RESEARCH PAPER

Design And Development Of Controlled Release Drug Delivery System Of Remogliflozin Etabonate

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ABSTRACT

The present research work focuses on the design and development of a controlled release matrix tablet of Remogliflozin Etabonate for effective management of Type 2 Diabetes Mellitus (T2DM). T2DM is a chronic metabolic disorder characterized by persistent hyperglycaemia and associated complications, necessitating sustained therapeutic control for improved patient outcomes. Remogliflozin Etabonate, a selective SGLT2 inhibitor with a short half-life (≈1.5–2 hours), requires frequent dosing, leading to fluctuating plasma drug levels. Therefore, a controlled release formulation was developed to prolong drug action and enhance patient compliance. Preformulation studies confirmed the identity and purity of the drug. The calibration curve demonstrated excellent linearity validating the analytical method. Matrix tablets were prepared using polymers such as Carbopol 934P and PVP K30 and optimized using a 3^2 factorial design. Pre- and post-compression parameters were within acceptable limits, indicating good flow properties and tablet integrity. The optimized formulation RF9 exhibited sustained drug release 99.45% over 24 hours with excellent swelling behaviour. Stability studies confirmed formulation robustness under accelerated conditions. Thus, the developed controlled release system provides a promising approach for sustained drug delivery, improved glycaemic control, and enhanced patient compliance.

Keywords: Remogliflozin Etabonate, Controlled Release, Matrix Tablet, Carbopol 934P.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a growing public health concern marked by persistent hyperglycaemia and progressive decline in β-cell function. Despite available therapies, many patients struggle to achieve stable glycaemic control due to fluctuating drug levels and poor adherence. In this context, drug delivery systems that provide consistent plasma exposure and reduced dosing frequency are increasingly recognized as a practical approach to improve both therapeutic outcomes and patient compliance.[1]

Remogliflozin etabonate, a selective SGLT2 inhibitor, lowers blood glucose by promoting urinary glucose excretion and has shown significant reductions in fasting glucose and HbA1c. However, its rapid absorption and short half-life (1.5–2 hours) may lead to peak–trough variations and require multiple daily dosing. These limitations make it a suitable candidate for controlled-release formulation.[2]

A sustained-release oral matrix system can effectively modulate drug release, prolong systemic exposure, and minimize fluctuations in plasma levels. Such an approach may reduce dosing frequency,

improve glycaemic stability, and enhance patient adherence, making it a promising strategy for optimized T2DM management.[3]

MATERIALS AND METHOD

MATERIALS: Excipients like Carbopol 934P, PVP K30, Microcrystalline Cellulose (MCC), Magnesium Stearate, Talc were obtained from Chemdyes Corporation, Rajkot, Gujarat.

METHOD: Controlled release tablets of Remogliflozin etabonate were prepared using the wet granulation method. All ingredients were accurately weighed and passed through sieve #30 to ensure uniform particle size. The drug and excipients, excluding talc and magnesium stearate, were thoroughly blended to obtain a homogeneous mixture. Granulation was carried out using water, and the wet mass was passed through sieve #16 to form granules. The prepared granules were dried in a hot air oven at 50–60°C for 30 minutes, followed by sizing through sieve #24 to achieve uniformity. The dried granules were then lubricated with talc and magnesium stearate to improve flow properties and prevent sticking during compression. Finally, the lubricated blend was compressed into tablets using a 12 mm punch.[4-5]

Statistical Optimization using 3^2 Factorial Design

The optimization of controlled-release tablets of Remogliflozin etabonate was carried out using a 3^2 factorial design based on preliminary trials. Two independent formulation variables - Carbopol 934P (X_1) and PVP K30 (X_2) were studied at three levels to evaluate their effect on key responses, namely percentage swelling index (Y_1) and percentage cumulative drug release (Y_2). Experimental data obtained from nine formulations were statistically analysed using ANOVA with Design-Expert software to determine the significance of each factor and their interactions.

The relationship between independent and dependent variables was described using a quadratic polynomial equation:

$$Y= B_0+ B_1X_1+ B_2X_2+ B_{12}X_1X_2+ B_{11}X_1^2+ B_{22}X_2^2+ E$$

where B_0 represents the intercept, B_1 and B_2 are coefficients of the main effects, B_{12} indicates the interaction effect, B_{11} and B_{22} correspond to quadratic terms, and E denotes experimental error.

The experimental design included nine formulations with Carbopol 934P and PVP K30 varied at low, medium, and high levels. This systematic approach enabled the identification of an optimized formulation with desirable swelling behaviour and controlled drug release characteristics. Formulation table is mentioned in table 1.

Table 1: Formulation Design of Controlled Release Tablets of Remogliflozin Etabonate

Ingredients (mg)	RF1	RF2	RF3	RF4	RF5	RF6	RF7	RF8	RF9
Remogliflozin Etabonate	100	100	100	100	100	100	100	100	100
Carbopol 934P	60	80	100	60	80	100	60	80	100
PVP K30	5	5	5	10	10	10	15	15	15
MCC PH102	125	105	85	120	100	80	115	95	75
Magnesium Stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
Purified Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Total Weight (mg)	300	300	300	300	300	300	300	300	300

Determination of Melting Point of Remogliflozin Etabonate

The melting point of Remogliflozin Etabonate was determined using a digital melting point apparatus. A small quantity of the drug was filled into a thin-walled capillary tube sealed at one end. The capillary tube was then placed in the melting point apparatus alongside a calibrated thermometer. The temperature range at which the drug sample melted was recorded. All measurements were performed in triplicate to ensure accuracy and reproducibility, and the average value was reported.[6]

Estimation of Remogliflozin Etabonate by UV spectroscopy method: 10 mg Remogliflozin Etabonate was dissolved in in 0.1 N HCl in 100 ml of

volumetric flask and diluted quantitatively with 0.1 N HCl to obtain a solution having a known concentration of 100 µg/ml. The standard solution of Remogliflozin Etabonate was subsequently diluted with 0.1 N HCl to obtain a series of dilutions containing 2, 4, 6, 8 and 10 µg/ml solution of Remogliflozin Etabonate. The absorbance of these solutions was measured in analytical technologies Limited, UV-Visible Spectrophotometer at 228 nm using 0.1 N HCl as blank.[7]

Determination of drug & Compatibility Study of Drug and Excipients by FTIR: FTIR was performed for determination of Remogliflozin Etabonate and was estimated for standard FTIR peaks. It was employed to identify the drug and excipients and assess their compatibility.[8]

Pre-Compression Parameters

Pre-compression parameters of the powder blend were evaluated to assess the flow characteristics and compressibility of the formulation prior to tablet compression.

Bulk Density[9-10]: Bulk density was determined by gently transferring a known mass of the powder blend into a graduated measuring cylinder without compacting the material. The volume occupied by the powder was recorded, and bulk density was calculated using the following equation:

$$\textbf{Bulk Density} = \frac{\textbf{Mass of powder (gm)}}{\textbf{Bulk volume of powder (ml)}}$$

Tapped Density[9-10]: Tapped density was measured using a mechanical tapping apparatus. A graduated cylinder containing a known quantity of powder blend was tapped repeatedly until a constant volume was obtained. The tapped density was then calculated using the following formula:

$$\textbf{Tapped Density} = \frac{\textbf{Mass of powder (gm)}}{\textbf{Tapped volume of powder (ml)}}$$

Compressibility Index (Carr's Index)[9-10]: The compressibility index indicates the flow properties of a powder blend and was calculated from the bulk and tapped densities using the following equation:

$$\textbf{Carr's index} = \frac{\textbf{Tapped Density} - \textbf{Bulk Density}}{\textbf{Tapped Density}} \boldsymbol{X\ 100}$$

Hausner's Ratio[9-10]: Hausner's ratio was calculated as the ratio of tapped density to bulk density and provides an indication of powder flowability. A Hausner's ratio value of ≤ 1.25 indicates good flow properties, whereas values greater than 1.25 indicate poor flow characteristics.

$$\textbf{Hausner's Ratio} = \frac{\textbf{Tapped Density}}{\textbf{Tapped Density}}$$

Angle of Repose[9-10]: The angle of repose was determined using the funnel method to evaluate the flowability of the powder blend. The powder was allowed to flow through a funnel positioned at a fixed height to form a conical heap on a flat surface. The height (h) and radius (r) of the powder cone were measured, and the angle of repose (θ) was calculated using the following equation:

$$\textbf{Tan}\ \theta = \frac{\textbf{Height of pile (h)}}{\textbf{radius of pile (r)}}$$

Post Compression Parameters

- **Thickness and diameter[11]:** Tablet thickness and diameter were measured by Digi-matic Vernier calipers. Five tablets were randomly collected and their thickness and diameter were measured by placing between two arms of Vernier calipers.
- **Weight variation[11]:** Twenty tablets were randomly collected and average weight was determined by using an electronic balance.
- **Hardness[12]:** Tablet hardness has been defined as the force required to break a tablet in a diametric compression test and was measured by using Monsanto type hardness tester.
- **Friability test[12]:** The friability of tablets was measured by Roche type friabilator. Twenty tablets were initially weighed and then tablets were placed in friabilitor at 25 rpm for 4 min then tablets were deducted and weighed again. Loss in weight should not be more than 1%. % friability determined by using following equation.

$$\%\ \textbf{Friability} = \frac{\textbf{Initial weight} - \textbf{Final weight}}{\textbf{Initial weight}} \times \textbf{100}$$

- **Drug content[13]:** Ten tablets were powdered and equivalent to 100 mg of Remogliflozin Etabonate was weighed and dissolved in 100 ml of 0.1 N HCl. The solution was filtered and 2 ml from filtrate was diluted to 10 ml and absorbance of this solution was analyzed by UV spectrophotometer at 228 nm.
- **Swelling Index[14]:** The extent of swelling was determined in terms of percentage weight gained

by the tablets. One tablet from each formulation was kept in dissolution apparatus USP type I (basket) containing volume of 900 ml 0.1N HCl. At regular time interval, tablets were withdrawn, soaked on tissue paper and weighed, and then percentage weight gain by the tablet was calculated using the formula.

$$\text{Swelling Index} = \frac{(\text{Initial weight of tablet} - \text{Final weight of tablet})}{\text{Final weight of tablet}} \times 100$$

- ***In Vitro* Drug release study[15]:** % drug release of Remogliflozin Etabonate Controlled Release tablet was determined by USP type II (paddle type) dissolution apparatus. This test performed using 900 ml of 0.1 N HCl at 37° ± 0.5 °C at 50 rpm. 5 ml sample solution was withdrawn from dissolution apparatus at regular time interval and the same quantity of sample was replaced with fresh dissolution media. The sample was filtered through 0.45 µm membrane filter. Absorbance of these samples was analyzed by using UV spectrophotometer at 228 nm.
- **Stability study of optimized batch[16]:** In the present study, stability study of optimized batch was carried out at 40° ± 2°C/ 75 ± 5% RH for time period of 1 month by wrapping the formulation in aluminium foil to prevent the formulation from exposure to light under the 40° ± 2 °C/ 75 ± 5% RH for 1 month as prescribed by ICH guidelines for accelerated stability study. After completion of 30 days tablets were evaluated for Hardness, Friability, Drug content, Wetting time, *In Vitro* Disintegration time and *In Vitro* Drug Release study.

RESULTS AND DISCUSSION

Melting point: Melting point determination is one of the popular techniques used to identify drug using melting point apparatus and melting point of Remogliflozin Etabonate was found in the range of 150 - 155 °C. Reported melting point of Remogliflozin Etabonate is 152 - 156 °C and is thus similar to the melting point of Remogliflozin Etabonate.

Estimation of drug by UV overlay spectra

The overlay spectra of drug were obtained by scanning different concentrations of solutions viz. 2, 4, 6, 8 and 10 ppm showed maximum absorption at 228 nm. The overlay spectra for Remogliflozin Etabonate is represented in Figure 1. The absorbance of different concentration of Remogliflozin Etabonate in 0.1 N HCl are shown in Table 2 and Figure 2.

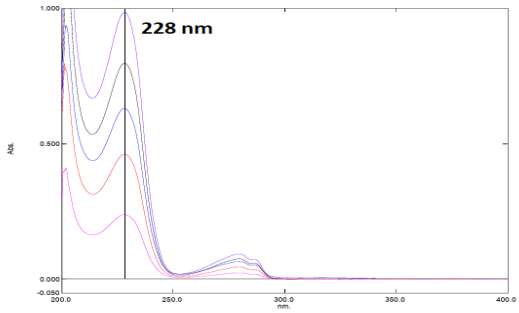

Figure 1: Overlay Spectra of Remogliflozin Etabonate

Table 2: Absorbance of different concentrations of Remogliflozin Etabonate in 0.1 N HCl

Sr. No.	Concentration (ppm)	Absorbance			Mean Absorbance ± SD
		I	II	III	
1	2	0.231	0.245	0.248	0.241 ± 0.009
2	4	0.451	0.455	0.459	0.455 ± 0.004
3	6	0.62	0.635	0.647	0.634 ± 0.013
4	8	0.799	0.801	0.805	0.802 ± 0.003
5	10	0.973	0.986	0.983	0.981 ± 0.006

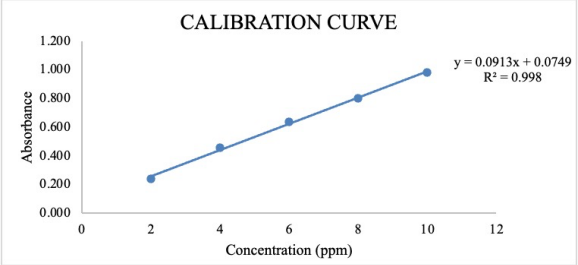

Figure 2: Calibration curve of Remogliflozin Etabonate in 0.1 N HCl

Identification of drug by FT-IR

Batch	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's index	Hausner's ratio	Angle of repose (Ø)
RF1	0.82 ± 0.04	0.93 ± 0.10	11.71 ± 11.66	1.15 ± 0.16	27.78 ± 1.06
RF2	0.53 ± 0.01	0.56 ± 0.00	4.92 ± 1.15	1.05 ± 0.01	27.35 ± 0.35
RF3	0.55 ± 0.01	0.58 ± 0.01	4.40 ± 2.15	1.05 ± 0.02	28.18 ± 0.37
RF4	0.86 ± 0.00	0.94 ± 0.05	8.05 ± 5.27	1.09 ± 0.06	29.05 ± 0.00
RF5	0.84 ± 0.02	0.98 ± 0.04	13.41 ± 5.64	1.16 ± 0.07	27.98 ± 0.72
RF6	0.81 ± 0.05	0.85 ± 0.07	4.38 ± 2.18	1.05 ± 0.02	28.18 ± 0.37
RF7	0.54 ± 0.01	0.56 ± 0.00	3.56 ± 1.20	1.04 ± 0.01	27.35 ± 0.35
RF8	0.88 ± 0.02	1.14 ± 0.05	22.29 ± 4.92	1.29 ± 0.08	30.23 ± 0.42
RF9	0.53 ± 0.01	0.58 ± 0.01	8.44 ± 2.02	1.09 ± 0.02	28.18 ± 0.37

The FTIR spectrum of Remogliflozin Etabonate clearly showed all the expected characteristic peaks associated with its key functional groups, confirming that the drug was authentic and correctly identified. When the spectra of the physical mixtures of the drug with excipients were compared with that of the pure drug, no notable changes such as peak shifts, disappearances, or formation of new peaks were observed. This indicates that Remogliflozin Etabonate remained chemically stable in the presence of all the excipients, suggesting good compatibility between the drug and the selected excipients.

Evaluation of Remogliflozin Etabonate Controlled Release Tablet Formulated by using 3^2 Factorial Design

Pre Compression Parameters: The factorial design batches (RF1–RF9) were evaluated for pre-compression parameters to assess their flow and packing characteristics prior to tablet compression.

Bulk density values ranged from 0.53 ± 0.01 to 0.88 ± 0.02 g/cm³, while tapped density varied between 0.56 ± 0.00 and 1.14 ± 0.05 g/cm³, indicating acceptable powder packing behavior across all formulations. Carr's index values were found in the range of 3.56 ± 1.20% to 22.29 ± 4.92%. Most batches exhibited Carr's index below 15%, suggesting good to fair flow properties, whereas RF8 showed comparatively higher compressibility, indicating slightly reduced flow. Hausner's ratio values ranged from 1.04 ± 0.01 to 1.29 ± 0.08, confirming that the majority of batches possessed good flowability suitable for direct compression. The angle of repose values was 27.35 ± 0.35° to 30.23 ± 0.42° further supported satisfactory flow characteristics of the powder blends (Table 3).

Overall, the pre-compression evaluation demonstrated that all factorial design batches possessed acceptable flow and compressibility properties, indicating their suitability for further tablet compression and post-compression evaluation.

Post Compression Parameters**:** The post-compression evaluation of factorial design batches RF1–RF9 was carried out to assess the physical quality and uniformity of the compressed tablets. All batches complied satisfactorily with pharmacopeial requirements, indicating robustness of the formulation design and compression process.

Table 3: Pre Compression Parameters data

Post compression parameters

The weight variation values ranged from 294.20 ± 26.91 mg to 301.10 ± 1.17 mg. All batches showed minimal deviation from the average tablet weight, confirming uniform die filling and acceptable flow behavior of the blends during compression. The tablet thickness varied between 2.80 ± 0.00 mm and 3.57 ± 0.12 mm, demonstrating consistent tablet dimensions across all batches. Such uniformity reflects controlled compression force and proper tooling alignment. Hardness values were found in the range of 6.67 ± 0.29 to 8.00 ± 0.50 kg/cm², indicating adequate

mechanical strength of the tablets to withstand handling, packaging, and transportation. Batches RF6, RF8, and RF9 exhibited comparatively higher hardness, which may contribute to enhanced matrix integrity and controlled drug release. The friability of all formulations was below 1% (0.71–0.87%), complying with pharmacopeial limits and confirming good resistance to abrasion. Slightly higher friability values observed in batches with increased polymer content still remained within acceptable limits, indicating no adverse impact on tablet integrity. The drug content ranged from 98.53 ± 0.47% to 99.60 ± 0.28%, demonstrating excellent content uniformity across all factorial batches (Table 4).

This confirms homogeneous distribution of the drug within the polymeric matrix and validates the suitability of the mixing process. Overall, the post-compression evaluation results indicate that all factorial design batches (RF1–RF9) possess satisfactory physical characteristics, mechanical strength, and uniform drug content. These findings confirm that the formulations are suitable for further *in-vitro* performance evaluation and optimization studies

Table 4: Post compression parameters data

Batch	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability	Drug Content
RF 1	300.30 ± 1.45	3.23 ± 0.47	6.67 ± 0.29	0.71	99.08 ± 0.64
RF 2	299.60 ± 1.43	3.30 ± 0.35	6.67 ± 0.58	0.75	99.37 ± 0.35
RF 3	300.35 ± 1.09	3.27 ± 0.40	7.50 ± 0.50	0.81	98.97 ± 0.55
RF 4	299.10 ± 1.25	3.20 ± 0.35	6.67 ± 0.29	0.73	98.80 ± 0.59
RF 5	300.75 ± 1.37	3.10 ± 0.17	6.83 ± 0.29	0.79	99.04 ± 0.57
RF 6	294.20 ± 26.91	2.83 ± 0.06	7.83 ± 0.76	0.84	99.60 ± 0.28
RF 7	299.85 ± 1.39	2.80 ± 0.00	6.67 ± 0.29	0.76	98.53 ± 0.47
RF 8	301.10 ± 1.17	2.93 ± 0.23	7.83 ± 0.76	0.82	99.12 ± 0.09
RF 9	299.60 ± 1.31	3.57 ± 0.12	8.00 ± 0.50	0.87	99.48 0.23

Swelling Index (%):

- The swelling behaviour of controlled release matrix tablets is a critical parameter influencing drug diffusion, matrix integrity, and overall release kinetics. The % swelling index of Remogliflozin etabonate controlled release tablets (RF1–RF9) was evaluated over a period of 24 hours, and the results demonstrated a clear time-dependent swelling pattern for all formulations.
- All batches exhibited an initial rapid swelling phase during the first 6–8 hours, which may be attributed to the immediate hydration and relaxation of polymeric chains upon contact with the dissolution medium. At 1 hour, swelling index values ranged from 55.18% (RF1) to 80.36% (RF9), indicating prompt water uptake by the hydrophilic matrix. This initial swelling is essential for gel layer formation, which governs controlled drug diffusion.
- Between 8 and 12 hours, a gradual and more controlled increase in swelling index was observed across all formulations. At 12 hours, RF1 showed a swelling index of 200.36%, whereas RF9 exhibited a significantly higher value of 280.36%, reflecting the influence of polymer concentration and composition on matrix expansion. This phase corresponds to stable gel layer formation, which contributes to sustained drug release by creating a diffusional barrier.
- At later time points (16–24 hours), swelling continued progressively, indicating sustained

hydration without structural disintegration of the matrix. After 24 hours, RF1 showed the lowest swelling index (290.22%), while RF9 demonstrated the highest swelling index (430.18%). The higher swelling observed with RF6–RF9 suggests increased polymer content or higher viscosity grades, leading to enhanced water retention and matrix swelling. Such behaviour is desirable for prolonged drug release, as it maintains matrix integrity and prevents dose dumping (Table 5 and Figure 3).

- Comparative evaluation revealed the swelling index order as RF9 > RF6 > RF8 > RF7 > RF5 > RF4 > RF3 > RF2 > RF1. Formulations exhibiting higher swelling indices are expected to provide better control over drug release due to increased gel strength and diffusional path length. Conversely, lower swelling formulations may result in comparatively faster drug diffusion.
- Overall, the swelling index study confirms that polymer concentration and formulation variables significantly influence matrix hydration and swelling behaviour. The sustained and controlled swelling observed, particularly in RF9, RF6, and RF8, supports their suitability for controlled release drug delivery of Remogliflozin etabonate over 24 hours.

Table 5: Swelling Index (%) of RF1 to RF9 Batch

Time (hrs)	RF1	RF2	RF3	RF4	RF5	RF6	RF7	RF8	RF9
0	0	0	0	0	0	0	0	0	0
2	55.18	60.45	70.22	58.18	68.22	78.36	65.36	75.22	80.36
4	75.36	80.42	90.36	78.22	88.36	98.22	85.22	95.18	100.18
6	105.18	115.18	130.42	110.22	125.18	140.36	120.36	135.22	145.22
8	135.36	142.36	160.18	140.36	160.18	180.22	150.22	170.18	185.18
10	165.22	175.18	200.45	170.36	195.18	220.36	190.36	215.18	225.22
12	200.36	220.36	250.18	210.18	240.36	270.22	230.18	260.42	280.36
14	230.18	250.18	285.36	240.36	275.18	310.45	260.36	300.22	320.22
16	260.36	285.42	325.18	275.18	315.36	355.22	300.22	340.45	365.36
18	290.22	320.22	370.36	310.36	360.18	410.45	340.45	390.18	430.18

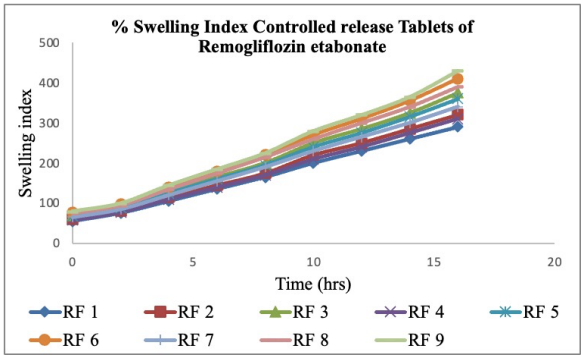

Figure 3: % Swelling Index vs Time of Batch RF1 to RF9

- **Cumulative Drug Release study**: *In-vitro* drug release studies were carried out to evaluate the controlled release performance of Remogliflozin etabonate matrix tablets (RF1–RF9) over a period of 24 hours. The % cumulative drug release profiles demonstrated a sustained and time-dependent release pattern for all formulations, confirming the suitability of the selected polymeric matrices for controlled drug delivery.
  - During the initial phase (0–2 hours), all formulations exhibited limited drug release, ranging from 12.18% to 21.36% at 1 hour and 20.32% to 28.92% at 2 hours. This controlled initial release suggests the absence of dose dumping and indicates effective formation of a hydrated gel barrier

on the tablet surface, restricting rapid drug diffusion. Between 4 and 8 hours, a gradual and uniform increase in drug release was observed. At 8 hours, the %CDR values ranged from 55.18% (RF1) to 65.22% (RF9). This phase corresponds to polymer swelling and matrix relaxation, allowing diffusion-controlled release of the drug through the hydrated polymer network. The consistency of release during this interval highlights the reproducibility and robustness of the matrix system. In the later phase (12–24 hours), all formulations showed sustained drug release with gradual progression towards completion. At 12 hours, drug release ranged from 65.22% (RF1) to 78.18% (RF9), while at 24 hours, RF1 exhibited the lowest release (88.45%) and RF9 showed the highest release (99.45%) (Table 6 and Figure 4)

- The increased drug release observed in RF6–RF9 may be attributed to optimized polymer concentration and composition, which provided a balance between matrix swelling, erosion, and diffusion. Comparative analysis revealed the order of drug release at 24 hours as RF9 > RF6 > RF8 > RF7 > RF5 > RF3 > RF4 > RF2 > RF1. Formulations with higher polymer swelling capacity exhibited enhanced control over drug diffusion, resulting in near-complete yet sustained drug release. In contrast, formulations with lower polymer content showed relatively slower and incomplete release within the same duration. Overall, the %CDR study confirms that formulation variables significantly influenced the release behaviour of Remogliflozin etabonate. Among all batches, RF9 demonstrated an optimal controlled release profile with approximately 99% drug release at 24 hours, indicating its suitability as the optimized formulation for once-daily controlled release therapy.

Table 6: Cumulative Drug Release RF1 to RF9 batch

Time (hrs)	RF1	RF2	RF3	RF4	RF5	RF6	RF7	RF8	RF9
0	0	0	0	0	0	0	0	0	0
1	12.18	15.85	19.26	14.36	17.48	20.56	18.93	16.15	21.36
2	20.32	23.48	27.36	22.18	25.18	28.1	26.05	24.36	28.92
4	32.36	36.489	40.22	35.22	38.26	40.28	39.05	37.26	42.36
6	45.18	48.15	52.48	47.36	51.56	53.49	52.45	50.22	55.18
8	55.18	58.32	61.48	57.22	60.18	62.42	62.36	60.36	65.22
12	65.22	70.36	75.42	68.36	73.6	76.89	74.26	72.18	78.18
16	75.45	80.22	85.22	78.22	83.69	84.56	85.18	82.36	88.45
20	82.18	88.36	92.42	85.36	90.28	92.45	91.25	89.58	95.18
24	88.45	93.22	97.22	92.18	95.36	98.22	95.18	97.36	99.45

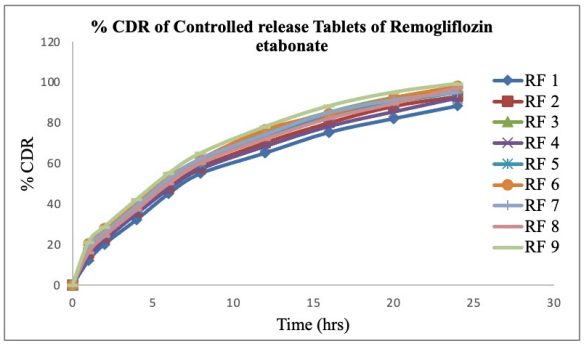

Figure 4: % CDR vs Time of batch RF1 to RF9

Statistical analysis for % Swelling Index at 18 hrs.

The swelling behavior of the formulations was well explained by the quadratic polynomial equation $Y_1 = 358.57 + 45.83B_1 + 29.17B_2 + 1.15B_{12} + 2.64B_1^2 - 2.56B_2^2$, indicating that both Carbopol 934P (X_1) and PVP K30 (X_2) contributed positively to the swelling index (Y_1). Among the two, Carbopol 934P had a stronger influence, as reflected by its higher coefficient value. The interaction term suggested a mild synergistic effect between the polymers, while the quadratic terms indicated that increasing Carbopol concentration continues to enhance swelling, whereas excessive amounts of PVP K30 may slightly reduce it at higher levels. The contour plot (Figure 5a) showed a gradual and uniform increase in swelling from lower to higher regions, suggesting a predictable and controlled response, with maximum swelling observed at higher polymer concentrations, especially Carbopol 934P. This trend was further supported by the 3D surface plot (Figure 5b), which displayed a smooth and steadily rising surface without abrupt changes, indicating good formulation stability. Moreover, the predicted vs. actual plot (Figure 5c) demonstrated a close agreement between experimental and predicted values, confirming the reliability and accuracy of the model. Overall, the findings highlight that Carbopol 934P plays a crucial role in governing swelling behavior, and its optimal combination with PVP K30 is important for achieving the desired controlled drug release profile.

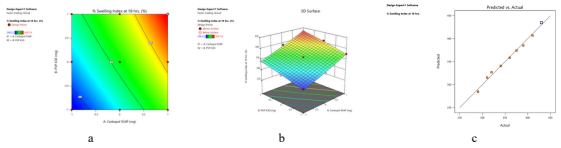

Figure 5: (a) Contour plot showing the effect Carbopol 934 P (X_1) and PVP K30 (X_2) on % Swelling Index at 18 hrs. (b) 3D surface plot showing the effect of Carbopol 934 P (X_1) and PVP K30 (X_2) on % Swelling Index at 18 hrs. (c)Actual value vs predicted value of % Swelling Index at 18 hrs.

6.4.2. Statistical analysis for % CDR at 24 hrs.

The cumulative drug release at 24 hours was described by the polynomial equation $Y_2 = 95.38 + 3.18B_1 + 2.18B_2 - 1.13B_{12} - 0.1967B_1^2 - 0.1067B_2^2$, which shows that both Carbopol 934P (X_1) and PVP K30 (X_2) contribute positively to drug release, with Carbopol having a slightly stronger effect. However, the negative interaction term indicates that when both polymers are used together at higher levels, their combined effect is not entirely additive. The negative quadratic terms suggest that increasing the concentration of either polymer beyond a certain level may slightly reduce drug release, likely due to the formation of a more viscous and dense gel matrix that slows down drug diffusion. The contour plot (Figure 6a) shows a smooth and gradual increase in drug release across the formulation range, with higher release observed at increased polymer concentrations. This behavior is further supported by the 3D surface plot (Figure 6b), which displays a steady and uniform surface without sharp changes, indicating consistent performance of the formulations. The predicted vs. actual plot (Figure 6c) demonstrates that the experimental values closely match the predicted values, confirming that the model is accurate and reliable. Overall, the findings suggest that while both Carbopol 934P and PVP K30 help in enhancing drug release, maintaining an optimal balance between them is important, as very high concentrations may slightly slow down the release due to increased matrix strength.

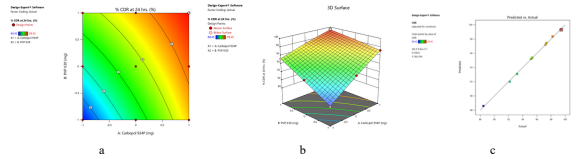

Figure 6: (a) Contour plot showing the effect of Carbopol 934 P (X_1) and PVP K30 (X_2) on % CDR at 24 hrs. (b) 3D surface plot showing the effect of Carbopol 934 P (X_1) and PVP K30 (X_2) on % CDR at 24 hrs. (c) Actual value vs predicted value of % CDR at 24 hrs.

Stability study

On the basis of all above parameters of Factorial Design batches it was concluded that the batch RF9 was an optimized batch, as it had good surface appearance, Mechanical strength and Drug Content. A stability study was carried out to check the stability of Controlled release tablets of the Optimized batch. A stability study carried out at 40°± 2 °C and 75 ± 5% RH for one month. After time period of one-month Hardness, Drug Content and *In-vitro* Drug Release study was carried out and results are shown

in Table 7 and 8. Comparison study between the result of optimized batch and after time period of stability of optimized batch is graphically illustrated in Figure 7.

Table 7: Result of the Stability study

Parameters	Optimized batch (RF9)	Optimized batch after 1 month
Hardness (kg/cm^2)	8.00 ± 0.50	8.80 ± 0.26
Drug Content (%)	99.48 ± 0.23	99.06 ± 0.10

Table 8: % Cumulative Drug Release of Stability batch

Time (hrs)	% CDR of Optimized Batch (RF9)	% CDR of Optimized batch after 1 Month
0	0	0
1	21.36	20.24
2	28.92	27.61
4	42.36	40.99
6	55.18	54.51
8	65.22	64.85
12	78.18	77.61
16	88.45	87.95
20	95.18	94.43
24	99.45	98.79

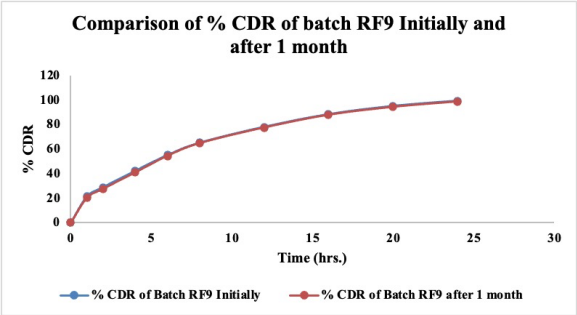

Figure 7: Comparison of % CDR of Optimized batch and Stability batch

Conclusion

The present study focused on the design and development of controlled-release matrix tablets of Remogliflozin etabonate for improved management of Type 2 diabetes mellitus. Preformulation studies confirmed the identity, purity, and compatibility of the drug with selected excipients, as no significant interactions were observed in FTIR analysis. Matrix tablets were successfully prepared using wet granulation with polymers Carbopol 934P and PVP K30. All formulations exhibited acceptable pre- and post-compression parameters, indicating good flow properties, mechanical strength, and content uniformity. Swelling and dissolution studies demonstrated that drug release was highly dependent on the type and concentration of polymer used. Among all the batches, Carbopol 934P-based formulations showed superior swelling behaviour and sustained drug release compared to other polymers. Optimization using a 3^2 factorial design revealed that both Carbopol 934P and PVP K30 significantly influenced swelling index and drug release. The optimized formulation (RF9) exhibited controlled drug release (~99.45%) over 24 hours with excellent matrix integrity and stability. The optimized formulation demonstrated desirable physicochemical properties, consistent drug release, and stability, making it suitable for once-daily administration. The use of Carbopol 934P in combination with PVP K30 proved effective in achieving controlled drug delivery. Overall, this formulation approach offers a promising strategy to enhance therapeutic efficacy, improve glycaemic control, and increase patient compliance in the management of Type 2 diabetes mellitus.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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