agreement with established theories of drug release from hydrophilic matrix systems, where swelling and erosion contribute alongside diffusion[26],[27].

Stability is a key requirement for pharmaceutical formulations intended for long-term use. The stability data presented in **Table 7** indicate that the optimized formulation (F1) maintained its physical appearance, drug content, and release profile over the study period under both room temperature and accelerated conditions. The minimal variations observed suggest that the polymeric system effectively protects the drug from degradation and maintains structural integrity over time.

The calibration curve shown in **Figure 1** confirmed the reliability and linearity of the analytical method used for drug quantification, ensuring accuracy in the evaluation of drug content and release studies.

Overall, the results demonstrate that the combination of HPMC K100M and Eudragit RLPO provides an effective platform for controlled transdermal delivery of glimepiride. The hydrophilic component facilitates swelling and drug diffusion, while the hydrophobic polymer modulates permeability, resulting in a sustained release profile. Such a system addresses the limitations associated with conventional oral therapy by maintaining steady plasma drug levels and potentially reducing the risk of hypoglycaemic episodes.

5.CONCLUSION

The present study successfully established a membrane-controlled transdermal delivery system for glimepiride with consistent performance and stability. The drug was found to possess suitable physicochemical characteristics for transdermal administration, as evidenced by its lipophilicity and compatibility with selected polymers. Compatibility studies confirmed that the drug remained stable within the polymeric matrix without any undesirable interactions, ensuring formulation integrity.

The prepared transdermal patches exhibited uniform physical characteristics, adequate mechanical strength, and satisfactory flexibility, indicating their suitability for practical application. Drug distribution within the patches was consistent, and the surface pH remained within a range compatible with skin, minimizing the likelihood of irritation.

The release studies demonstrated a controlled and prolonged delivery of glimepiride over 24 hours. The optimized formulation achieved a balanced release profile, avoiding rapid drug depletion while ensuring sufficient drug availability throughout the dosing period. The release mechanism was predominantly governed by diffusion through the hydrated polymer matrix, supported by polymer swelling behaviour.

Stability evaluation confirmed that the optimized system maintained its structural properties, drug content, and release characteristics under both normal and accelerated conditions, highlighting its robustness and potential for long-term storage.

Overall, the developed transdermal system provides a viable alternative to conventional oral therapy by offering sustained drug delivery, reduced dosing frequency, and improved therapeutic consistency. This approach has the potential to enhance patient adherence and minimize fluctuations in plasma drug levels, thereby contributing to better management of Type 2 diabetes mellitus.

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