RESEARCH PAPER

Development and Statistical Optimization of Remogliflozin Etabonate Transdermal Drug Delivery System Using DoE

Ayushi Jain[1*], Akhlesh Kumar Singhai[1]

[1] School of Pharmacy, LNCT University, Bhopal (Madhya Pradesh)

[*] **Corresponding Author:** Ayushi Jain. Email: ayushijain131195@gmail.com

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ABSTRACT

The present study aimed to optimize and evaluate transdermal patches of Remogliflozin Etabonate using a Box–Behnken design (BBD). Independent variables such as HPMC K4, Eudragit RLPO, and Eudragit RSPO were systematically varied to study their effect on critical quality attributes including drug content, folding endurance, and patch thickness. A total of 13 experimental runs were performed, and the optimized formulation was selected based on the desired responses. The results showed that drug content ranged from 95.12% to 99.12%, folding endurance from 162 to 192, and patch thickness from 0.228 mm to 0.272 mm. The optimized formulation (F11) exhibited drug content of 99.12%, folding endurance of 172, and patch thickness of 0.258 mm, with values closely matching predicted responses, confirming model validity. Evaluation studies indicated acceptable physicochemical properties including weight variation, surface pH, moisture content, and tensile strength. In vitro drug release studies demonstrated sustained drug release up to 88.95% over 12 hours. Release kinetics analysis revealed that the optimized formulation followed the Korsmeyer–Peppas model, indicating a non-Fickian diffusion mechanism. Stability studies conducted as per ICH guidelines confirmed that the formulation remained stable under both intermediate and accelerated conditions. In conclusion, the study successfully optimized transdermal patches of remogliflozin etabonate with desirable properties, controlled drug release, and good stability, suggesting its potential as an effective transdermal drug delivery system for diabetes management.

Keywords: Remogliflozin etabonate, Transdermal patch, Box–behnken design, Doe, Hpmc k4, Eudragit rlpo, Drug content, Folding endurance, Controlled release, Stability study.

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Introduction

Transdermal drug delivery systems (TDDS) have gained significant attention as an effective alternative to conventional oral and parenteral routes due to their ability to provide controlled drug release, improve patient compliance, and avoid first-pass metabolism [1]. These systems deliver drugs across the skin into systemic circulation, maintaining steady plasma drug concentrations over an extended period. The development of transdermal patches is particularly advantageous for drugs with short half-lives and those requiring sustained therapeutic action [2].

Remogliflozin Etabonate is a sodium-glucose co-transporter-2 (SGLT2) inhibitor used in the management of type 2 diabetes mellitus. It works by inhibiting glucose reabsorption in the kidneys, thereby promoting glucose excretion and reducing blood glucose levels. However, its oral administration is associated with certain limitations such as variable bioavailability and the need for frequent dosing. Therefore, the development of a transdermal drug delivery system for remogliflozin etabonate can offer improved therapeutic efficacy and patient compliance [3-4].

The formulation of transdermal patches requires careful selection and optimization of polymers to achieve desired mechanical strength, drug release profile, and stability. Polymers such as hydroxypropyl methylcellulose (HPMC) and Eudragit derivatives are widely used due to their

film-forming ability and controlled release characteristics. The interaction between formulation variables significantly influences the quality attributes of the final product, making optimization a critical step in formulation development [5].

Design of Experiments (DoE) is a systematic and efficient statistical approach used to study the effects of multiple variables and their interactions on formulation performance. Among various DoE techniques, the Box–Behnken design (BBD) is widely used for optimization studies as it requires fewer experimental runs while providing reliable results. It helps in developing mathematical models, generating response surface plots, and identifying optimal formulation conditions [6].

In the present study, a Box–Behnken design was employed to optimize the formulation of remogliflozin etabonate transdermal patches by evaluating the effects of independent variables such as polymer concentrations on critical responses including drug content, folding endurance, and patch thickness. The optimized formulation was further evaluated for physicochemical properties, in vitro drug release, and stability to ensure its suitability as a controlled drug delivery system.

Material and Methods

Material

Remogliflozin Etabonate was used as the active pharmaceutical ingredient. Hydroxypropyl methylcellulose (HPMC K4), Eudragit RLPO, and Eudragit RSPO were used as film-forming polymers. Polyethylene glycol (PEG-400) was employed as a plasticizer to enhance flexibility of the patches. Solvents such as methanol and distilled water were used for preparation of the casting solution. All other reagents and chemicals used in the study were of analytical grade and procured from standard suppliers.

Methods

Preparation of Remogliflozin Etabonate Transdermal Patches Using DoE

Transdermal patches containing Remogliflozin etabonate were prepared by the solvent evaporation technique and optimized using Design of Experiments (DoE) based on Box–Behnken Design (BBD). Initially, a 2% polyvinyl alcohol (PVA) solution was poured into a glass mold to form the backing membrane and dried at 60°C for 6 hours. The drug reservoir layer was prepared by dissolving HPMC K4, Eudragit RLPO, and Eudragit RSPO in a chloroform:methanol (1:1) solvent system according to the polymer ratios suggested by the experimental design. Dibutyl phthalate (15% w/w of total polymer weight) was added as a plasticizer to improve film flexibility. Remogliflozin etabonate (50 mg) dissolved in 5 mL of the solvent mixture was incorporated into the polymer solution under continuous stirring to obtain a homogeneous dispersion. The resulting solution was cast onto the prepared PVA backing membrane and allowed to dry at room temperature for 24 hours to form transdermal films[7]. The dried patches were carefully removed, cut into appropriate sizes, and stored in a desiccator between wax paper sheets until further evaluation. The prepared patches were subsequently characterized to determine the effect of formulation variables on the properties of the transdermal system.

Table 1: Independent variables (factors) selected for BBD

Factor Code	Independent Variable	Low Level (-1)	Medium Level (0)	High Level (+1)
A	HPMC K4 (mg)	150	200	250
B	Eudragit RLPO (mg)	0	50	100
C	Eudragit RSPO (mg)	50	100	150

Table 2: Selection of dependent variables (responses) for optimization

Response Code	Response	Objective
Y1	Drug content (%)	Maximize
Y2	Folding endurance	Maximize
Y3	Patch thickness (mm)	Control

Table 3: Experimental Design Matrix and Responses for the Preparation of Remogliflozin Etabonate Transdermal Patches Using DoE

F. Code	Std	Run	Factor 1	Factor 2	Factor 3
			A:HPMC K4	B:Eudragit RLPO	C:Eudragit RSPO
			(mg)	(mg)	(mg)

F1	7	1	150	50	150
F2	9	2	200	0	50
F3	11	3	200	0	150
F4	5	4	150	50	50
F5	4	5	250	100	100
F6	6	6	250	50	50
F7	12	7	200	100	150
F8	10	8	200	100	50
F9	3	9	150	100	100
F10	8	10	250	50	150
F11	17	11	200	50	100
F12	1	12	150	0	100
F13	2	13	250	0	100

Final Equation in Terms of Coded Factors

Drug content = +98.58 + 0.7963A + 0.3388B + 0.0325C − 0.0350AB + 0.4675AC + 0.5625BC − 1.46A² − 0.0915B² − 0.6490C²

Final Equation in Terms of Actual Factors

Drug content = +73.64275 + 0.231765(HPMC K4) − 0.009265(Eudragit RLPO) + 0.003920(Eudragit RSPO) − 0.000014(HPMC K4 × Eudragit RLPO) + 0.000187(HPMC K4 × Eudragit RSPO) + 0.000225(Eudragit RLPO × Eudragit RSPO) − 0.000585(HPMC K4²) − 0.000037(Eudragit RLPO²) − 0.000260(Eudragit RSPO²).

Final Equation in Terms of Coded Factors

Folding Endurance = 169.60 + 8.63A + 3.00B + 4.38C + 2.75AB + 3.00AC + 2.25BC − 0.0500A² + 6.20B² + 4.45C²

Final Equation in Terms of Actual Factors

Folding Endurance = 186.05 + 0.0055(HPMC K4) − 0.4980(Eudragit RLPO) − 0.5535(Eudragit RSPO) + 0.0011(HPMC K4 × Eudragit RLPO) + 0.0012(HPMC K4 × Eudragit RSPO) + 0.0009(Eudragit RLPO × Eudragit RSPO) − 0.00002(HPMC K4²) + 0.00248(Eudragit RLPO²) + 0.00178(Eudragit RSPO²).

Final Equation in Terms of Coded Factors

Patch Thickness = 0.2482 + 0.0133A + 0.0075B + 0.0083C + 0.0010AB + 0.0025AC − 0.0035BC − 0.0021A² + 0.0049B² + 0.0014C².

Final Equation in Terms of Actual Factors

Patch Thickness = 0.165100 + 0.000481(HPMC K4) + 0.000014(Eudragit RLPO) − 0.000077(Eudragit RSPO) + 4.00000E−07(HPMC K4 × Eudragit RLPO) + 1.00000E−06(HPMC K4 × Eudragit RSPO) − 1.40000E−06(Eudragit RLPO × Eudragit RSPO) − 8.40000E−07(HPMC K4²) + 1.96000E−06(Eudragit RLPO²) + 5.60000E−07(Eudragit RSPO²).

Evaluation of Remogliflozin Etabonate Transdermal Patches

Drug Content

Drug content of the prepared transdermal patches was determined to evaluate the uniform distribution of the drug in the polymeric matrix. A patch of known area (1 cm²) was cut into small pieces and transferred into a volumetric flask containing 10 mL of methanol. The solution was sonicated for 30 minutes to ensure complete extraction of the drug. The resulting solution was filtered through Whatman filter paper No. 1 and suitably diluted with methanol. The absorbance of the solution was measured using a UV–Visible spectrophotometer at the λmax of Remogliflozin Etabonate. The drug content was calculated using the previously prepared calibration curve [8].

Folding Endurance

Folding endurance was determined to evaluate the mechanical strength and flexibility of the transdermal patches. A small strip of the patch (2.5 cm × 2.5 cm) was repeatedly folded at the same place until it broke. The number of times the patch could be folded without breaking or developing visible cracks was recorded as the folding endurance value [9].

Patch Thickness

The thickness of the prepared patches was measured using a digital vernier caliper or micrometer screw gauge. The thickness was measured at three different points of each patch, and the average value was calculated to ensure uniformity of the prepared films [10].

Weight Variation

Three patches of equal size were randomly selected and weighed individually using a digital balance. The average weight was calculated and compared to determine the uniformity of the prepared patches[11].

Surface pH

The surface pH of the transdermal patches was determined to ensure that the formulation does not cause skin irritation. The patch was allowed to swell in 1 mL of distilled water for 1 hour, and the pH was measured using a digital pH meter by placing the electrode on the surface of the patch[12].

Moisture Content

The prepared patches were weighed individually and placed in a desiccator containing fused calcium chloride for 24 hours. After drying, the patches were reweighed and the percentage moisture content was calculated [13].

$$\text{Moisture Content (\%)} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Final Weight}} \times 100$$

Moisture Uptake

The patches were weighed accurately and placed in a desiccator containing saturated potassium chloride solution (84% RH) at room temperature for 24 hours. The patches were then removed and weighed again to calculate the percentage moisture uptake [14].

$$\text{Moisture Uptake (\%)} = \frac{\text{Final Weight} - \text{Initial Weight}}{\text{Initial Weight}} \times 100$$

Tensile Strength

Tensile strength of the patches was determined using a tensile testing apparatus. The patch was fixed between two clamps and force was applied until the patch broke [15]. The tensile strength was calculated using the formula:

$$\text{Tensile Strength} = \frac{\text{Force at Break}}{\text{Cross-sectional Area}}$$

In-vitro drug release study

The in-vitro drug release study was carried out using a Franz diffusion cell. The transdermal patch was placed on a cellophane membrane, which was mounted between the donor and receptor compartments. The receptor compartment was filled with phosphate buffer (pH 7.4) maintained at 37 ± 0.5°C and stirred continuously using a magnetic stirrer to maintain sink conditions. At predetermined time intervals of 0.5, 1, 2, 3, 4, 6, 8, 10, and 12 hours, 1 mL of the sample was withdrawn from the receptor compartment and replaced with an equal volume of fresh buffer to maintain constant volume. The withdrawn samples were filtered and analyzed using a UV–Visible spectrophotometer at the λmax of Remogliflozin Etabonate, and the cumulative percentage drug release was calculated [16].

Stability Studies

Stability studies of the optimized Remogliflozin Etabonate transdermal patches were carried out according to the International Council for Harmonisation (ICH) guidelines to evaluate the stability of the formulation under different environmental conditions. The optimized patches were wrapped in aluminium foil and stored in stability chambers maintained at 25 ± 2°C / 60 ± 5% relative humidity (RH) for long-term stability and 40 ± 2°C / 75 ± 5% RH for accelerated stability conditions. The study was conducted for a period of three months, and samples were withdrawn at predetermined time intervals of 0, 1, 2, and 3 months. The withdrawn samples were evaluated for physical appearance, drug content, folding endurance, patch thickness, and in-vitro drug release. The obtained results were compared with the initial values to assess any significant changes in the physicochemical properties of the formulation. The optimized formulation showed no significant changes in the evaluated parameters, indicating that the prepared Remogliflozin Etabonate transdermal patches were stable under the tested storage conditions [17].

Results and Discussion

The present study aimed to optimize and evaluate transdermal patches of Remogliflozin Etabonate using a Box–Behnken design (BBD). The selection of independent variables, namely HPMC K4 (A), Eudragit RLPO (B), and Eudragit RSPO (C), at three different levels (Table 1), allowed a systematic investigation of their influence on critical quality attributes. The dependent variables, including drug content, folding endurance, and patch thickness, were selected based on formulation requirements (Table 2).

The experimental design matrix (Table 3) demonstrated the effect of formulation variables on the responses. The results (Table 4) indicated that drug content ranged from 95.12% to 99.12%, folding endurance from 162 to 192, and patch thickness from 0.228 mm to 0.272 mm, suggesting good formulation uniformity and mechanical properties.

The normal probability plots of residuals for drug content, folding endurance, and patch thickness (Figure 1, Figure 2, and Figure 3) showed a linear distribution, indicating normality of residuals and confirming the adequacy of the statistical model. Furthermore, predicted vs. actual plots demonstrated a close correlation, validating the reliability of the design model.

The contour plots and 3D response surface plots (Figure 1–3) revealed that polymer concentrations significantly influenced the responses. An increase in HPMC K4 concentration improved drug content and

folding endurance due to enhanced film-forming properties, while Eudragit RLPO and RSPO contributed to mechanical strength and controlled thickness of the patches.

Among all formulations, F11 was identified as the optimized formulation (Table 5), with experimental values of drug content (99.12%), folding endurance (172), and patch thickness (0.258 mm), which were in close agreement with predicted values. This confirms the robustness and predictability of the optimization model.

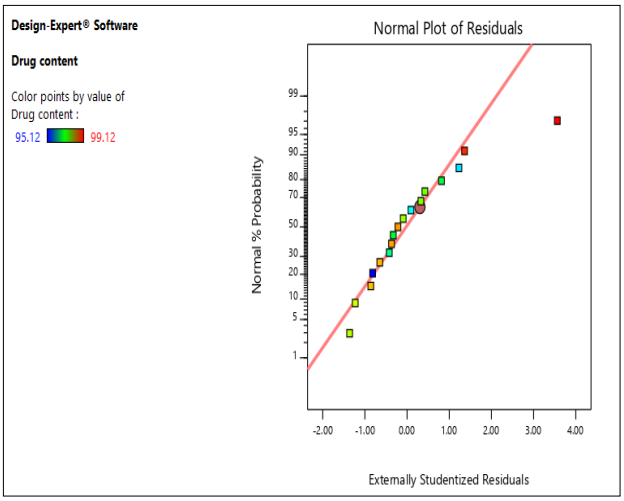
The evaluation parameters (Table 6) showed that all formulations exhibited acceptable weight variation, surface pH (6.39–6.62), moisture content, and tensile strength, indicating suitability for transdermal application without causing skin irritation.

The in vitro drug release study (Table 7) demonstrated a sustained release pattern for all formulations, with the optimized formulation F11 showing 88.95% drug release at 12 hours. This indicates effective controlled drug delivery, which is essential for maintaining therapeutic levels over an extended period.

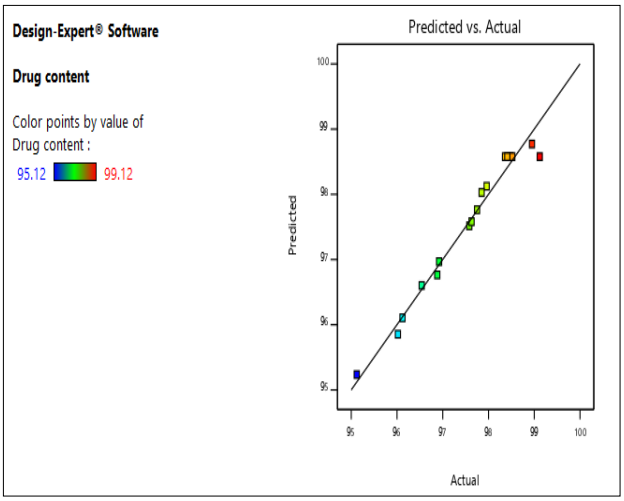
The release kinetics study (Table 8 and Table 9) revealed that the optimized formulation followed Korsmeyer–Peppas model (R^2 = 0.9809), indicating non-Fickian diffusion involving both diffusion and polymer relaxation mechanisms. The high correlation with first-order and Higuchi models further supports controlled drug release behavior.

Stability studies conducted as per ICH guidelines (Table 10) demonstrated that the optimized formulation remained stable under both intermediate and accelerated conditions. There were no significant changes in drug content, folding endurance, thickness, or drug release, and the physical appearance remained unchanged throughout the study period.

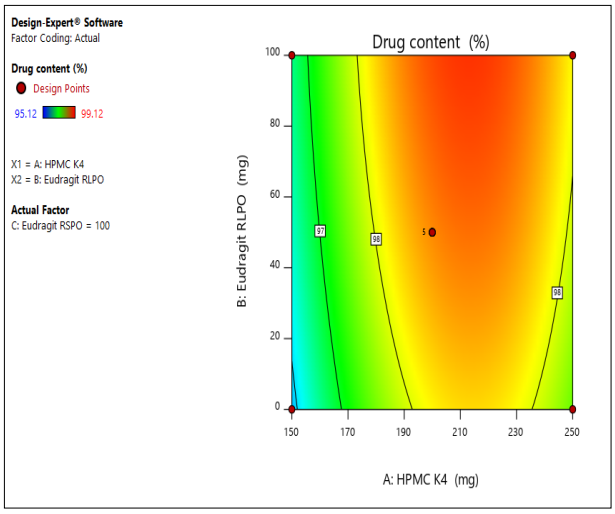
The study confirms that the application of DoE using Box–Behnken design is an efficient approach for optimizing transdermal formulations. The optimized formulation (F11) exhibited desirable physicochemical properties, controlled drug release, and good stability, making it a promising candidate for transdermal delivery of remogliflozin etabonate in the management of diabetes.

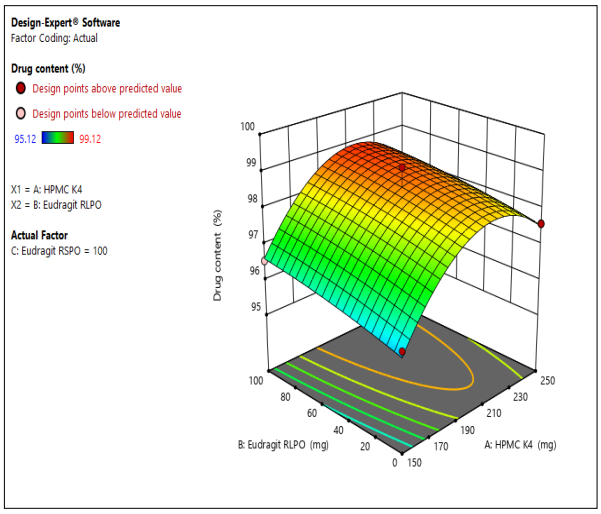


Normal Probability Plot of Residuals for Drug Content of Remogliflozin Etabonate Transdermal Patches (DoE Model Validation)



Predicted vs. Actual Plot

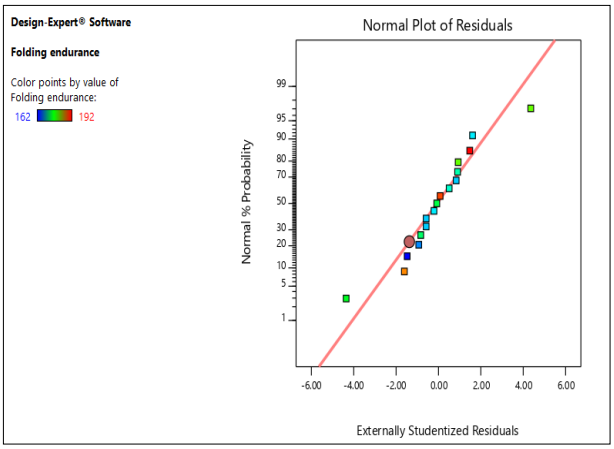


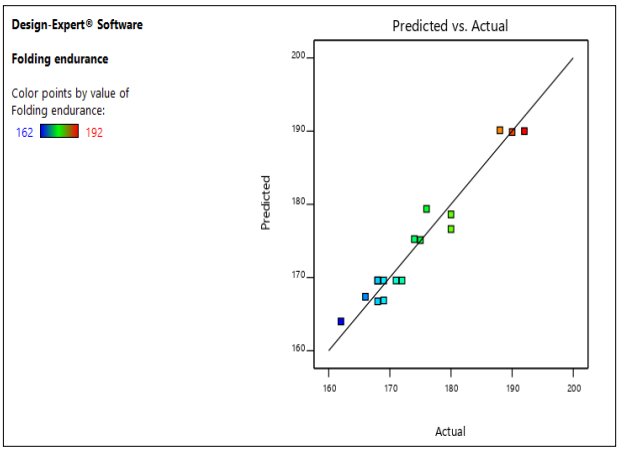


Contour plots between HPMC K4 and Eudragit RLPO **3D plots between HPMC K4 and Eudragit RLPO**

Figure 1: Graph of Normal Probability Plot of Residuals for drug content

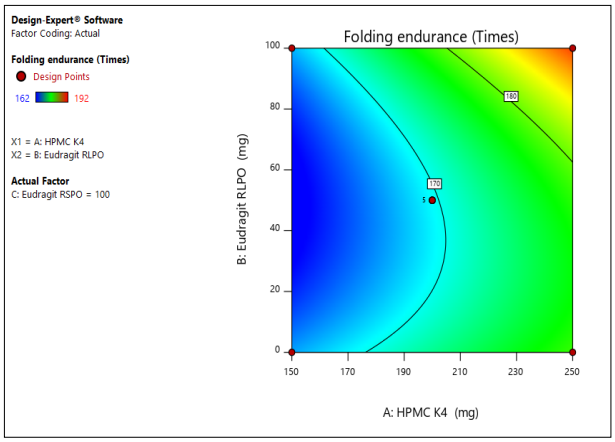
Normal Probability Plot of Residuals for folding endurance of Remogliflozin Etabonate Transdermal Patches

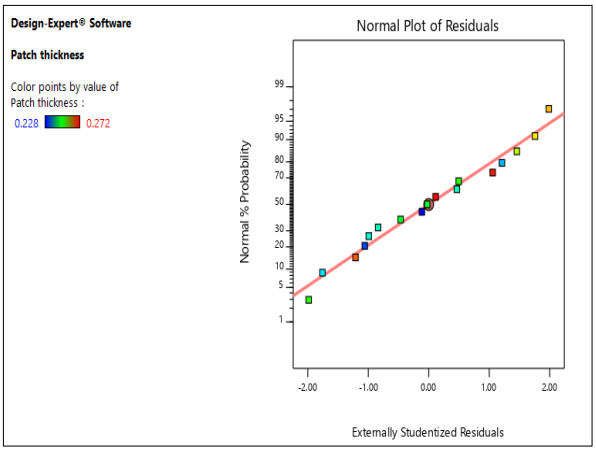


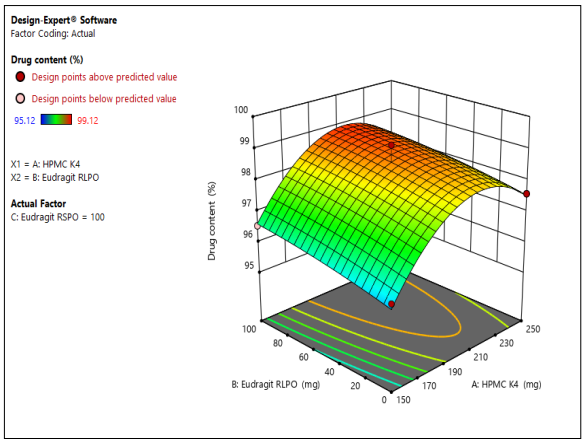


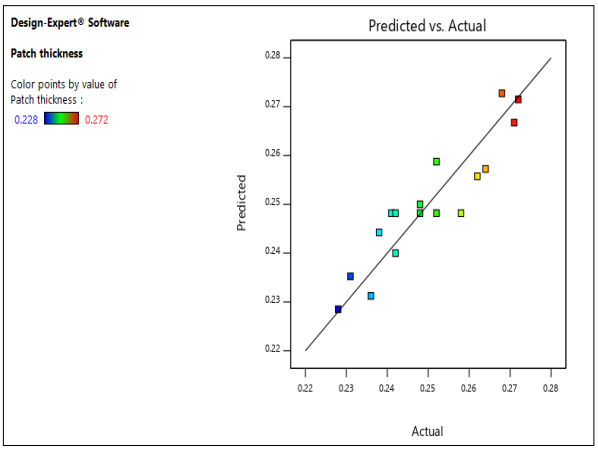
Normal Probability Plot

Predicted vs. Actual Plot







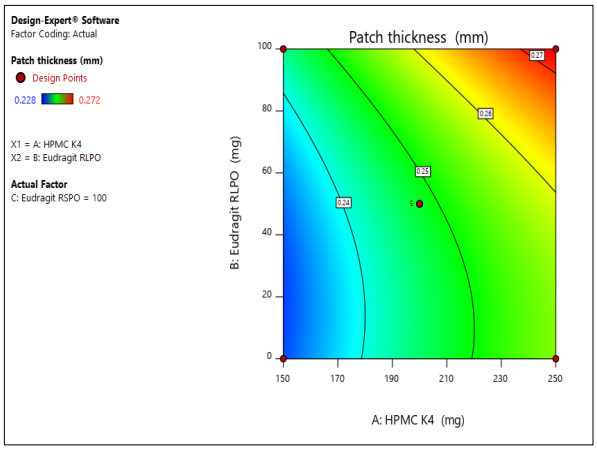


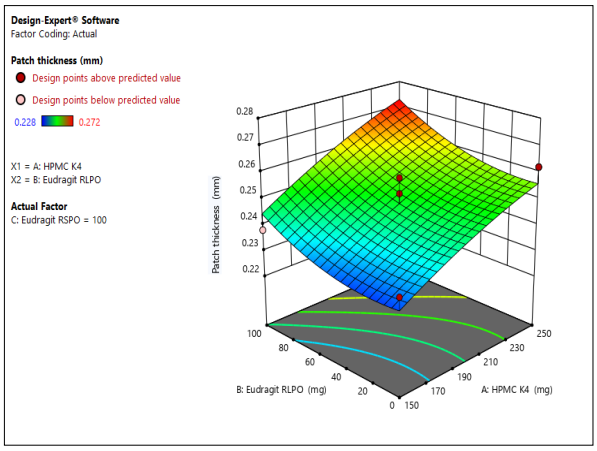
Contour plots between HPMC K4 and Eudragit RLPO **3D plots between HPMC K4 and Eudragit RLPO**

Figure 2: Graph of Normal Probability Plot of Residuals for folding endurance

Normal Probability Plot

Predicted vs. Actual Plot





Contour plots between HPMC K4 and Eudragit RLPO **3D plots between HPMC K4 and Eudragit RLPO**

Figure 3: Graph of Normal Probability Plot of Residuals for Patch thickness

Table 4: Results of Drug content, Folding endurance and Patch thickness

F. Code	Response 1	Response 2	Response 3
	Drug content	Folding endurance	Patch thickness
	%	Times	mm
F1	95.12	168	0.242
F2	97.85	175	0.231
F3	96.92	176	0.252
F3	96.12	162	0.228
F4	97.96	188	0.268
F6	96.88	174	0.248
F7	98.95	190	0.271
F8	97.63	180	0.264
F9	96.54	166	0.238
F10	97.75	192	0.272
F11	99.12	172	0.258
F12	96.02	169	0.236
F13	97.58	180	0.262

Table 5: Optimized Formulation of Remogliflozin Etabonate Transdermal Patches Showing Experimental and Predicted Responses

F. Code	HPMCK4 (mg)	Eudragit RLPO (mg)	Eudragit RSPO (mg)	Drug Content (%) Actual	Drug Content (%) Predicted	Folding Endurance Actual	Folding Endurance Predicted	Patch Thickness (mm) Actual	Patch Thickness (mm) Predicted
F11	200	50	100	99.12	98.58	172	169.60	0.258	0.2482

Table 6: Evaluation Results of Remogliflozin Etabonate Transdermal Patches (F1–F13)

F. Code	Weight Variation (mg)	Surface pH	Moisture Content (%)	Moisture Uptake (%)	Tensile Strength (kg/cm²)
F1	205 ± 2.15	6.45 ± 0.04	2.12 ± 0.11	3.24 ± 0.15	3.15 ± 0.08
F2	210 ± 2.32	6.52 ± 0.06	2.28 ± 0.12	3.36 ± 0.13	3.32 ± 0.07
F3	215 ± 2.18	6.47 ± 0.05	2.36 ± 0.10	3.48 ± 0.17	3.45 ± 0.06
F4	202 ± 2.10	6.39 ± 0.03	2.05 ± 0.09	3.15 ± 0.12	3.02 ± 0.05
F5	225 ± 2.45	6.58 ±	2.52 ± 0.14	3.65 ± 0.16	3.65 ± 0.09

		0.04			
F6	220 ± 2.31	6.50 ± 0.05	2.40 ± 0.12	3.52 ± 0.14	3.55 ± 0.07
F7	230 ± 2.52	6.60 ± 0.06	2.68 ± 0.15	3.72 ± 0.18	3.72 ± 0.08
F8	228 ± 2.47	6.57 ± 0.05	2.60 ± 0.14	3.70 ± 0.16	3.68 ± 0.09
F9	212 ± 2.22	6.48 ± 0.04	2.30 ± 0.11	3.40 ± 0.13	3.40 ± 0.06
F10	235 ± 2.60	6.62 ± 0.05	2.75 ± 0.16	3.80 ± 0.19	3.85 ± 0.10
F11	222 ± 2.28	6.55 ± 0.04	2.45 ± 0.13	3.58 ± 0.15	3.60 ± 0.08
F12	208 ± 2.16	6.44 ± 0.03	2.18 ± 0.10	3.30 ± 0.12	3.20 ± 0.07
F13	218 ± 2.25	6.51 ± 0.05	2.34 ± 0.11	3.45 ± 0.14	3.48 ± 0.06

Table 7: In-Vitro Drug Release Profile of Remogliflozin Etabonate Transdermal Patches (F1–F13)

Time (h)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**	**F13**
0.5	18.25	19.85	20.45	16.85	22.95	21.85	24.12	23.75	20.10	25.45	26.85	18.75	21.15
1	28.65	30.25	31.12	25.45	33.85	32.75	35.65	34.85	30.45	37.25	38.65	29.25	32.15
2	38	41	42	35	45	44	47	46	41	49	51	39	43
	.85	.15	.25	.15	.85	.35	.85	.65	.75	.85	.25	.75	.25
3	46.75	49.25	50.65	41.85	54.25	52.85	56.15	55.45	49.35	58.65	60.25	47.85	51.45
4	53.65	56.45	57.85	48.25	61.85	60.45	63.75	62.65	56.15	66.25	67.95	54.85	58.25
6	61.25	64.45	66.15	56.85	71.45	69.85	73.15	72.25	64.35	76.45	78.15	62.85	66.25
8	67.85	70.65	72.45	62.95	77.25	75.65	79.25	78.15	70.15	82.65	84.25	68.95	72.85
10	70.85	73.45	75.65	66.85	80.25	78.45	82.15	81.25	73.95	85.25	87.15	71.85	76.25
12	**72.85**	**75.42**	**78.25**	**69.35**	**82.46**	**80.12**	**84.65**	**83.25**	**76.85**	**86.75**	**88.95**	**73.65**	**79.52**

Table 8: Release Kinetics Profile of Remogliflozin Etabonate optimized Transdermal Patches F11

Time (h)	**Cumulative Drug Release (%)**	**Cumulative Drug Remaining to be Released (%)**	**Log Time**	**Log Cumulative Drug Release**	**Square Root of Time (√t)**	**Log Cumulative Drug Remaining**
0.5	26.85	73.15	-0.30	1.429	0.707	1.864

			1			
1	38.65	61.35	0.000	1.587	1.000	1.788
2	51.25	48.75	0.301	1.710	1.414	1.688
3	60.25	39.75	0.477	1.780	1.732	1.599
4	67.95	32.05	0.602	1.832	2.000	1.506
6	78.15	21.85	0.778	1.893	2.449	1.339
8	84.25	15.75	0.903	1.925	2.828	1.197
10	87.15	12.85	1.000	1.940	3.162	1.109
12	88.95	11.05	1.079	1.949	3.464	1.043

Table 9: Release Kinetic Model Fitting for Optimized Formulation (F11) of Remogliflozin Etabonate Transdermal Patch

S. No.	Kinetic Model	Correlation Coefficient (R^2)
1	Zero Order	0.8534
2	First Order	0.9725
3	Higuchi Model	0.9559
4	Korsmeyer–Peppas Model	0.9809

Table 10: Stability Study Results of Optimized Remogliflozin Etabonate Transdermal Patch (F11) According to ICH Guidelines

Time (Months)	Storage Condition	Drug Content (%)	Folding Endurance	Patch Thickness (mm)	Drug Release at 12 h (%)	Physical Appearance
0	Initial	99.12 ± 0.54	172 ± 2	0.258 ± 0.01	88.95 ± 0.94	Smooth, uniform
1	25 ± 2°C / 60 ± 5% RH	98.85 ± 0.48	171 ± 2	0.257 ± 0.01	88.42 ± 0.88	No change
2	25 ± 2°C / 60 ± 5% RH	98.62 ± 0.51	170 ± 3	0.256 ± 0.01	87.95 ± 0.91	No change
3	25 ± 2°C / 60 ± 5% RH	98.40 ± 0.46	169 ± 2	0.255 ± 0.01	87.65 ± 0.87	No change
1	40 ± 2°C / 75 ± 5% RH	98.52 ± 0.49	170 ± 2	0.256 ± 0.01	87.85 ± 0.90	No change
2	40 ± 2°C / 75 ± 5% RH	98.28 ± 0.47	168 ± 3	0.255 ± 0.01	87.25 ± 0.85	No change
3	40 ± 2°C / 75 ± 5% RH	98.05 ± 0.50	167 ± 2	0.254 ± 0.01	86.85 ± 0.82	No change

Conclusion

The present study successfully developed and statistically optimized transdermal patches of Remogliflozin Etabonate using a Box–Behnken design approach. The systematic optimization of formulation variables, including HPMC K4, Eudragit RLPO, and Eudragit RSPO, significantly influenced the critical quality attributes such as drug content, folding endurance, and patch thickness. The optimized formulation (F11) exhibited excellent physicochemical properties with high drug content, adequate mechanical strength, and uniform thickness.

In vitro drug release studies demonstrated a controlled and sustained release profile over 12 hours, following the Korsmeyer–Peppas kinetic model, indicating a non-Fickian diffusion mechanism. Stability studies confirmed that the formulation remained stable under both intermediate and accelerated conditions without significant changes in performance characteristics. The study highlights the effectiveness of the DoE approach in optimizing transdermal drug delivery systems and suggests that the developed formulation is a promising alternative for controlled delivery of remogliflozin etabonate in the management of diabetes mellitus.

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