

# Statistically 2 Level Factorial by Design Expert: *In-vitro* Design and Formulation of Levitiracetam Extended Release Tablets

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## ABSTRACT

**Background:** Levitiracetam is an antiepileptic medication that falls into the BCS Class I drug classification. It is used to treat specific types of seizures in adults and children with epilepsy because of its high solubility and permeability. **Aim:** The objective of the present study is to evaluate the extended release tablets of levitiracetam by direct compression using HPMCK100, HPMCK15 and Xanthan gum/Ethyl cellulose effect of the dissolution rate by 2 level factorial designs by Design expert software. **Materials and Methods:** The Design Expert software used to 2 level factorial designs, the three independent components of X1: drug: HPMCK 100, X2: HPMC K15 and X3: Ethyl cellulose/Xanthan gum was used to do analysis of variance (ANOVA), 3D surface plots, counter plots, optimization, and desirability. Fourier-transform infrared spectroscopy was used to investigate drug-excipient compatibility. **Results and Conclusion:** The drug release from all the tablets was diffusion control as indicated by the linear Higuchi plots. The release data was analyzed Peppas equation the release exponent (n) was found to be in the range 0.76-0.93. Amount all the levitiracetam tablets prepared formulation F2 formulated employing HPMC K100 60 mg, HPMCK15 25 mg, Xanthane gum 25 mg. In the all cases formulations F1, F3, F4, F5, F8 Indicates nonfickain diffusion and F2, F6, F7 Indicates super case II transport as release mechanism. The formulation F2 was released 100% drug release in a 8 hr. It is fulfill specifications for extended release tablets. The results of ANOVA of dependent variables indicated that the individual and combined effect of the 3 factors is significant ( $p < 0.05$ ). The design expert software used to find 2 level factorial design, surface, counter plots, optimization and desirability. The optimized formula did better on the desirability level (1.0), indicating that it was a good fit. The FTIR spectra of pure drug and mixture with various excipients, indicates no chemical interaction between drug and excipients.

**Keywords:** Extended release, Design expert software, Levitiracetam, Direct compression, Drug release 8hr.

## INTRODUCTION

Levitiracetam is a widely prescribed antiepileptic medicine that belongs to the BCS Class I drug classification. It has a high solubility and permeability and is used to treat specific types of seizures in adults and children with epilepsy and recent formulations are reported.<sup>1-7</sup> The purpose of this study is to analyze levitiracetam extended-release tablets using HPMC K100, HPMC K15, and Xanthan gum/Ethyl cellulose. The hydration of HPMC, which forms the gel barrier through which

the drug diffuses, is known to limit drug release from the hydrophilic matrix tablet. Concentration increases the diffusion path length for the drug due to the formation of more gel, which delays drug release from the formulation. The recent research found by HPMC polymers are reported.<sup>8-14</sup> The HPMC K100LV or K4M slows the release of the medication by 4 or 8 hr, respectively. The HPMC K100M was preferred for a sustained-released period of more than 12 hr, and the percentage of HPMC K100M in

Submission Date: 18-09-2021;

Revision Date: 03-05-2022;

Accepted Date: 07-07-2022.

DOI: 10.5530/ijper.56.4.180

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formulations grew to 41%. The viscosity of HPMC was increased, the release rate was decreased in 12 hr, and the concentration of HPMC K4M, K15M, and K100M was 89.662.3, 84.28±1.11% and 76.22±1.44% mg/tablet. To examine the individual main effects and combined effects of the three components involved, the study uses 2<sup>3</sup> factorial designs. Simple experiments that look at one element at a time reveal not just the influence of that factor, but also the number of combination or interaction effects of two or more factors reported various statistical and other researchers reported.<sup>15-28</sup> A 2<sup>3</sup> factorial design was used in the formulation of tablets in this investigation. Individual and combined effects of three factors, each at two levels, were explored. HPMC K100 (factor X1), HPMC K15 (factor X2), and Xanthan gum/Ethyl cellulose are the three factors studied (factor X3).

## MATERIALS AND METHODS

Levetiracetam A Gifted sample from Aurobondo pharma. pvt. Ltd, Pydibhimavaram. Xanthene gum Purchased from Yarrow chemie. pvt. ltd, Mumbai, HPMC K100 Purchased from Yarrow chemie. pvt. ltd, Mumbai, HPMC K15 Purchased from Yarrow Chemie. pvt. ltd, Mumbai, Ethylcellulose Purchased from Loba Chemie Pvt, ltd., Lactose Purchased from Lobachemie Pvt, ltd, Magnesium Stearte, Lobachemie Pvt, ltd Loba Chemise Pvt, ltd, Sodium Hydroxide Loba Chemie Pvt, ltd Mark Life Science Pvt, Talc Loba Chemie Pvt, ltd.

### Design

Design expert software was used to create 2<sup>3</sup> factorial design, responses are predicted in this approach by calculating the influence of each Independent variable and their interactions in a specific experimental region computationally. HPMCK100, HPMCK15, and, Xantangum(XG)/Ethyl cellulose (EC) concentrations were used as independent variables (X1, X2, and X3, respectively). HPMC K100 was 60 mg and 30 mg in XG 25 mg and EC 15 mg, respectively, while HPMC K15 was 50 mg and 25 mg in XG 25 mg and EC 15mg. Three central points were established to range from X1- 45 mg, X2- 37.5mg, and X3-20 mg. To identify ideal formulations of four response variables: cumulative amount of drug release (CDR) 2hr (percent; Y1), cumulative amount of drug release (CDR) 5hr (percent; Y2), CDR 8hr (%; Y3) and T50 (hr's; Y4) (time for 50% release) were used. As shown in Design and responses shown in Tables 1 and 2, 11 different experimental runs were recommended; as a result, experiments were carried out using the supplied combinations. Y1 had a range of 5.90 to 68.55 percent, Y2 had a range of

**Table 1: Design for selected Independent variables.**

Independent variables(mg)	(X1) HPMC K100		(X2) HPMC K15		(X3) XG/EC	
	60 (+)	30 (-)	50 (+)	25 (-)	25 (+)	15 (-)
Central Point	45		37.5		24.57	
Dependent variables	Optimization (Prediction value)		Range			
Y1	15.068	5.9	68.55			
Y2	41.36	14.25			96.1	
Y3	62.194	26.5			100	
Y4	6.00	1			15.5	

**Table 2: Combination of Experimental Responses with Runs.**

Runs	(X1) HPMC K100(mg)	(X2) HPMC K15(mg)	(X3) EC/XG (mg)	(Y1) CDR 2hr (%)	(Y2) CDR 5hr (%)	(Y3) CDR 8hr (%)	(Y4) T50 (hr's)
F1	30	25	15	29.49	46.47	69.57	5.33
F2	60	25	15	8.85	32.07	69.80	5.67
F3	30	50	15	5.90	32.74	62.13	7.17
F4	60	50	15	33.23	57.72	70.90	9.83
F5	30	25	25	10.22	14.25	26.50	15.5
F6	60	25	25	12.43	65.06	100	3.57
F7	30	50	25	10.76	65.07	88.66	3.75
F8	60	50	25	68.55	96.0	100	1
Central Points							
F9	45	37.5	20	24.57	56.12	87.30	4.83
F10	45	37.5	20	24.57	56.12	87.30	4.83
F11	45	37.5	20	24.57	56.12	87.30	4.83

14.25 to 96.01 percent, Y3 had a range of 26.50 to 100 percent, and Y4 had a range of 1 to 9.83 hr. As per the factorial design approach, on the produced tablets. The responses were evaluated using a statistical model that included interactive and polynomial terms, i.e.  $Y=X_0+1X_1+2X_2+12(X_1X_2)+3(X_3)+13(X_1X_3)+2,3(X_2X_3)-123.(X_1X_2X_3)$ .

### Preparation of tablets

Each tablet containing 60 mg of medicine and polymers was made using different ratios according to the formula Design for selected Independent variables in Table 1. The appropriate proportions of drug, ethyl cellulose polymers, HPMC K100, and HPMC K15 were all passed through sieve no 16 in that order. Then, using a mortar and pestle, all of the components were well combined.

**Table 3: Analysis of variance for Experimental Responses.**

Source	Df	CDR 2hr			CDR 5hr			CDR 8hr			Q50		
		S.S	F	P	S.S	F	P	S.S	F	P	S.S	F	P
Model	6	3129.23	216.14	0.0005	4051.89	6.68	0.0448	3383.55	2.71	0.221	135.11	11.48	0.035
A-HPMC K100	1	555.94	230.40	0.0006	1067.68	8.80	0.0413	1100.86	5.28	0.105	17.05	8.70	0.060
B-HPMC K15	1	412.56	170.97	0.0010	1099.34	9.06	0.0396	389.55	1.87	0.264	8.65	4.41	0.126
C-EC/XG	1	74.97	31.07	0.0114	638.67	5.26	0.0835	228.50	1.10	0.371	2.18	1.11	0.368
AB	1	1340.33	555.46	0.0002	634.75			359.32	1.73	0.280	16.53	8.43	0.062
AC	1	355.24	147.22	0.0012	611.45	5.23	0.0842	718.87	3.45	0.160	39.07	19.93	0.020
BC	1	390.18	161.70	0.0010	53.14	5.04	0.0882	586.45	2.82	0.192	51.61	26.32	0.014
Curvature	1	10.00	4.15	0.1346	485.51	0.44	0.5444	418.79	2.01	0.251	5.92	3.02	0.180
Residual	3	7.24			485.51			624.90			5.88		
Lackof Fit	1	7.24			0.000			624.90			5.88		
Pure Error	2	0.000			4590.54			0.000			0.000		
CorTotal	10	3146.47						4427.23			146.91		

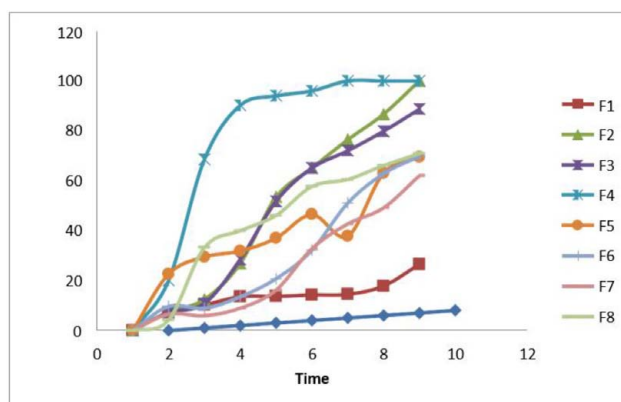
**Table 4: Statistical analysis for the measured responses.**

Parameter	CDR 2hr	CDR 5hr	CDR 8hr	Q50
Std. Dev.	1.55	11.02	14.43	1.40
Mean	23.01	52.53	77.22	6.03
C.V.%	6.75	20.97	18.69	23.23
PRESS	463.30	7768.13	39993.58	376.48
-2Log Likelihood	26.61	72.88	75.65	24.33
R-Squared	0.9977	0.8930	0.8441	0.8748
AdjR-Squared	0.9931	0.7592	0.5323	-1.6703
PredR-Squared	0.8523	-0.7120	-8.9773	12.142
AdeqPrecision	47.293	9.313	5.972	41.12
BIC	43.40	87.26	92.44	75.66
AICc	77.95	105.88	126.99	

**Table 5: Drug release Parameters of Tablets Prepared.**

Sl. No.	Formulation	Release exponent ('n' value)	Release rate		T50 (h.min)
			K1(h <sup>-1</sup> )	Ko(mg/h)	
1	F1	0.80	0.0364	2.5475	>8
2	F2	0.93	0.0612	5.596	3.40
3	F3	0.86	0.0390	3.720	3.45
4	F4	0.83	0.5097	14.65	1
5	F5	0.76	0.285	6.093	5.20
6	F6	0.90	0.0554	4.543	5.40
7	F7	0.92	0.025	0.7785	7.10
8	F8	0.89	0.0226	14.035	>8

The lubricants, such as talc and magnesium stearate, were fed via mesh no 16 into the blended powder after thorough mixing. These were also mixed in the mortar with the pestle once more. On a rotating multi-station

**Figure 1: Dissolution profile of Levitracetam prepared Tablets Prepared.**

punching machine, the tablet blend was compressed into tablets.

### **In vitro Dissolution**

The tablets were dissolved in 0.1 N hydrochloric acid for the first 2 hr and then in pH 6.8 phosphate buffers for the remaining 6 hr, using DISSO 8000 (LABINDA) 8 station dissolution test apparatus with a paddle rotating at 75 rpm at a temperature of 37°C throughout the study. Each dissolution media test sample (5ml) was withdrawn through a filter at various intervals of time and examined at 210 nm. Each dissolution samples replicated four times ( $n=4$ ), with the sample of dissolution fluid withdrawn at each time being replaced with fresh fluid.

### **FTIR Studies**

On a Perkin Elmer IR spectrophotometer with KBr disc, FTIR spectra of the medication and its combinations

were recorded. The resolution was  $2\text{ cm}^{-1}$  and the scanning range was  $400\text{ to }4000\text{ cm}^{-1}$ .

### Data Analysis

Data analysis is performed using the first order and zero order kinetics models. ANOVA was used to determine the individual and combined effects of the three components involved in the dissolution rate constant.

## RESULTS AND DISCUSSION

Angle repose of prepared blends was determined to be outstanding to good flow property, and Carr's index of all prepared blends reveals good flow property. Therefore mentioned blend worked better in direct compression, but the results aren't shown here. Figure 2 show the Fourier-transform infrared spectrum of levetiracetam and excipients in the  $400\text{--}4000\text{ cm}^{-1}$  range. The primary characteristic absorption bands in the spectra are  $3196.43(\text{N-H})$ ,  $2991.05$ ,  $2938.98$ ,  $2911.02$ ,  $2890.77$  (aliphatic C-H),  $1675.84$ ,  $1649.8$  (C=O),  $1383.68$  (C-N),  $1213.01$  (C-O),  $1082.83$  (C-C), and  $702.926$ ,  $636.394$ ,  $545.756\text{ cm}^{-1}$  for N-H,  $2991.05$ ,  $2938$  (ring deformation). The IR absorption peaks of levetiracetam can be seen in the FTIR spectra of a drug mixture with various excipients. Pure medication and mixtures with varied excipients have similar FTIR spectra. It means there is not any chemical interaction between the drug and the excipients Figure 1 and Table 5. Illustrate the dissolution profile and specifications of tablets manufactured. The dissolution data were analyzed using zero order and first order kinetics, as well as Higuchi and Pappas kinetics. The correlation coefficient value ( $r$ ) was calculated for each model. The ' $r$ ' value in zero order models was always higher than in first order models. The medication release from tablets is depicted using zero order

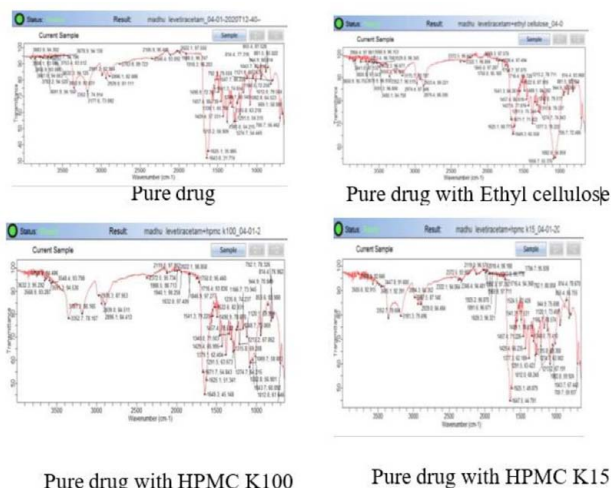


Figure 2: FTIR Spectrums.

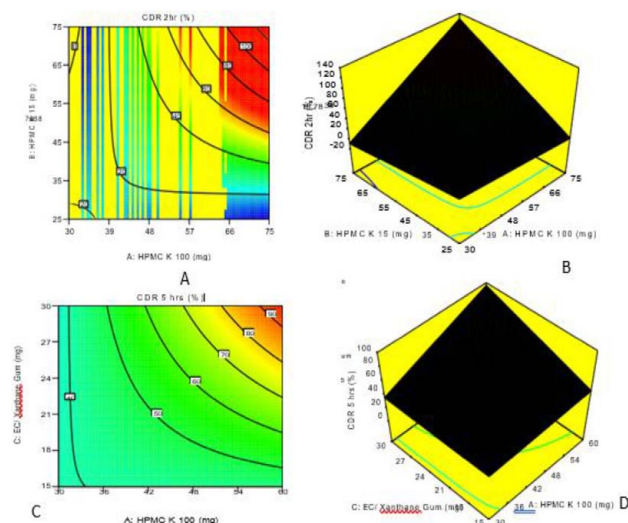


Figure 3: Counter plots CDR 2hr and 5hr A, C. 3D Surface plots B, D.

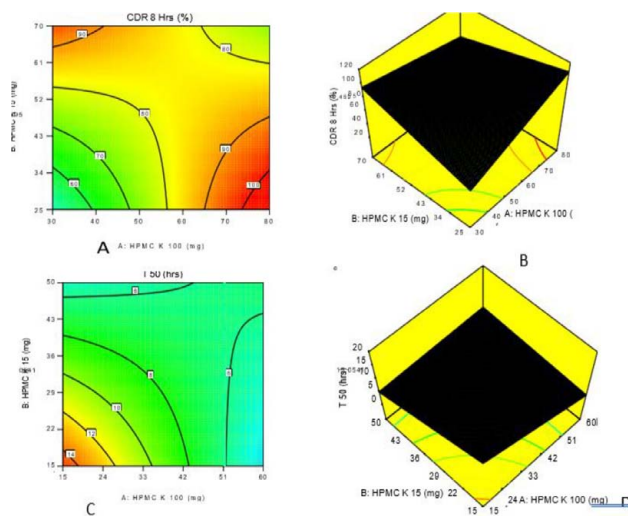


Figure 4: Counter plots CDR 8hr and T50 A, C. 3D Surface plots B, D.

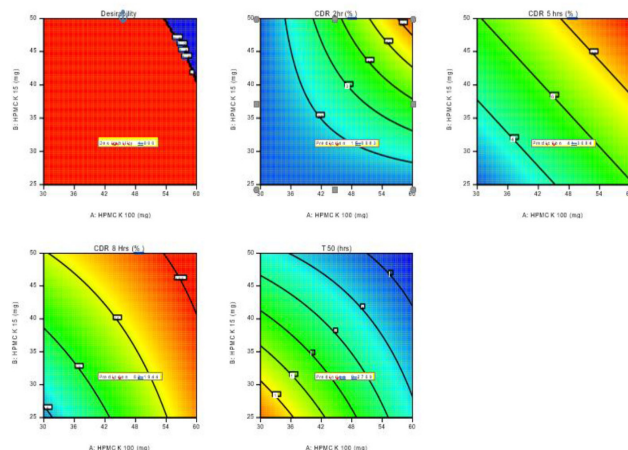


Figure 5: Desirability for all responses.



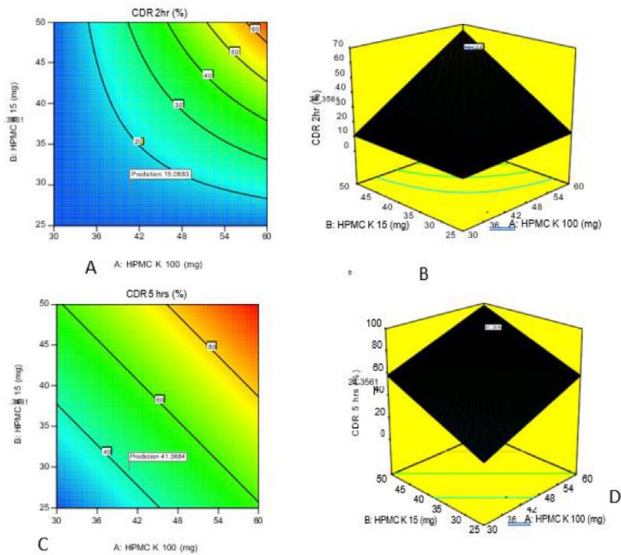


Figure 6: Optimization Surface B, D and counter plots A, C of CDR 2hr and CDR 5hr.

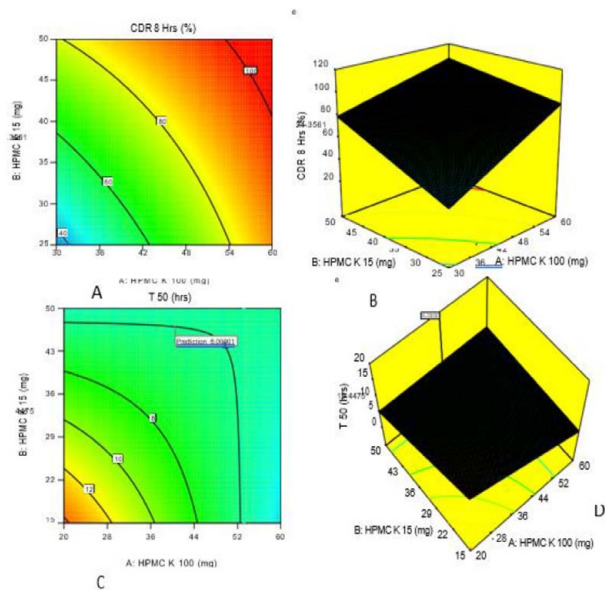


Figure 7: Optimization Counter plots CDR 8hr and T50 A, C. 3D Surface plots B, D.

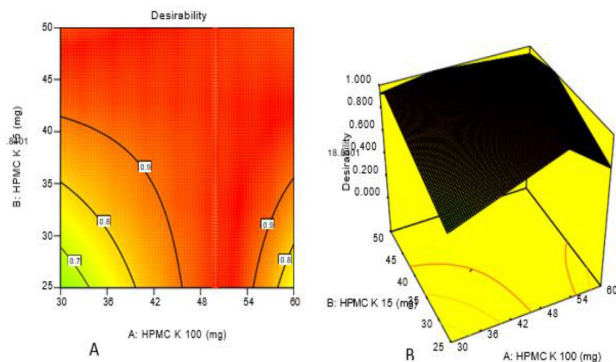


Figure 8: Desirability of Counter plot A, surface plot B.

Table 6: Correlation–Coefficient(r) values in the analysis of released at a sample prepared as per different kinetic model.

SI. No.	Formulation	Zero order	First order	Higuchi	Peppas
1	F1	0.9019	0.8073	0.93430	0.806469
2	F2	0.990	0.9611	0.92799	0.935645
3	F3	0.979	0.974	0.93351	0.862530
4	F4	0.9560	0.95602	0.95149	0.831480
5	F5	0.979	0.9832	0.97797	0.768419
6	F6	0.9663	0.918	0.87605	0.901453
7	F7	0.9669	0.947	0.87075	0.926659
8	F8	0.7063	0.637	0.63345	0.894028

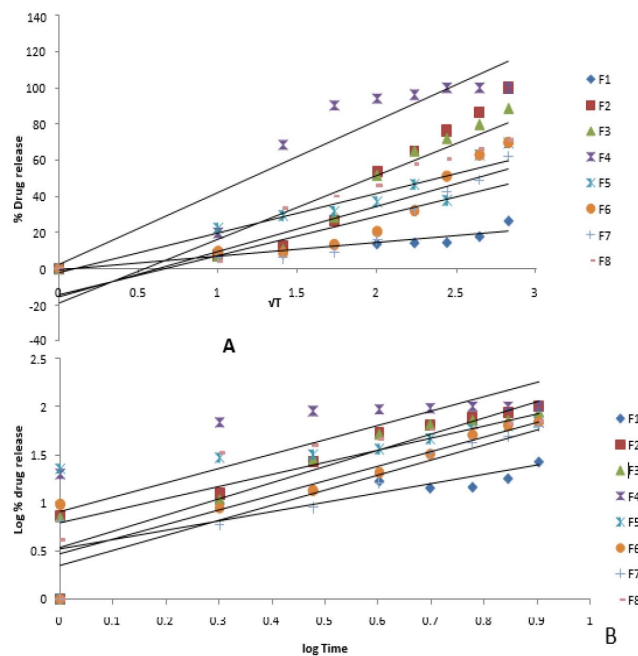


Figure 9: A. Higuchi Dissolution plots B. Peppas plots.

kinetics. Table 6 shows the correlation coefficient(r) value of medication release. Zero order kinetic models were created for the drug release from all of the tables. The linear Higuchi plots showed that the drug release from all of the tablets was diffusion controlled. The data analyzed for the release. The release exponent (n) in Peppas equation was determined to be in the range of 0.76-0.93, as indicated in Table 6 and Figure 9. F1, F3, F4, F5, F8 Indicates Non Fickian Diffusion F2, F6, F7 Indicates super case II transport as the drug release mechanism. Due to formulation factors, there were several variances in the dissolution rate  $K_0$  values of various tablets. At two levels, the individual and combined effects of three components were evaluated. A total of 8 treatments corresponding to  $2^3$  factorial

studies were tested in tablet form. The dissolution profile of all produced tablets was given in Figure 1. Formulation F1 drug release is 26% in 8 hr, Formulation F2 drug release is 100% in 8 hr, Formulation F3 drug release is 88.66% in 8 hr, Formulation F4 drug release is 100% in 8 hr, Formulation F5 drug release is 69.5 percent in 8 hr, Formulation F6 drug release is 69.8% in 8 hr, Formulation F7 drug release is 62 percent in 8 hr, and Formulation F8 drug release is 70.90 percent in 8 hr.  $F4 < F2 < F3 < F8 < F6 < F5 < F7 < F1$  is the medication release order. Amount of all levetiracetam tablets manufactured using HPMCK100 60mg, HMPCK15 25mg, and xanthane gum 25mg in formulation F2. The formulation F2 had a 100% drug release time of 8 hr. It satisfies all criteria and is suitable for long-term use.

### Statistical Analysis

Table 4 shown in Statistical analysis for the measured responses lists each statistical Variable. The standard error of regression (S) was calculated as a measure of how well the current model fits the data. Furthermore, model with a higher  $R^2$  is preferable, where  $R^2$  shows the model's prediction accuracy, lack of fit indicates data variability around the fitted model, and a good model provides statistically significant ( $p < 0.05$ ) results. The findings of the analysis of variances for the four responses are shown in Table 3. Each response was influenced by at least one of the linear effect parameters (X1, X2, and X3).

### Dependent Variable Y1 (CDR 2hr)

The model's  $F$ -value of 216.14 indicates that it is significant. An  $F$ -value of this magnitude has a 0.05 percent chance of occurring due to noise. Model terms are significant if the "Prob >  $F$ " value is less than 0.0500. X1, X2, X3, X1.X2, X1.X3, X2.X3 are important model terms in this scenario. The "Curvature  $F$ -value" of 4.15 indicates that the design space's curvature is not substantial in comparison to the noise. A "Curvature  $F$ -value" of this magnitude has a 13.46 percent chance of occurring due to noise. The "Pred R-Squared" of 0.8523 is within 0.2 of the "AdjR- Squared" of 0.9931, indicating that the difference is less than 0.2. The signal-to-noise ratio is measured using "Adeq Precision." A ratio greater than 4 is desirable; ratio of 47.293 indicate an adequate signal. Based on polynomial equation described below

$$Y1 = +244.47898 - 3.81000X1 - 4.76680X2 - 7.57625X3 + 0.069033X1.X2 + 0.088850X1.X3 + 0.11174X2.X3.$$

### Dependent variable Y2 (CDR 5hr)

The model's  $F$ -value of 6.68 indicates that it is significant. Model terms are significant if the "Prob >  $F$ " value is less than 0.0500. The curvature (as assessed by the difference between the average of the centre points and the average of the factorial points) in the design space is not significant in comparison to the noise, according to the "Curvature  $F$ -value" of 0.44. A "Curvature  $F$ -value" of this value has a 54.44 percent chance of occurring due to noise. The overall mean may be a better predictive response than the present model if the "Pred R-Squared" is negative. The signal-to-noise ratio is measured using "Adeq Precision." A signal with are to greater than 4 is desired; a signal with are ratio of 9.313 is appropriate. Based on polynomial Equation described below.

$$Y2 = + 158.76591 - 1.60517X1 - 1.85980X2 - 8.80300X3 + 0.11877X1.X3 + 0.13988X2.X3.$$

### Dependent Variable Y3 (CDR 8hr)

The model's  $F$ -value of 2.71 indicates that it is not significant in comparison to the noise. A large  $F$ -value has a 22.17 percent likelihood of being due to noise, and Prob >  $F$  less than 0.0500 indicates that model terms are meaningful. The "Curvature  $F$ -value" of 2.01 indicates that the design space's curvature is not substantial in comparison to the noise. A "Curvature  $F$ -value" of this magnitude has a 25.12 percent chance of Occurring due to noise. The overall mean may be a better predictor of reaction than the present model if the "Pred R-Squared" is negative. The signal-to-noise ratio is measured using "Adeq Precision." A ratio of more than 4 is preferable, and a ratio of 5.972 suggests a sufficient signal. This model can be used to navigate the design space. Based on polynomial equation described below.

$$Y3 = +155.89847 - 0.40542X1 - 0.57310X2 - 9.75588X3 - 0.035743X1.X2 + 0.12639X1.X3 + 0.13699X2.X3$$

### Dependent Variable Y4 (Q50)

The model's  $F$ -value of 11.48 indicates that it is significant. An  $F$ -value of this magnitude has a 3.54 percent chance of occurring due to noise. Due to noise, there is an 18.06 percent probability that a "Curvature  $F$ -value" this large will occur. The overall mean may be a better predictor of your reaction than the present model if the "Pred R-Squared" is negative. The signal-to-noise ratio is measured using "Adeq Precision." A ratio of more than 4 is preferable, and a ratio of 12.142 indicates a good signal. Based on polynomial equation

described below  $Y_4 = -28.44432 + 0.20450X_1 + 0.38460X_2 + 2.74550X_3 + 7.66667E-003X_1.X_2 - 0.029467X_1.X_3 - 0.040640X_2.X_3$ . The size of each regression coefficient's effects on responses was assessed. The factors with a positive sign have a positive relationship with the responses, whilst those with a negative sign have a negative relationship with the responses. A desirability function was used to optimize three independent variables. Table 1 shows the composition of the optimized formulation, with Y1, Y2, Y3, and Y4 being 15.0683 percent, 41.3684 percent, 62.1944 percent, and 6.00001 hr, respectively, with a desire function of 1.000. In order to determine their liability and accuracy of the range, a comparison was made between the predicted values and the experimental values. Figures 3 and 4 show the contour and response surface plots for all responses of all formulation components, whereas Figures 5, 6, and 7 show the optimized formulation. The response surface's contour and response plots as a function of three elements at once are more useful in comprehending both the primary and interaction impacts of the factors. The feasibility was based on the optimum formulations and the intended function of surface and response plots (see Figure 8). The calculated percentage prediction errors of all replies were sufficiently low, implying that the numerical values for optimization were dependable and accurate.

## CONCLUSION

A two-level factorial design was used to successfully generate levetiracetam formulations. CDR 2hr (percent; Y1) 15.0683 percent, CDR 5hr (percent; Y2) 41.3684 percent, CDR 8hr (percent; Y3) 62.1944 percent, and T50 (hr's; Y4) 6.00001 hr. The article illustrates how universal 2 level factorial designs were used to successfully optimize direct compression results.

## ACKNOWLEDGEMENT

The Author Thankful to Sri Venkateswara College of Pharmacy, Etcherla, Srikakulam Provides research facilities and design expert software developed by P.V. Bhaskar, GSK, Pvt, Ltd., literature and edited by Dr. Ch. Taraka Ramarao and S. Madhuri.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**HPMC:** Hydroxy Propyl Methyl Cellulose; **ANOVA:** Analysis of Variance; **BCS:** Biopharmaceutical Classification System; **XG:** Xanthan Gum; **EC:** Ethyl Cellulose; **CDR:** Cumulative amount of Drug Release; **FTIR:** Fourier-transform Infrared Spectroscopy.

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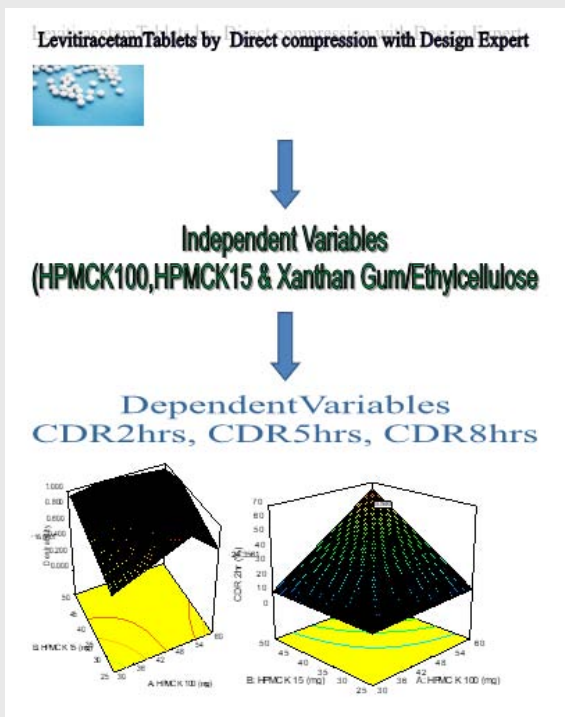
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## SUMMARY

The extended release Levitracetam tablets had prepared to stay in prolonged period of time for the blood stream to treat specific types of seizures in adults and children with epilepsy. The formulated after identifying the formulation variables using 2 level factorial design and then prepared by using direct compression technique. The Design Expert software used to 2 level factorial designs, the three independent components of X1: HPMCK 100, X2: HPMC K15 and X3: Ethyl cellulose/Xanthan gum was used to do analysis of variance (ANOVA), 3D surface plots, counter plots, optimization, and desirability. The Angle repose of prepared blends was determined to be outstanding to good flow property, and Carr's index of all prepared blends reveals good flow property. The IR absorption peaks of levetiracetam can be seen in the FTIR spectra of a drug mixture with various excipients. Pure medication and mixtures with varied excipients have similar FTIR spectra. It means there is not any chemical interaction between the drug and the excipients. The ANOVA was used to determine the individual and combined effects of the independent variables by using Design Expert software. The *In vitro* dissolution data were analyzed using zero order and first order kinetics, as well as Higuchi and Pappas kinetics. The correlation coefficient value (*r*) was calculated for each model. The '*r*' value in zero order models was always higher than in first order models. The linear Higuchi plots showed that the drug release from all of the tablets was diffusion controlled. The release exponent (*n*) in Peppas equation was determined to be in the range of 0.76-0.93, as F1, F3, F4, F5, F8 and Non Fickian Diffusion F2, F6, F7 Indicates super case II transport as the drug release mechanism. The formulation F2 had a 100% drug release time of 8 hr. It satisfies all criteria and is suitable for long-term use. The statistical analysis for the measured responses lists each statistical Variable. The standard error of regression (S) was calculated as a measure of how well the current model fits the data. Furthermore, model with a higher R2 is preferable, where R2 shows the model's prediction accuracy, lack of fit indicates data variability around the fitted model, and a good model provides statistically significant ( $p < 0.0500$ ) in all dependent variables. The optimized formulation, with Y1, Y2, Y3, and Y4 being 15.0683%, 41.3684%, 62.1944%, and 6.00001 hr, respectively, with a desirability function of 1.000. In order to determine their liability and accuracy of the range, a comparison was made between the predicted values and the experimental values.



**PICTORIAL ABSTRACT**



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**Cite this article:** Ramarao Ch T, Madhuri S. Statistically 2 Level Factorial by Design Expert: *In-vitro* Design and Formulation of Levitiracetam Extended Release Tablets. Indian J of Pharmaceutical Education and Research. 2022;56(4):994-1002.