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Research Article

Design And Optimization Of Compression-Coated Nateglinide Tablets: Modulation Of Drug Release And Release-Kinetic Mechanism

Mistri Ripal¹

¹ Assistant Professor, Indubhai Patel College of Pharmacy and Research Centre, Dharmaj.

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ABSTRACT

The aim of the current investigation is to develop oral once daily controlled release matrix tablets of nateglinide using compression coating technique. Nateglinide is a novel, highly physiologic, mealtime glucose regulator recently approved for the treatment of Type II diabetes mellitus. Nateglinide has a rapid onset and short duration of insulinotropic action that results in reduction of mealtime glucose rise and lowers the postabsorptive potential for hypoglycemia in humans. We designed a single unit type-controlled release tablet containing nateglinide to decrease both postprandial blood glucose level (PBG) and fasting blood glucose level (FBG). The tablet contains 60 mg of nateglinide in an immediate release portion, and 90 mg of nateglinide in a controlled release portion. The Inner Erosion Matrix tablet was prepared using different concentration of HPMC K4 to achieve desired 24 hour drug release profile. Compressible enteric coating were optimized using 32 factorial design. Outer coating of immediate release was done using MCC and Lactose. 32 factorial design was applied in present study using Design Expert software. Eudragit L 100(X1) and HPMC K4(X2) as Independent variables and T2(% drug release at 2 hr), T12(% drug release at 12 hr) and T24(% drug release at 24 hr) as Dependent variables. A checkpoint batch of the tablets was prepared by changing the value of independent variables within the range used in the preparation of factorial batches of tablets to check the validity of the evolved optimized mathematical model. In-vitro release profiles of optimized formulations was carried out which shows 24 hour drug release with desired limit.

INTRODUCTION

Vast amounts of literature have been written about the current and growing epidemic of diabetes mellitus (DM) and its associated complications.

Diabetes mellitus, or simply diabetes, is a chronic disease that occurs when the pancreas is no longer able to make insulin, or when the body cannot make good use of the insulin it produces.^[1] Type 2 diabetes accounts for approximately 85 to 90

***Corresponding Author:** Mistri Ripal

Address: Assistant Professor, Indubhai Patel College of Pharmacy and Research Centre, Dharmaj

Email ✉: rx.ripalmistry@gmail.com

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percent of all the diabetics in the country.^[2] Nateglinide is a novel D-phenylalanine derivative that inhibits ATP-sensitive K⁺ channels in pancreatic β -cells in the presence of glucose and there by stimulates the prandial release of insulin.^[3,4] During past few decades, significant advance have been made in the area of controlled release as evidenced by an increasing number of patents, publication, as well as commercial controlled release products for the delivery of variety of pharmaceutical compounds. With a controlled release formulation a predictable and reproducible release rate can be achieved, at the target site for desired duration.^[5] New Enteric coated chemical entity often is first formulated as a wet coating for encapsulation of tablet. During the course of clinical development, the drug containing granulation usually is modified for compaction into a tablet product. The tablet product subsequently may be film coated for taste masking, identification, or other purposes.^[6,7] The purpose of the study is to formulate and evaluate the controlled release tablet of Nateglinide. In this regard, we considered an erosion matrix tablet as the controlled release portion, and a dry coating of tablet as entric coating and outer prosion for immediate release of the nateglinide.

MATERIALS AND METHODS:

Materials

Nateglinide was obtained as gift sample (Cadila Chemical SBU, Ankleshwar, Gujarat.) HPMC K4M were obtained as gift samples (Crystal chemicals, Himmatnagar, Gujarat.), Eudragit L 100 was obtained as gift sample (Vikram Thermo Pvt. Ltd., Ahemdabad, Gujarat.). Distilled water was prepared in laboratory using all steel distillation apparatus. Other materials used in the study were of analytical grade.

Development of UV spectroscopy method in 0.1 N HCl:^[8]

From the stock solution, appropriate aliquots were taken into different volumetric flasks and volume was made up to 10 ml with 0.1 N HCl so as to get drug concentrations of 5, 10, 15, 20, 25 and 30 μ g/ml. The absorbencies of these drug solutions were estimated at λ_{max} 210 nm. This procedure was performed in triplicate to validate the calibration curve.

Development UV spectroscopy method in Phosphate Buffer (pH 6.8) solution:^[8]

From the stock solution, appropriate aliquots were taken into different volumetric flasks and volume was made up to 10 ml with phosphate buffer (pH 6.8) solution so as to get drug concentrations of 5, 10, 15, 20, 25 and 30 μ g/ml. The absorbencies of these drug solutions were estimated at λ_{max} 210 nm. This procedure was performed in triplicate to validate the calibration curve.

Drug–Excipient Compatibility Studies:^[9]

Preformulation studies regarding the drug-polymer interaction for selecting appropriate polymers by FT-IR spectroscopy. The pure drug and drug with excipient were scanned separately. Potassium bromide was mixed with drug and/or polymer in 9:1 ratio and the spectra were taken. FT-IR spectrum of nateglinide was compared with FT-IR spectra of nateglinide with polymer. The peaks were observed for any kind of interaction between the drug and excipient.

Formulation Development:

Dose Calculation^[10-12]

Dose calculation for controlled release tablet was carried out and theoretical drug release profile was developed. So, in the present study attempts were



made to design controlled release tablets of nateglinide using 60 mg in immediate release portion and 90 mg as Controlled release portion

according to the developed theoritcal drug release profile.

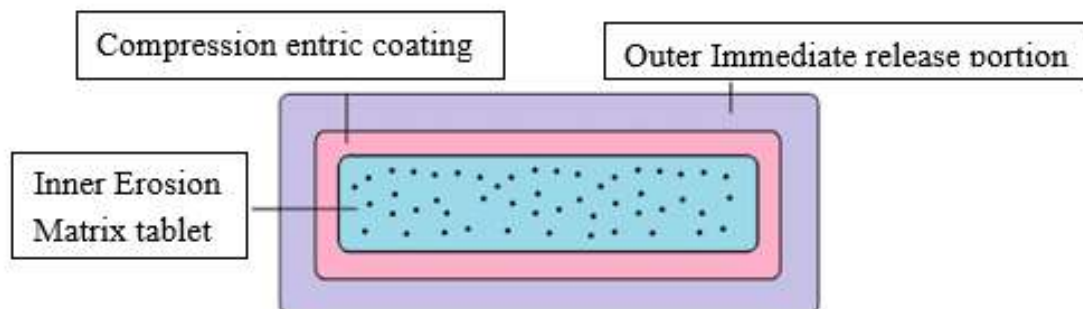


Figure 01: Nateglinide controlled release dry coated tablet containing erosion matrix tablet

Procedure for Inner Core (Erosion matrix tablet): Wet Granulation Method

Nateglinide, HPMC K 4, MCC were mixed, make it granules with HPMC in Water (5%) granulating medium. The blend was passed through 10# sieve and after dry at 70° C. Passed these granules through 22# and 44# sieve. Take granules obtained from 44 # sieve and added 5% fine, magnesium stearate in granules. Then mixed it and punched the tablets. The granules was then compressed on 8-station rotary punching machine using concave faced punches 8 mm.

Procedure for Enteric coating: Direct Compression Method

Eudragit L 100, HPMC K 4, MCC was mixed and passed through 22# and 44# sieve. Then blend it properly. Fill half die cavity of 10 mm die with the blend and put inner core tablet and fill remaining half cavity with blend then compressed.

Procedure for Outer coat (immediate release portion): Direct Compression Method

Nateglinide, MCC, Lactose mixed and was passed through 22# and 44# sieve. Then blend it properly. Fill half die cavity of 12 mm die with the blend and

put enteric coated tablet and fill remaining half cavity with blend then compressed.

Evaluation of granules and tablets ^[10-17]

The prepared granules were evaluated for angle of repose, bulk density, tapped density, compressibility index, and Hausner ratio. The prepared tablets were evaluated for weight variation, friability, hardness, thickness, and disintegration time.

The *in vitro* drug release study was carried out in a United States Pharmacopoeia (USP) dissolution apparatus I (Electrolab, Mumbai, India) using a rotating Basket at 50 rpm in 900 mL of 0.1 N HCl±0.5% sodium lauryl sulphate as dissolution medium and Phosphate Buffer (pH 6.8) solution while maintaining the temperature at 37 ± 0.5°C (12). An aliquot of 10 mL was withdrawn at different time intervals and an equal volume of fresh dissolution medium was added to maintain the sink condition. Samples were suitably diluted and analysed in a UV-visible spectrophotometer at 210 nm to determine the amount of drug released (13). The fresh dissolution medium replacement was considered in the calculation of the amount of drug released.

Table 01: Preliminary Batches of Inner Core (Erosion matrix tablet)

Ingredient	P1	P2	P3	P4	P5	P6	P7
Inner core							
Nateglinide	90	90	90	90	90	90	90
Eugragit L 100	39	-	-	-	-	-	-
HPMC k 4	-	29	29	39	110	110	110
MCC	-	-	-	-	89	89	89
Mg stearate	1	1	1	1	1	1	1
Grannulating Medium		water	Water: IPA(1:1)	PVP K 90 5% in IPA	PVP K 130 5% in IPA	HPMC 10% in water	HPMC 5% in Water
Punch Used	6 mm	6 mm	6 mm	6 mm	8 mm	8 mm	8 mm
Weight	105±0.2	107±0.06	104±0.09	108±0.05	222±0.73	219±0.45	225±0.06

*All values are in milligram

Table 02: Formulation Batches of inner Core using Different concentration of HPMC K4

Ingredient	F1	F2	F3	F4	F5
Nateglinide	90	90	90	90	90
HPMC k 4	5%	10%	15%	20%	50%
MCC	118	107	96	85	19
Mg stearate	1	1	1	1	1

*All values are in milligram

Table 03: Preliminary Batches of enteric Coating

Ingredient	C1	C2	C3	C4	C5
Inner Core	P1	F4	F4	F4	F4
Outer Coat					
Nateglinide	60 mg	-	-	-	-
Lactose	160 mg	-	50 %	-	-
Eugragit L 100	-	100 %	50 %	50 %	50 %
MCC	-	-	-	25 %	20 %
HPMC k 4	-	-	-	25 %	30 %

Table 04: Preliminary Batches of outer Coat

Ingredient	O1	O2
Enteric Coated	C5	C5
Outer Coat		
Nateglinide	60	60
MCC	50%	75%
Lactose	50%	25%

Full factorial design ^[18-20]

In preliminary studies Eudragit L 100, HPMC K 4 and MCC were selected as Coating agent for the

preparation of tablets. In order to investigate the effect of formulation variables on the response that predict an optimized formulation, a 3² factorial design was adopted using software Design Expert.



Nine batches were prepared as per the design combination of independent variables that give the layout. In the present work, a 3^2 full factorial desired values of dependent variables. design was adopted to find out the optimum

Table 05: Selection of Independent variables and Dependent variables

3^2 full factorial design				
Independent Variables		Dependent Variables		
X1	X2	Y1	Y2	Y3
Eugragit L 100	HPMC k 4	T2%(% Drug Release at 2 hr)	T12%(% Drug Release at 12 hr)	T24%(% Drug Release at 24 hr)

Table 06: Selection of levels for independent variables

Independent Variables	Level		
	Low	Intermediate	High
	-1	0	1
X1 : Eudragit L 100	40 %	50 %	60 %
X2 : HPMC K 4	30 %	35 %	40 %

Table 07: 3^2 Factorial design

Experiment	coded value		uncoded value		Eudragit L 100	HPMC K 4
	X1	X2	X1%	X2%	X1(mg)	X2(mg)
E1	-1	-1	40	30	48	36
E2	0	-1	50	30	60	36
E3	1	-1	60	30	72	36
E4	-1	0	40	35	48	42
E5	0	0	50	35	60	42
E6	1	0	60	35	72	42
E7	-1	1	40	40	48	48
E8	0	1	50	40	60	48
E9	1	1	60	40	72	48

RESULT AND DISCUSSION:

Calibration curve of nateglinide in 0.1 N HCl solution was prepared which has linearity equation $y = 0.0278x + 0.016$ and regression coefficient value is 0.998. Calibration curve of nateglinide in phosphate buffer solution (pH 6.8) was prepared which has linearity equation $y = 0.0287x + 0.0128$ and regression coefficient value is 0.9946. A drug-excipient interaction study at an early stage of product development is an important exercise in the development of a stable dosage form. The

peaks of NTG and excipient were not affected and prominently same as observed in FT-IR spectrum of NTG alone.

Batches for selection of Inner core (Erosion matrix tablet) :

Preliminary batches P1-P4 were made to prepare the tablets using 6 mm punch on 'B' tooling punching machine using ingredients shown in the Table 01. Maximum weight of the inner core tablet is 100 mg whereas of dose of nateglinide in the



inner core is 90 mg. Hence for controlling 90 mg of nateglinide we have add more polymer so have to move on the 8 mm Punch. Batches P-5 to P-7 were prepared using 8 mm punch on 'B' tooling punching machine by increasing the total weight of tablet 200-250 mg. From the results of the above batches it was found that Batch P7 shows the good Hardness (4.7 ± 0.6 kg/cm²) and also pass the friability test so Batch P7 was selected for further optimization of polymer concentration.

Batches for selection of concentration of Polymer:

Batches F1-F5 were made to prepare the tablets using 8 mm punch on 'B' tooling punching machine using different concentration of HPMC K4. Drug release profile of F-1 to F-3 of the formulations mentioned above did not appear to be closer to the theoretical drug release profile as it not release up to 24 hrs. As F-4 showed 102.76 % of drug release in 24 hours.

Table 08: Evaluation of granules and tablets of preliminary batches of inner core

Item	P1	P2	P3	P4	P5	P6	P7
Evaluation of granules							
Angle of repose(θ)	27.34	25.67	28.73	32.71	30.48	25.84	25.69
Compressibility (%)	36.36	7.69	9.25	34.3	10.37	12.46	23.07
Hausner ratio	1.571	1.083	1.02	1.304	1.025	1.05	1.3
Evaluation of tablets							
Hardness (kg/cm ²)	4.5 ± 0.8	1.2 ± 0.1	2.5 ± 0.2	2.9 ± 0.4	1.5 ± 0.2	1 ± 0.2	4.7 ± 0.6
Friability (%)	0.015	3.2	2.9	0.79	1.7	1.23	0.036

Table 09: Evaluation of granules and tablets of formulation batches of inner core

Item	F1	F2	F3	F4	F5
Evaluation of granules					
Angle of repose(θ)	27.34	28.67	28.73	32.71	30.48
Compressibility (%)	25.99	32.46	25.72	22.71	25.37
Hausner ratio	1.37	1.479	1.02	1.28	1.33
Evaluation of tablets					
Hardness(kg/cm ²)	4.5 ± 0.8	4.8 ± 0.1	4.5 ± 0.2	4.9 ± 0.4	4.5 ± 0.2
Friability(%)	0.015	0.027	0.029	0.023	0.027

Table 10: Dissolution data of F1-F5

Time(hours)	Cumulative percentage of drug released*AM + SD				
	F1	F2	F3	F4	F5
2	52.33 ± 2.3	16.79 ± 3.4	11.22 ± 2.4	8.08 ± 4.2	0.07 ± 3.9
6	101.96 ± 3.4	45.59 ± 3.6	34.59 ± 4.4	27.52 ± 5.2	5.68 ± 2.9
14		103.7 ± 63.6	80.50 ± 2.8	57.75 ± 4.3	16.54 ± 3.6
18			101.9 ± 36.3	80.72 ± 5.2	19.00 ± 4.5
22				102.76 ± 2.5	22.21 ± 4.7



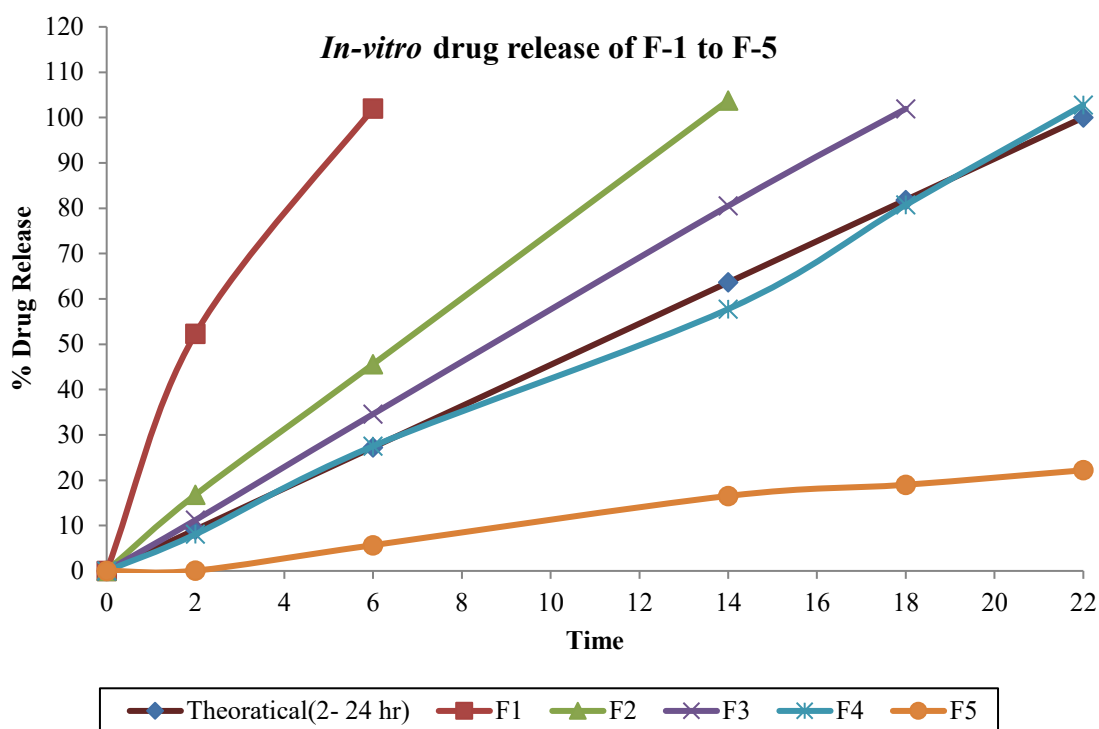


Figure 02: Comparison of *in vitro* release of nateglinide from the tablets of the batches F-1 to F-5 with theoretical drug release profile for 2 to 24 hr.

Batches for selection of Enteric coating :

Batches C-1 to C5 were prepared by using different concentration of Eudragit L100 , and

HPMC K4. Batch C1 fails the disintegration test of enteric coated tablets. In 0.1 N HCl it disintegrates completely within 15 min.

Table 11: Evaluation of granules and Enteric tablets

Item	C1	C2	C3	C4	C5
Evaluation of granules					
Angle of repose (θ)	35.2	34.5	33.5	32.2	30.5
Compressibility index (%)	28.2	24.4	22.3	20.2	18.2
Hausner ratio	1.39	1.32	1.28	1.25	1.22
Evaluation of tablets					
Hardness(kg/cm ²)	4.5 $\pm$ 0.8	1.8 $\pm$ 0.1	2.4 $\pm$ 0.2	2.9 $\pm$ 0.4	4.5 $\pm$ 0.2
Friability(%)	0.015	0.027	0.029	0.023	0.027

Batches C2, C3 and C4 shows lamination during the compression coating (Figure no a). This might be because of lake binding proprieties of Eudragit L 100. In Batch C5 addition of HPMC MCC solved the problem of lamination (Figure no a) and also passes the disintegration test for enteric

coating. it can with stand in 0.1 N HCl for 2 hr as it is (Figure no b). Though there is a scope for further improvement, amongst the batches tested the formulation C-5 is considered as the best batch, which needs to be finally optimized. Further



optimization of coating was carried out by using experimental design.



(a)



(b)

Figure 03: a) Tablet laminate. b) It can withstand for 2 hr in 0.1 N HCl

Batches for outer coat (immediate release portion):

The outer coat containing immediate release portion of drug (60 mg) was added by coating the enteric coated tablets using 12 mm punch as per

methodology described earlier. Batch O2 show good coating and showing good constancy. So final outer coat was done using 12 mm punch keeping final weight 630 mg. This formula was also used in for coating of enteric coated tablet in factorial design.

Table 12: Evaluation of granules and Outer coated tablets

Item	O1	O2
Evaluation of granules		
Angle of repose (θ)	28.5	26.9
Compressibility index (%)	28.9	38.2
Hausner ratio	1.38	1.6
Evaluation of tablets		
Hardness (kg/cm^2)	3.5 ± 0.8	5.8 ± 0.1
Friability	1.015	0.045

Formulation of batches as per factorial design:

The controlled release tablets were manufactured for the batches E1 to E9 using the ingredients

shown. The properties of the manufactured tablets are shown in the below table.

Table 13: Evaluation Factorial design batches

Batch code	Hardness (kg/cm^2)	Thickness (mm)	% Drug release at 2 hr	% Drug release at 12 hr	% Drug release at 24 hr
------------	--------------------------------------	----------------	------------------------	-------------------------	-------------------------

E1	5.02 ± 0.08	3.72 ± 0.23	46.63±0.03	75.49±0.09	104.74±0.09
E2	4.55 ± 0.11	3.79 ± 0.20	45.12±0.07	73.98±0.06	102.79±0.05
E3	6.52 ± 0.04	3.70 ± 0.14	40.37±0.02	69.25±0.06	100.13±0.02
E4	4.72 ± 0.25	3.73 ± 0.13	40.80±0.06	64.69±0.08	97.24±0.05
E5	5.85 ± 0.28	3.78 ± 0.17	41.02±0.06	62.88±0.04	95.57±0.00
E6	6.14 ± 0.37	3.75 ± 0.12	40.80±0.03	60.98±0.09	93.52±0.01
E7	4.21 ± 0.14	3.70 ± 0.32	40.80±0.06	58.82±0.09	91.24±0.07
E8	5.89 ± 0.13	3.74 ± 0.23	40.59±0.07	54.13±0.02	90.12±0.03
E9	5.88 ± 0.25	3.70 ± 0.30	40.59±0.02	52.85±0.02	89.81±0.09

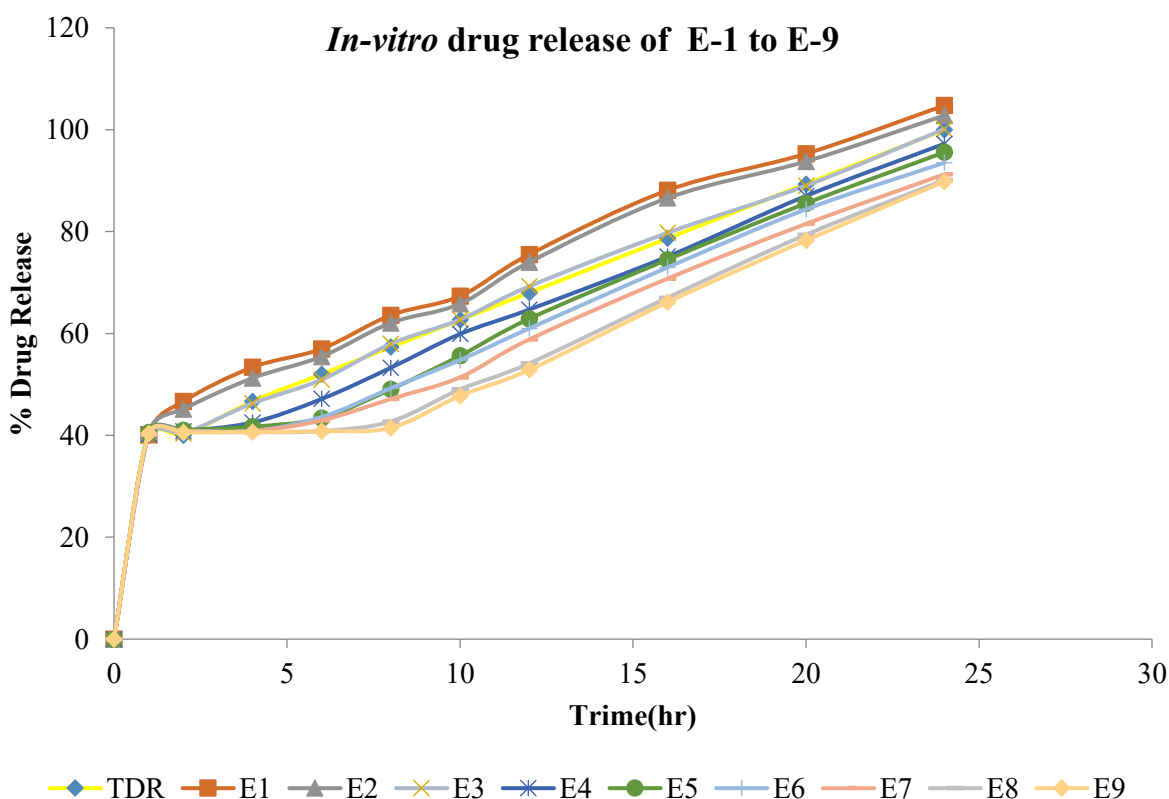


Figure 04: Comparison of *in vitro* release of nateglinide from the tablets of the batches E-1 to E-5 with theoretical drug release profile

The amount of Eudragit L 100 (X₁) and HPMC K4 (X₂) were chosen as independent variables in a 3² full factorial design using Design Expert Software. A statistical model incorporating interactive and polynomial terms was used to evaluate the responses.

$$Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}X_1^2 + b_{22}X_2^2 \dots \dots \dots \text{Eq. 1}$$

where, Y is the dependent variable, b_0 is the arithmetic mean response of the 9 runs, and b_1 is the estimated coefficient for the factor X₁. The main effects (X₁ and X₂) represent the average result of changing one factor at a time from its low to high value. The interaction terms (X₁X₂) showed how the response changes when two factors are simultaneously changed. The polynomial terms (X₁² and X₂²) are included to

investigate nonlinearity. As shown in Table 13, % drug release for 2 hr, 12 hr, and 24 hr for the 9 batches (E1 to E9) showed a wide variation. The data indicates that the dependent variables such as

% drug release for 2 hr, 12 hr, and 24 hr are dependent on the selected independent variables such as concentration of Eudragit L 100 and HPMC K4.

Table 14: Anova value for X1 and X2

Effect	Sum of squares	Df	Mean ss	F ratio	P value	R ²
Anova value for X1 and X2 on Y1 using Response Surface 2FI model						
Model	33.28	3	11.09	5.75	0.0446	0.775
X1-Eudragil l 100	6.98	1	6.98	3.62	0.1154	
X2-HPMC k 4	17.15	1	17.15	8.9	0.0307	
X1X2	9.14	1	9.14	4.74	0.0813	
Anova value for X1 and X2 on Y2 using Response Surface Linear model						
Model	509.2	2	254.6	176.39	< 0.0001	0.983
X1-Eudragil l 100	42.29	1	42.29	29.3	0.0016	
X2-HPMC k 4	466.91	1	466.91	323.48	< 0.0001	
Anova value for X1 and X2 on Y3 using Response Surface Linear model						
Model	237.8	2	118.9	141.11	< 0.0001	0.9792
X1-Eudragil l 100	15.9	1	15.9	18.88	0.0049	
X2-HPMC k 4	221.89	1	221.89	263.35	< 0.0001	

Table 14 shows the results of the analysis of variance (ANOVA), which was performed to identify significant factors. In Design Expert software it suggests to choose model so for Y1 *Two Factor Interaction* model and for Y2 and Y3 *Response Surface Linear* model was selected. So it will give reduce equation only as per below,

$Y1 = 41.86 - 1.69X2$, In this case X2 is a significant model term.

$Y2 = 63.68 - 2.65X1 - 8.82X2$, In this case X1, X2 are significant model terms.

$Y3 = 96.13 - 1.63X1 - 6.08X2$, In this case X1, X2 are significant model terms.

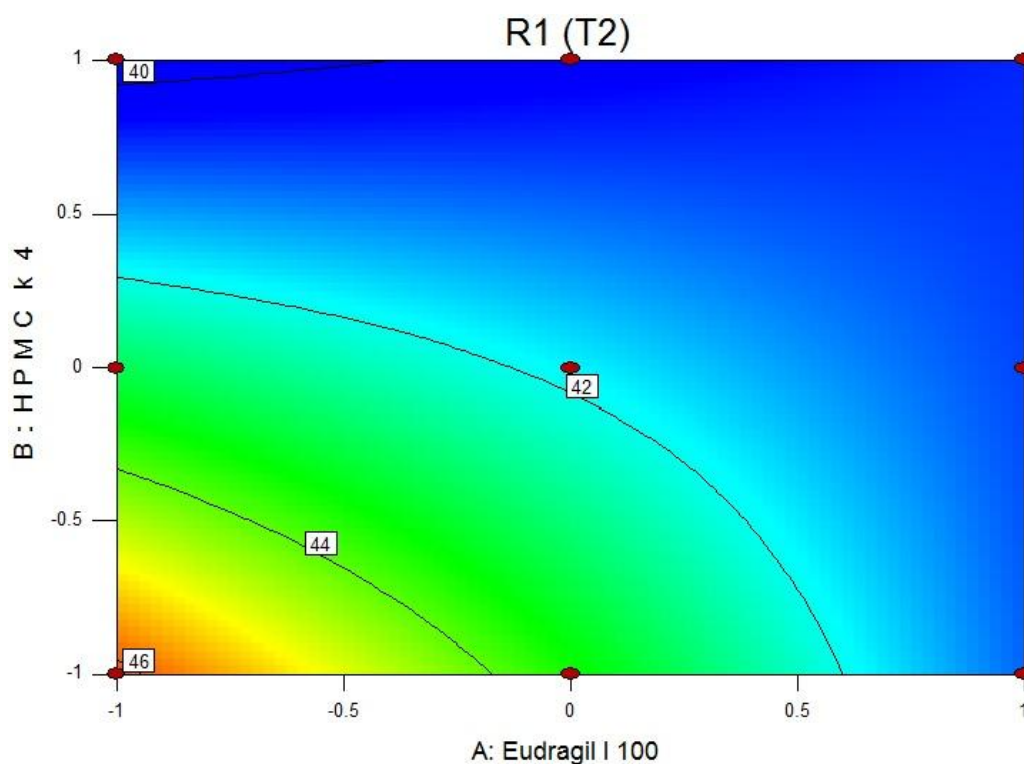


Figure 05: Contour plot of X1 and X2 on Y1

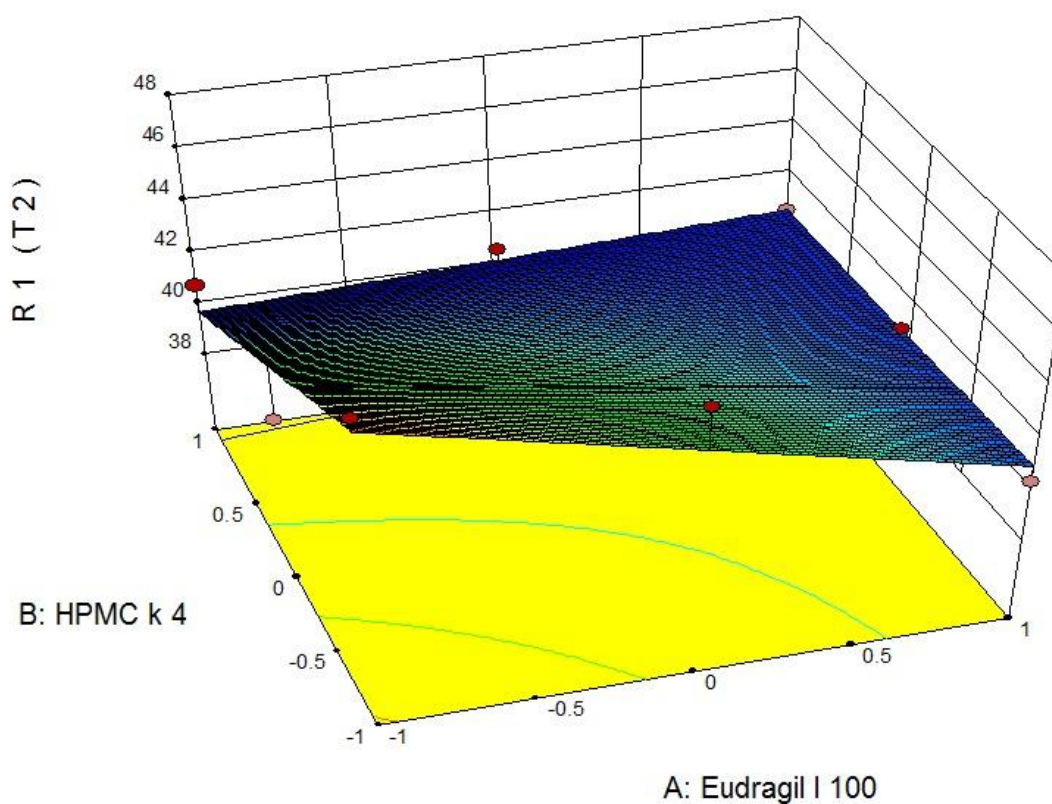


Figure 06: Three-dimensional surface plot showing for X1 and X2 on Y1

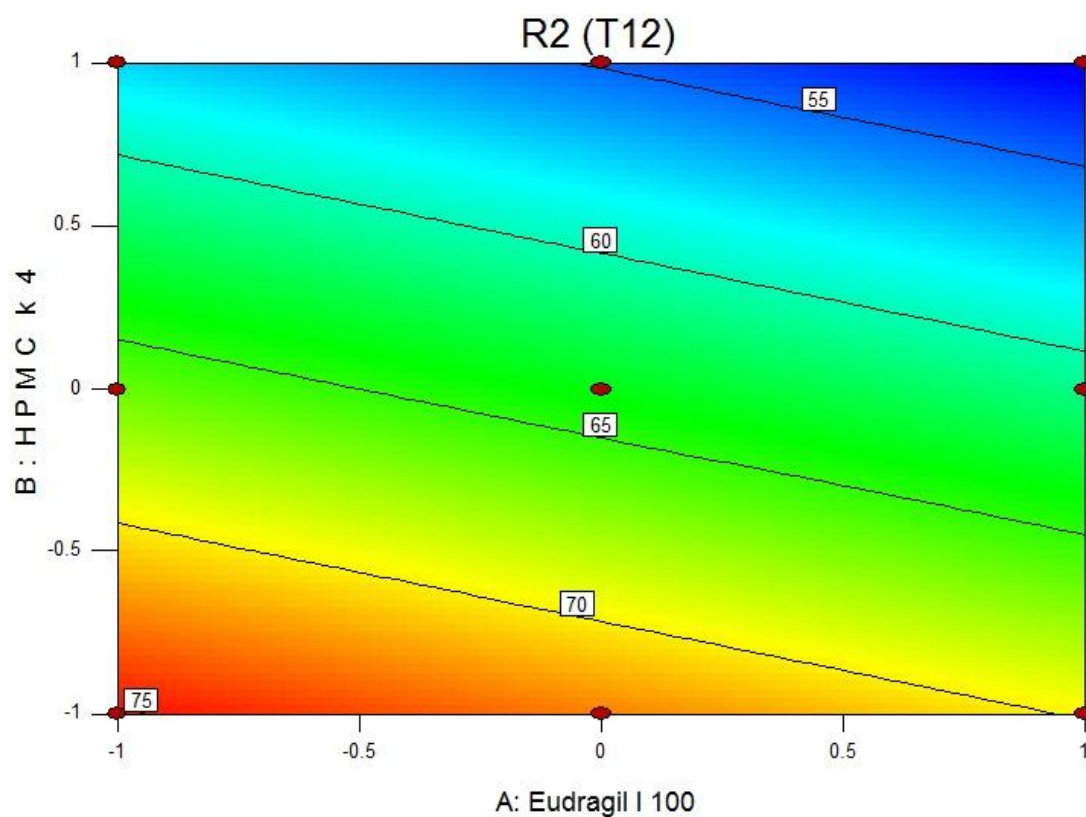


Figure 07: Contour plot of X1 and X2 on Y2

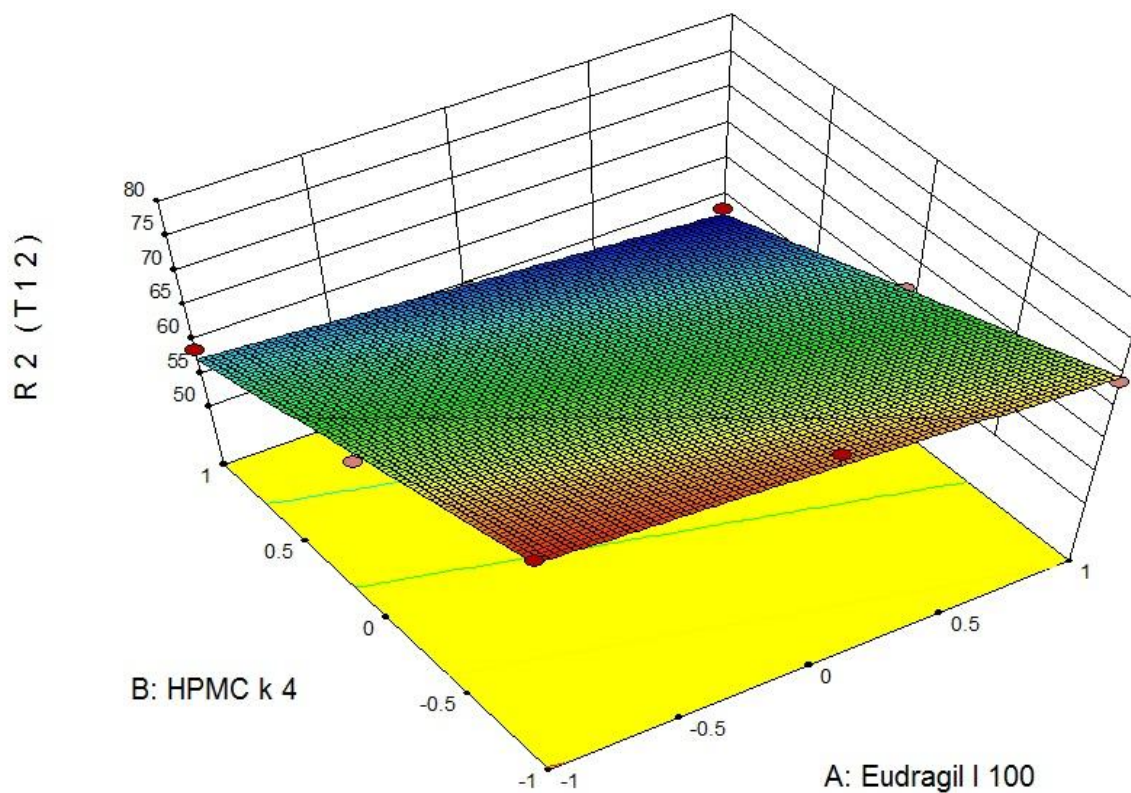


Figure 08: Three-dimensional surface plot showing for X1 and X2 on Y2

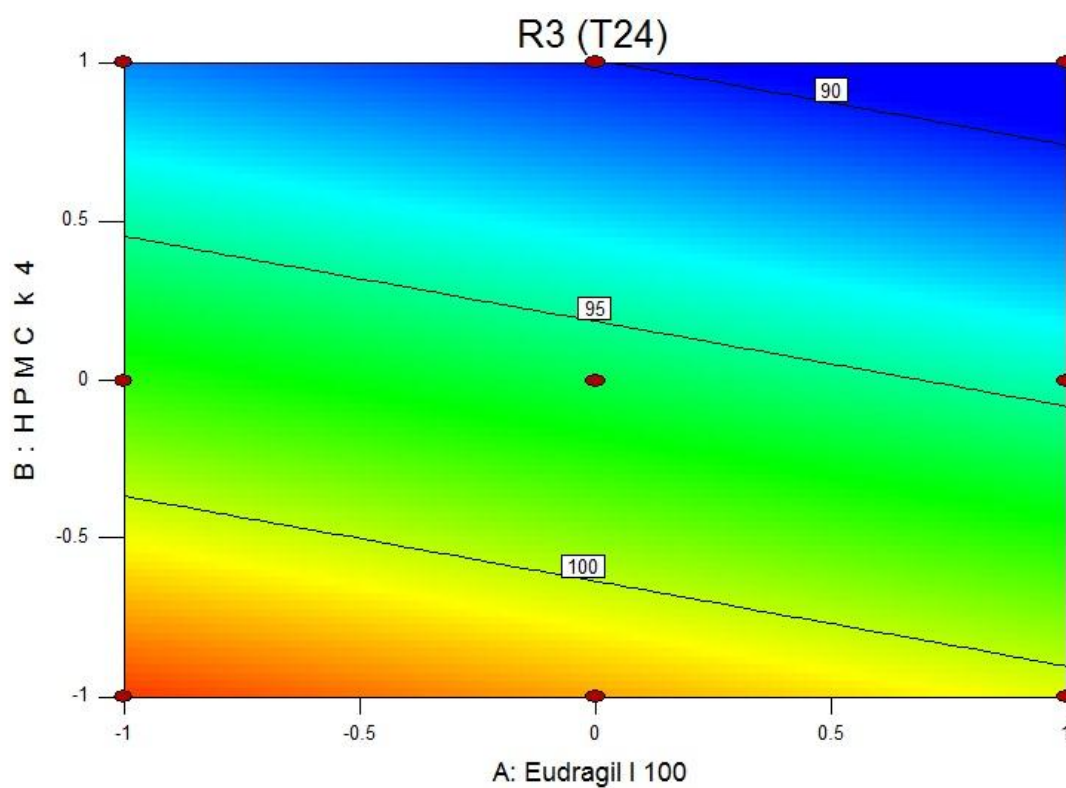


Figure 09: Contour plot of X1 and X2 on Y3

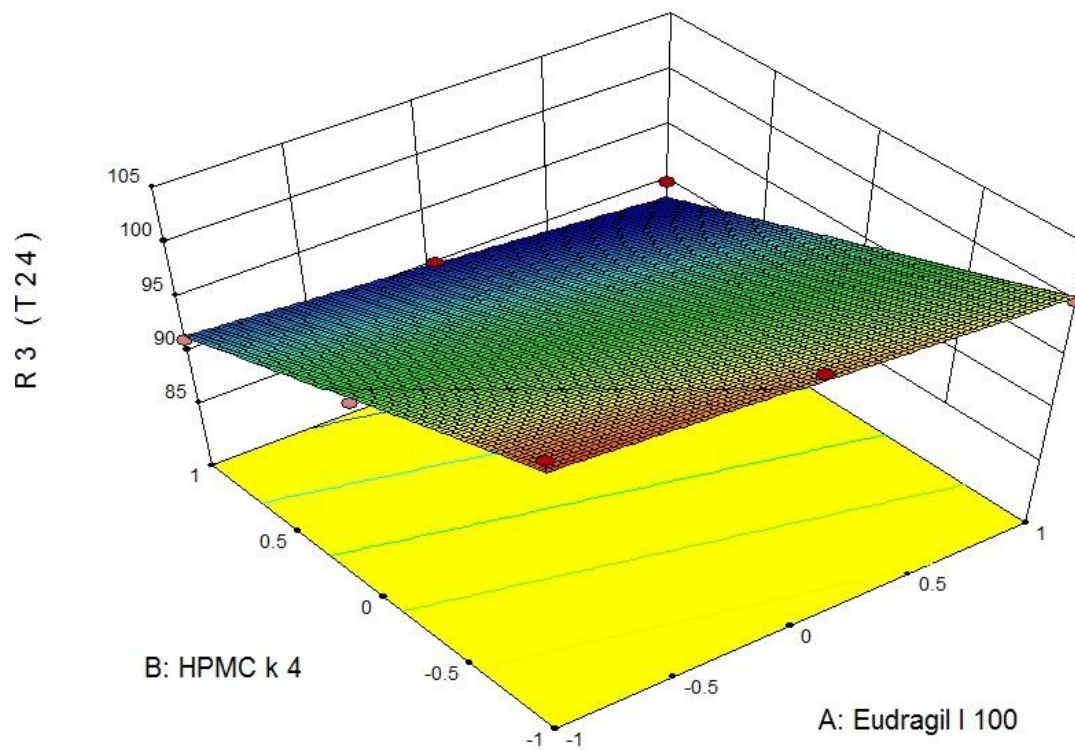


Figure 10: Three-dimensional surface plot showing for X1 and X2 on Y3

The response surface plot and three-dimensional plot of X1 and X2 versus response are shown in Figures 04 to 09, respectively. The response plot

showed that there is a significant effect of both factors on selected response.

Check point :

Table 15: Check point value

Check point	Coded Value		Transformed Values	
	X1	X2	X1(%)	X2(%)
1	-0.5	0.5	45 %	32.5%
2	0.5	-0.5	32.5%	37.5%

Table 16: Evaluation of check point batches

Checkpoint	Predicted			Observed		
	T2%	T12%	T24%	T2%	T12%	T24%
1	41.17	60.59	93.90	41.35±0.4	61.01±0.8	94.07±0.6
2	41.79	66.76	98.36	41.83±0.2	67.9±0.1	98.04±0.8

From the check point two batches were prepared and evaluated. Thus, from the results of statistical optimization techniques it can be concluded that all of the models are mathematically significant.

The model predicts the required drug release for Y1(T2%), Y2(T12%) and Y3(T24%) from point prediction, at X1 is 1 level and X2 is -0.791 level i.e. X1 (%) is 60 % X2(%) is 23.73% (E-3). The response T2% was predicted at 40.925% and T12% at 68.000% and T24% at 99.313.

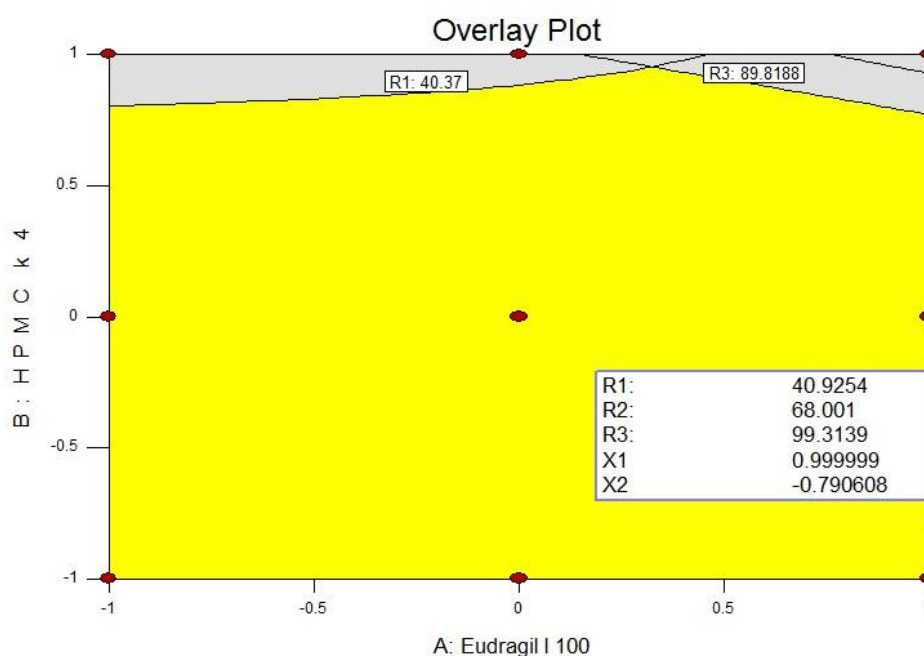


Figure 11: overlay plot for optimized batch



CONCLUSION:

In this study, the formulation of controlled release tablet of NTG was prepared by using different polymer using compression coating technology and a Tab in Tab in Tab was prepared. 20% HPMC K4 was give desire drug release profile same as theoretical drug release. Enteric coating was done successfully with suitable ratio of polymer. The results of a 3² full factorial design revealed that the amount of eudragit L 100 and HPMC K4 of the coating significantly affect the dependent variables, % drug release at 2 hr, 12 hr and 24 hr. It is concluded that by adopting a systematic formulation approach, an optimum point can be reached in the shortest time with a minimum effort. Tablets containing 60% of Eudragit L 100 and HPMC K4 23.73 % met the required drug release at desire time.

REFERENCES

1. Sheehan MT, "Current Therapeutic Option in Type 2 Diabrtes Mellitus: A Pratical Approach." Clinical Medicine. 2003,189-200.
2. Diabetes Atlas : <http://www.idf.org/diabetesatlas/5e/south-east-asia>.
3. Dunn CJ, "Nateglinide." Adis New Drug Profile. 2000. Volume 60(3), 607-615.
4. Margaret Weaver, "Pharmacokinetics And Metabolism Of Nateglinide In Humans." Drug Metabolism And Disposition. 2000. Volume 29, 415-421.
5. SP, Khar RK., Controlled drug delivery: Concepts And Advances. 1st ed. Delhi: Vallabh Prakashan; 2002.
6. Hariharan M. "A Novel Compression-Coated Tablet Dosage Form." Pharmaceutical Technology. 2001, Volume 1(1),14-19.
7. RR Patel. "Novel technologies of oral controlled release drug delivery system." Syst Rev Pharm. 2010. Volume 1(2),128-132.
8. Indian Pharmacopoeia. The Controller of Publications, Ministry of health
9. and welfare, New Delhi: 1996.
10. European Medicines Agency, Evaluation of Medicines for Human Use London, 27 July 2006, Doc.Ref.: EMEA/CHMP/87018/2006 ,Procedure No. EMEA/H/C/656.
11. Chisato Makino,Nobutaka Ninomiya," Effect of Decrease in Both Postprandial Blood Glucose (PBG) and Fasting Blood Glucose (FBG) Levels in Normal Beagle Dogs with Nateglinide Enteric Coated Granules and Immediate Release Tablets",volume 54 ,Issue 4 page no 409-414.
12. Brahmankar DM, Jaiswal SB. Biopharmaceutics and pharmacokinetics a treatise. 1st ed. New Delhi: Vallabh Prakashan; 1995.
13. Yubing Zhu MS, Qian Zhang, "Relative Fasting Bioavailability of Two Formulations of Nateglinide 60 mg in Healthy Male Chinese Volunteers: An Open-Label, Randomized-Sequence, Single-Dose, Two-Way Crossover Study", Clinical Therapeutics,Volume 34, Number 7, 2012,page no 1505.
14. Subrahmanyam CVS. Textbook of physical pharmaceutics. Vallabh Prakashan: Delhi; 2005.
15. Ripal Mistry, "Review-Selection-Of-Dissolution-Media." Pharmatutor, Sep 2013,
16. <http://www.pharmatutor.org/articles/review-selection-of-dissolution-media>.
17. Lachman L, Liberman HA, Kanig JL,"The Theory and Practice of Industrial Pharmacy", 3rd ed. Varghese Publishing House, Mumbai, India, 1987; pp. 66-99.
18. Lindberg N, Pålsson M, Pihl A, Freeman R, Freeman T, Zetzener H, Enstad G. "Flowability measurements of pharmaceutical powder mixtures with poor flow using five different techniques". Drug Dev Ind Pharm. 2004; 30:785-791.



19. US Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER). Guidance for Dissolution testing. Rockville, MD, USA, 2007.
20. Bolton S. Pharmaceutical Statistics, 2nd ed. Marcel Decker Inc., New York, USA, 1990; p. 234.
21. Mendenhall W, Sincich T. Multiple regression. 3rd ed., Dellen Publishing Co., San Francisco, CA, USA, 1989; pp. 141-226.
22. Franz RM, Browne JE, Lewis AR. Experiment design, modeling and optimization strategies for product and process development. In: Pharmaceutical Dosage Forms: Disperse Systems, Vol 1. 1st ed., Marcel Decker Inc., New York, NY, USA, 1988; pp. 427-519.

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