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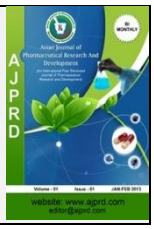

Open Access Research Article

Combined Effects of % Er Coating and Ec: Pvp Ratio on Release Profile of Topiramate Extended Release Pellets

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ABSTRACT

The main purpose of this study was to investigate the influence of %ER coating and EC: PVP ratio on the release profile of topiramate extended release pellets. This formulation comprises of an extended releasecomponent (ethyl cellulose) which retards the release of drug coated on the core pellets. The extent of extended release coat and concentration of extended release component is optimized to achieve predetermined dissolution profile. Formulating modified release drug delivery system for highly soluble drug is difficult.Presentresearchcomprisesofethylcelluloseactsasratecontrollinghydrophobicbarrier while povidone k-30 acts as pore former component which helps in release of drug. Reservoir technology by using wurster coating process was used to develop extended release pellets where, subsequent coating is applied on corepellets. In drug layering stage, drug solution prepared was dispersion solution. Therefore viscosity played animportantroleindruglayering. 4% barrier coating using Opadry clear was done to smoothen the drug layered pellets for the ease of subsequent coating process. Extended release coat applied on the barrier layer coated pellets, determines the release of the drug from the formulation. Thus, in present research ratio of EC: PVP K-30 and % ER coating were optimized to 75:15 and 13% respectively to obtain desired drug releaseprofile.

Keywords: Modified release drug delivery system, Rate controlling hydrophobic barrier, Pore former, Reservoir technology

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1. INTRODUCTION

Multi unit particulate system can be defined as "converting granules or fine powder of drug and excipients into small, spherical and free flowing form by using agglomeration process is known as pelletization." Size range of multiunit particulate system is generally in 0.5-1.5 mm. Use of Multi particulate system is advantageous in developing the modified release dosage forms with or without gastro retentive characteristics[1]. They are also used to achieve extended release drug dissolution profile and sometimes for site specific delivery usually in colon targeted drug delivery system multiunit particulate system is used[2,3].For specific drug delivery system that defines the specific action of formulation. Depending on that, formulation development, design and component as well as method of preparation of formulation are selected. Modified release dosage form or targeted drug delivery can be formulated in solid orals are generally formulated as multiunit system or a single unit system[4]. Multiunit system includes pellets or micro particles filled in capsule and single unit system includes tablet formulated by matrix or reservoir technology[5].

Pellets provides greater flexibility in formulation and also prevents the chances of dose dumping as compare to tablet and thus, efficiency and safety point of view pellets are highly preferable[6]. Moreover, in multiunit particulate system, two different strength of drug or two incompatible drugs can be in corporate into one formulation. Acid labile drug can be efficiently delivered by subsequent coatingoncorepelletsthisisgenerallyusedincaseofcolontarget eddrugdelivery. Over single unit dosage form it is also advantageous pharmacokinetically[7].

Due to the smaller particle size and increased surface area, pellets can be uniformly dispersed in GIT which enhances

the absorption characteristic of drug and decreases the local side effect caused by the long retention at the mucosal membrane[8]. Inter patient as well as inter variable variability can be prevented by using multiunit particulate system.

In present research, the antiepileptic drug used for the treatment of epileptic seizure is acts by blocking the action potentials caused by a sustained depolarization of the neurons and blocks the action of sodium channels[9,10]. It also increases the action of the neurotransmitter gamma-amino butyrate (GABA) at $GABA_A$ receptor. This drug is BSC class 3 drug having high solubility in aqueous media. Immediate release formulation for this drug is available in market. But this drug is having some sever evaders effect which include somnolence, speech disorder, ataxia, Abnormal vision, problem associated with memory, diplopia, paresthesia and acute myopia can also be take place[11].Thus, nevertheless drug is having long biological half-life of 19-21 hours, it is generally not prescribed as once a daily dose as fluctuation in plasma drug concentration after administering single high dose lead to precipitation of side effect[10]. For this reason, drug is prescribed in twice daily dose but after taking each dose there is increase in plasma drug concentration followed by decrease concentration which again rise after administration of second dose, which results in to peak and valleys plasma concentration vs. time profile which is very harm full for the patient. Thus, it was required to formulate once daily dose for this drug[12].Therefore, there is a need for a formulation of topiramate, which reduces or eliminates the side effects associated with peaking and fluctuating plasma levels of the drug and preferably may be administered in a once-daily regimens. New, highly soluble and bioavailable forms of topiramate are also needed in order to increase the safety and effectiveness of the drug. For this purpose, extended release formulation of this drug is formulated[13]. Multiunit particulate system is advantageous over tablet is that, as it is made up of several micro sized pellets, each of them release the drug independently to other pellet results in very rare chances of dose dumping. Moreover, particle size of pellets is in microns results in higher surface area which helps in controlling the release in more efficient way from the formulation.

Delivering sparingly water-soluble drugs for a controlled release from polymer coated pellets remains a huge challenge[14]. Drug release is affected by multiple factors, such as drug solubility, pore-former types and levels, coating thickness, and osmotic pressure gradient across the membrane[15-17].It is well-accepted that the primary mechanism controlling drug release from polymer coated formulations is diffusion of the dissolved drug from the systems[18,19]. As dissolved molecules alone can diffuse, the solubility or dissolution rate of drugs plays an important role in governing drug release of the coated pellets[20]. Factors affecting the saturation solubility or dissolution rate of drugs in coated pellets, be they process or formulation variables, have positive effect on the release of coated pellets[21].

Polymer blend coatings of water insoluble ethyl cellulose and water soluble PVP K-30 can be utilized to control drug release from pellets in oral solid dosage forms, in which PVP K-30 act as a pore-former. More importantly, water-soluble pore-former has excellent wetting properties and readily forms films and providing appropriate mechanical film coating stability when osmotically active pellet/ capsule/tablet cores generate considerable hydrostatic pressure within the systems during drug release[22].

2. MATERIALS AND METHODS

2.1 Materials

MCC Sphere (CP 307) as a core pellets, Povidone (K-90) as a binder, Polyethylene glycol (400) as a plasticizer, Opadry clear as a film former, Ethyl cellulose as a rate controlling polymer, Povidone (K-30) as a pore-former, Triethyl citrate as a plasticizer, Talc as a anti-static agent, Isopropyl Alcohol and Dichloro methane were used for polymer dissolution.

2.2 Methods

2.2.1 Solubility of Topiramate

Solubility study of the drug was carried out by using different solvents. Saturated solutions were prepared by addition of excess of drug to the solvents and shaking them on shaker for 24 hrs under continuous vibration. After that, the solutions of drug were filtered and analysed.

2.2.2 Preparation of pellets

PVP K-90, PEG and Drug were added respectively in to the sufficient amount of water and drug loading was done on MCC Sphere by using wurster technology. For Barrier layer coating, Opadry clear and talc were added in to water and coating was done on drug loaded pellets. In a beaker, IPA and DCM were taken in a ratio of 60:40. After that PVP, TEC, EC, and Talc were added respectively in above solution and solution was coated on barrier layer pellets for ER coating. Drug Layering II and Barrier layer coating II was done same as Drug Layering I and Barrier layer coating I. finally, Pellets were lubricated by using Talc.

Table 1 : Formulation table of preliminary batches (F1-F6)

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Drug layering 1						
MCC Sphere	180	180	180	180	180	180
Topiramate USP	180	180	180	180	180	180
HPMC E 15	-	-	-	-	-	-
Povidone K90	10.8	10.8	10.8	10.8	10.8	10.8
PEG 400	3.6	3.6	3.6	3.6	3.6	3.6
Barrier Coating -1						

Opadry Clear	14.98	14.98	14.98	14.98	14.98	14.98
Talc	3.74	3.74	3.74	3.74	3.74	3.74
ER Coating						
Ethyl Cellulose	24.57	29.48	35.38	26.80	35.38	41.28
HPC-L	-	-	-	-	-	-
Povidone K30	19.65	23.59	28.30	26.80	17.69	11.79
Tri Ethyl citrate	2.46	2.95	3.54	2.68	2.95	2.95
Talc	2.46	2.95	3.54	2.68	2.95	2.95
Drug Layering -2						
Topiramate USP	20	20	20	20	20	20
HPMC E-15	-	-	-	-	-	-
Povidone K90	0.6	0.6	0.6	0.6	0.6	0.6
PEG 400	0.2	0.2	0.2	0.2	0.2	0.2
Barrier Coating -2						
Opadry Clear	18.52	18.92	19.38	18.92	18.92	18.92
Talc	4.63	4.73	4.85	4.73	4.73	4.73
Lubrication						
Talc	4.86	4.97	5.08	4.97	4.97	4.97
Total weight	**491.07**	**501.51**	**513.99**	**501.51**	**501.51**	**501.51**

2.2.3 *In-vitro* drug release

The in vitro dissolution study was carried out by dissolution testing apparatus USP-I. Sample was placed in 900ml of 0.1N HCl pH 1.2 followed by 6.8 pH Phosphate buffer and rotated at 100 rpm at 37±0.5°C. The sample was collected at specified time points up to 16 hrs. The sample was filtered through 1µm pore size of filtrate. The absorbance was measured by a HPLC using refractive index detector[23].

2.2.4 Related substance

Sample solution of 6 mg/ml of topiramate in Methanol and Water (1:4) was made. Vigorously shake the sample solution for at least 30 min, and passed a portion through a chemical resistant 0.45-um filter (PTFE). The sample was measured by a HPLC using refractive index detector.

2.2.5 Assay

Sample solution of 6 mg/ml of topiramate in Methanol and Water (1:4) was made. Shake vigorously for at least 30 min, and passed a portion through a chemical resistant 0.45-um filter (PTFE). The sample was measured by a HPLC using Methanol and Buffer(1:4)[24,25].

2.2.6 Water content

The process uses an organic base, sulphur dioxide, iodine and alcohol. During the titration, iodine was added to sample and the amount of iodine used to consume all the water contained in the sample was measured.

$$\%\ of\ water = \frac{Vs * F * 100}{W}$$

Where, Vs = Vol. of Kf reagent required

F = Factor of Kf reagent used in mg/ml

W = Wt. of sample in mg

2.2.7 Optimization by using 3^2 full factorial design

Table 2: Layout of optimization

Independent factors		**-1**	**0**	**+1**	**Dependent factors**
X1 = % ER Coating	Numeric	13	15	17	Y1 = % drug release at 4 hrs
X2 = EC:PVP Ratio	Numeric	65:25	70:20	75:15	Y2 = % drug release at 10 hrs

Table 3: Coded and Actual value of Independent variables

Run	**Coded value**		**Actual value**	
Batch Code	X1	X2	X1(%)	X2
B1	-1	-1	13	65:25
B2	-1	0	13	70:20
B3	-1	+1	13	75:15
B4	0	-1	15	65:25
B5	0	0	15	70:20

B6	0	+1	15	75:15
B7	+1	-1	17	65:25
B8	+1	0	17	70:20
B9	+1	+1	17	75:15

2.2.8 Composition of design batches

Table 4: Composition of design batches (B1-B5)

Ingredients (mg)	B1	B2	B3	B4	B5
Drug layering – 1					
MCC Sphere	180	180	180	180	180
Topiramate USP	180	180	180	180	180
Povidone K90	10.8	10.8	10.8	10.8	10.8
PEG 400	3.6	3.6	3.6	3.6	3.6
Barrier layer coating – 1					
Opadry Clear	14.98	14.98	14.98	14.98	14.98
Talc	3.74	3.74	3.74	3.74	3.74
ER coating					
Ethyl Cellulose	33.22	35.77	38.33	38.33	41.28
Povidone K30	12.78	10.22	7.67	14.74	11.79
Tri Ethyl citrate	2.56	2.56	2.56	2.95	2.95
Talc	2.56	2.56	2.56	2.95	2.95
Drug layering – 2					
Topiramate USP	20	20	20	20	20
Povidone K90	0.6	0.6	0.6	0.6	0.6
PEG 400	0.2	0.2	0.2	0.2	0.2
Barrier layer coating – 2					
Opadry Clear	18.60	18.60	18.60	18.94	18.92
Talc	4.65	4.65	4.65	4.73	4.73
Lubrication					
Talc	4.88	4.88	4.88	4.97	4.97
Total weight	**493.17**	**493.17**	**493.17**	**501.51**	**501.51**

Table 5: Composition of design batches (B6-B9)

Ingredients (mg)	B6	B7	B8	B9
Drug layering – 1				
MCC Sphere	180	180	180	180
Topiramate USP	180	180	180	180
Povidone K90	10.8	10.8	10.8	10.8
PEG 400	3.6	3.6	3.6	3.6
Barrier layer coating – 1				
Opadry Clear	14.98	14.98	14.98	14.98
Talc	3.74	3.74	3.74	3.74
ER coating				
Ethyl Cellulose	44.23	43.44	46.78	50.12
Povidone K30	8.85	16.71	13.37	10.02
Tri Ethyl citrate	2.95	3.34	3.34	3.34
Talc	2.95	3.34	3.34	3.34
Drug layering – 2				
Topiramate USP	20	20	20	20
Povidone K90	0.6	0.6	0.6	0.6
PEG 400	0.2	0.2	0.2	0.2
Barrier layer coating – 2				
Opadry Clear	18.92	19.23	19.23	19.23
Talc	4.73	4.81	4.81	4.81
Lubrication				
Talc	4.97	5.05	5.05	5.05
Total weight	**501.52**	**509.84**	**509.84**	**509.84**

2.2.9 Stability study

One month Accelerated stability study was carried out for B3 (optimized batch). Here, two different packaging materials were used are: Alu- Alu Blister and HDPE Bottle + 2 gm silica.

Procedure

Proper Labeled blister and well labeled and sealed HDPE bottle are kept in humidity chamber at 40° ± 2°C & RH75 % ± 5% and samples were withdrawn at initially and after 1 month.

3. RESULT AND DISCUSSION

a. Solubility of drug

Table 6: Solubility of drug in different pH

Sr. No.	Type of media	mg/ml
1	Water	11.5±0.0816
2	pH 2.1	11.9±0.216
3	pH 4.5	11.6±0.169
4	pH 6.8	11.4±0.0471
5	pH 7.5	11.5±0.169
***Each observation values are expressed as a mean±S.D. of n=3**		

Discussion:

Solubility data of drug indicates that drug exhibits nearly pH-independent solubility.

3.2 Evaluations of Preliminary batches

3.2.1*In-vitro* drug release

Table 7: In - vitro drug release (F1-F6)

Time (hrs)	% In – vitro drug release						
	Ref.	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
0	0	0	0	0	0	0	0
1	13.5	12	10.8	11	11.5	11.2	10.8
2	20.1	19.9	19.5	18.9	19.4	19.8	19.9
4	40.5	60.5	55.2	52.4	60.5	49.3	37.3
6	55.9	74.2	69.5	65.5	78.9	63.8	52.7
8	72.8	88.6	82.5	79.8	86.7	78.2	70.1
10	85.2	92.1	89.5	90.5	96.4	90.4	82.9
12	93.1	94.8	95.8	94.7	98.5	96.4	91.7
16	99.8	98.9	99.2	98.9	100	99.1	99.8
F2	-	48.36	55.59	60.86	46.08	65.21	81.09
F1	-	13.58	10.17	8.32	15.89	7.05	3.26

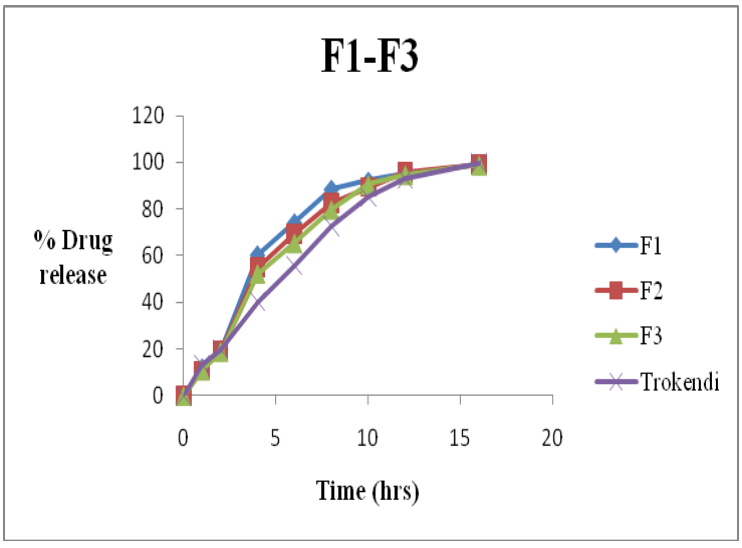

Figure 1: In – vitro drug release (F1 – F3)

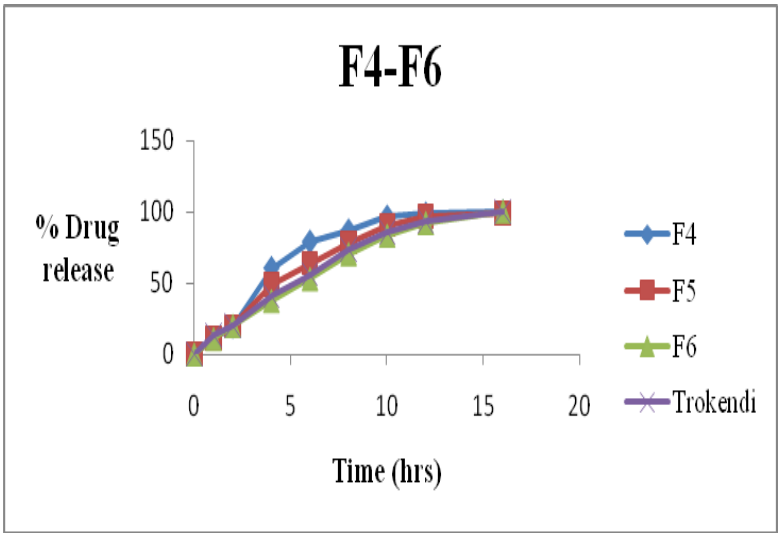

Figure 2: In – vitro drug release (F4 – F6)

3.2.2 Related substance

Table 8: Estimation of Related substance

Batch no.	Related substance			
	Test-AD(-) fructose	Test-B related compound A	Unknown impurity	Total degradation product
F1	ND	0.02	ND	0.02
F2	ND	ND	ND	ND
F3	ND	0.01	ND	0.01
F4	ND	ND	ND	ND
F5	ND	ND	ND	ND
F6	ND	ND	ND	ND
***ND = Not detected**				

3.2.3 Assay and Water content

Table 9: Estimation of Assay and Water content

Batch no.	Assay (%w/w)	Water content (%)
F1	101.5±0.081	1.56±0.020
F2	99.9±0.0471	0.52±0.021
F3	99.7±0.124	1.34±0.021
F4	98.5±0.163	1.06±0.094
F5	102.3±0.471	1.55±0.0124
F6	99.8±0.081	0.98±0.008
***Each observation values are expressed as a mean±S.D. of n=3**		

3.3Evaluations of design batches (B1 – B9)

3.3.1 *In-vitro* drug release

Table 10: In – vitro drug release (B1 – B4)

Time (hrs)	% In – vitro drug release				
	Ref.	B1	B2	B3	B4
0	0	0	0	0	0
1	13.5	10.8	10.9	11.8	10.7
2	20.1	19.7	19.8	19.9	19.8
4	40.5	51.3	43.5	41.1	45.9
6	55.9	73.8	68.7	57.3	61.3
8	72.8	87.9	80	73.4	76.4
10	85.2	96.2	87.9	86.2	92.4
12	93.1	98.4	94.8	93.9	95.2
16	99.8	100	98.3	99.5	98.9
F2	-	50.87	63.77	93.52	69.80
F1	-	13.18	6.61	1.37	5.76

Table 11: In – vitro drug release (B5 – B9)

Time (hrs)	% In – vitro drug release				
	B5	**B6**	**B7**	**B8**	**B9**
0	0	0	0	0	0
1	10.8	10.8	11.1	10.9	11.1
2	19.9	19.7	19.8	20	19.8
4	37.3	30.6	38.4	32.7	25
6	52.7	45.9	55.6	47.2	32.4
8	70.1	57.8	73.4	61.4	44.1
10	82.9	68.4	85.2	73.7	56.3
12	91.7	75.8	95.4	86.3	64.8
16	99.8	88.2	99.8	94.6	78.5
F2	81.09	47.28	88.90	56.65	34.59
F1	3.26	17.40	1.66	11.24	30.96

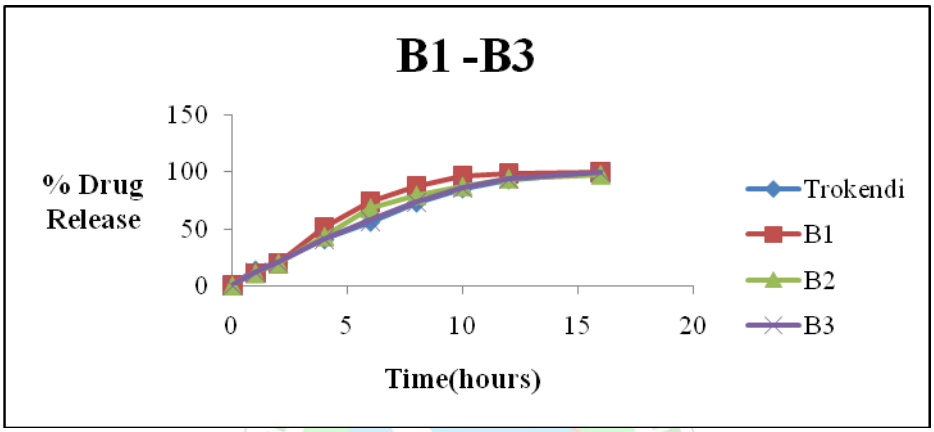

Figure 3: In – vitro drug release (B1 – B3)

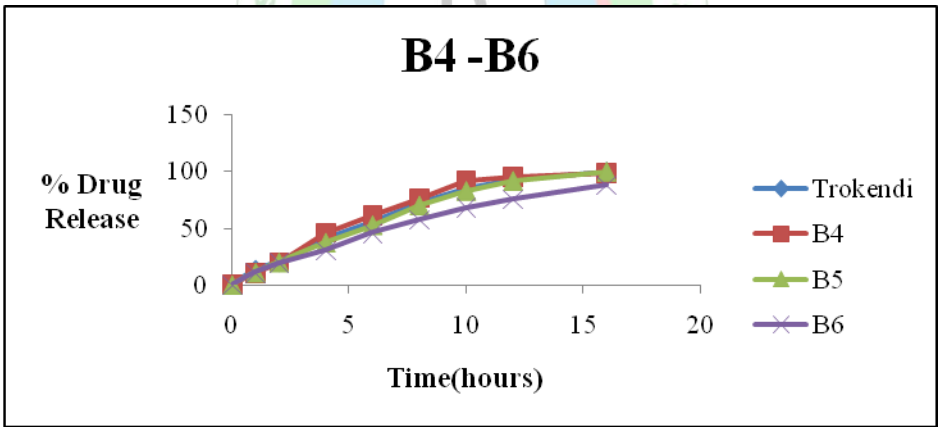

Figure 4: In – vitro drug release (B4 – B6)

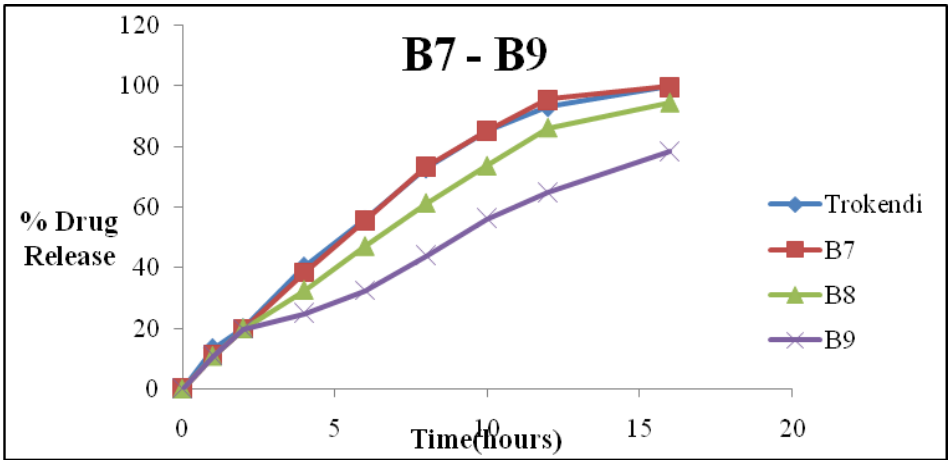

Figure 5: In – vitro drug release (B7 – B9)

3.3.2 Related substance

Table 12: Estimation of Related substance

Batch no.	Related substance			
	Test-AD(-) fructose	Test-B related compound A	Unknown impurity	Total degradation product
B1	ND	0.01	ND	0.01
B2	ND	0.01	ND	0.01
B3	ND	ND	ND	ND
B4	ND	ND	ND	ND
B5	ND	ND	ND	ND
B6	ND	0.01	ND	0.01
B7	ND	0.02	ND	0.02
B8	ND	0.02	ND	0.02
B9	ND	ND	ND	ND
***ND = Not detected**				

Discussion:

Related substance: These are the substances which are structurally related to a drug substance. These substances may be identified or unidentified degradation product or impurities arising from a manufacturing process or during storage of a material. The purpose of a test for related substances is to control degradation impur

3.3.3 Assay and Water content

Table 13: Estimation of Assay and Water content

Batch no.	Assay (%w/w)	Water content (%)
B1	99.8±0.163	0.86±0.012
B2	99.7±0.047	0.92±0.004
B3	99.8±0.082	0.77±0.008
B4	100.2±0.518	0.97±0.0126
B5	99.6±0.496	0.53±0.009
B6	99.7±0.169	0.65±0.020
B7	99.4±0.124	0.83±0.016
B8	99.2±0.543	0.95±0.021
B9	99.9±0.205	0.63±0.018
***Each observation values are expressed as a mean±S.D. of n=3**		

Discussion:

Assay: It is an analysis which is used to determine the presence of a substance and the amount of that substance. Assay of all formulations was found to be in the range of99.2±0.543 to 100.2±0.518 % w/w.

Water content: It is an analysis which is used to find out presence of moisture in the formulation. Water content of all the formulations was found to be in the range of 0.53±0.009 to 0.97±0.0126 %.

3.4 Analysis of Variance

Table 14: ANOVA for % Drug release at 4 hrs

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	525.68	5	105.14	84.84	< 0.0001	Significant
A-% ER coating	264.01	1	264.01	213.05	< 0.0001	
B-EC:PVP Ratio	252.20	1	252.20	203.52	< 0.0001	
AB	2.56	1	2.56	2.07	0.1938	
A^2	1.78	1	1.78	1.44	0.2694	
B^2	2.51	1	2.51	2.03	0.1976	
Residual	8.67	7	1.24			
Lack of Fit	8.67	3	2.89			
Pure Error	0.0000	4	0.0000			
Cor Total	534.35	12				

Table 15: ANOVA for % Drug release at 10 hrs

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	1263.04	5	252.61	72.19	< 0.0001	Significant
A-% ER coating	506.00	1	506.00	144.60	< 0.0001	
B-EC:PVP ratio	659.40	1	659.40	188.44	< 0.0001	
AB	89.30	1	89.30	25.52	0.0015	
A^2	1.58	1	1.58	0.4522	0.5229	
B^2	3.70	1	3.70	1.06	0.3382	
Residual	24.49	7	3.50			
Lack of Fit	24.49	3	8.16			
Pure Error	0.0000	4	0.0000			
Cor Total	1287.53	12				

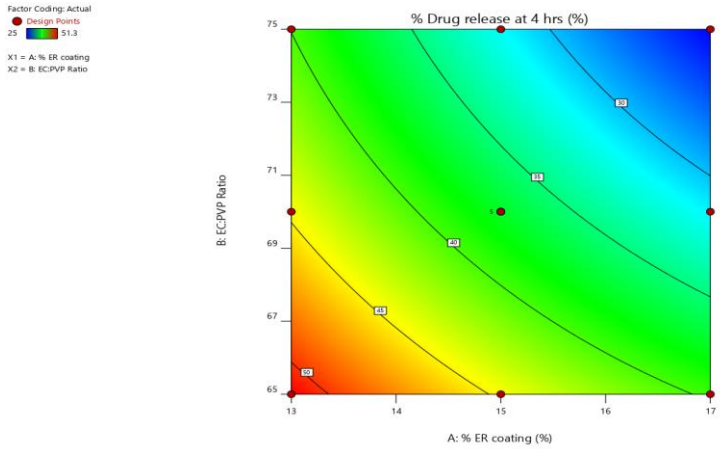

Figure 6: Contour plot showing the effect of % ER coating and EC:PVP ratio on response R1 (% Drug release at 4 hrs)

Final equation in terms of coded factors

% Drug release at 4 hrs = + 37.23–6.63 * A –6.48 * B –0.8000 * AB +0.8034 * A^2 + 0.9534 * B^2

Final equation in terms of actual factors

% Drug release at 4 hrs = + 325.81408–3.74253 * % ER coating– 5.43598 * EC:PVP ratio–0.080000 * % ER coating * EC:PVP ratio + 0.200862 * % ER $coating^2$+ 0.038138 * EC:PVP $ratio^2$

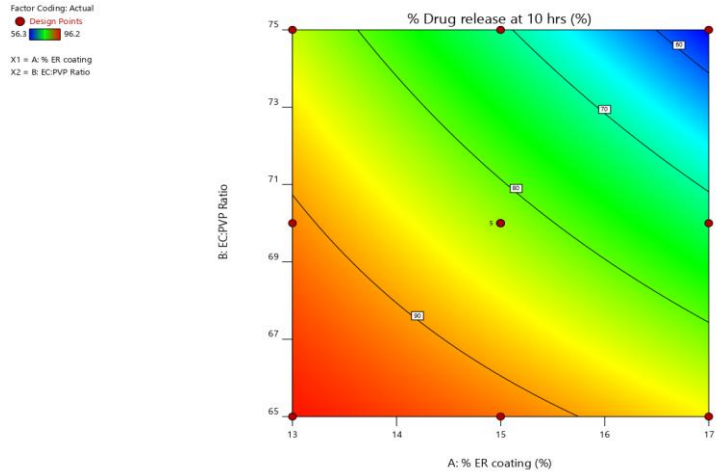

Figure 7: Contour plot showing the effect of % ER coating and EC:PVP ratio on response R2 (% Drug release at 10 hrs)

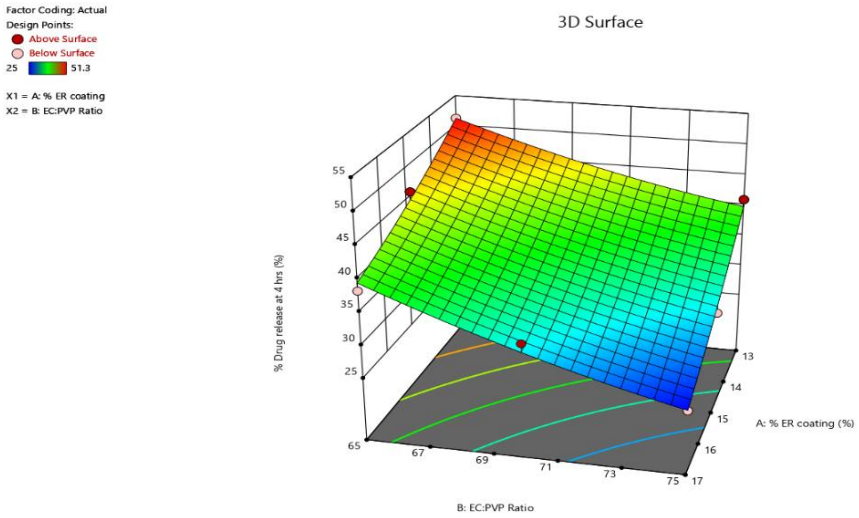

Figure 8: Response surface plot showing the effect of % ER coating and EC:PVP ratio on response R1 (% Drug release at 4 hrs)

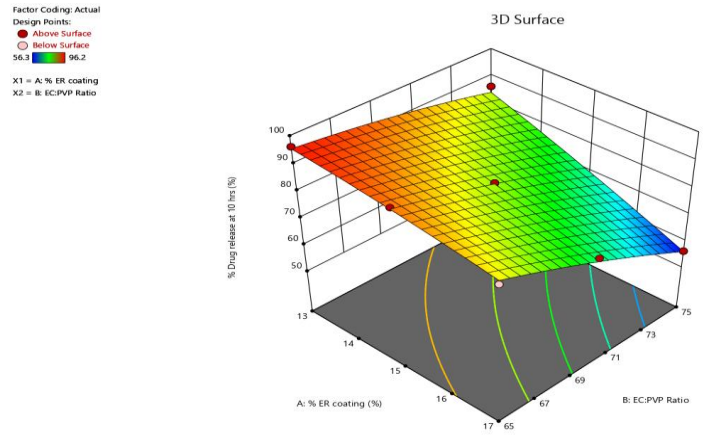

Figure 9: Response surface plot showing the effect of % ER coating and EC:PVP ratio on response R2 (% Drug release at 10 hrs)

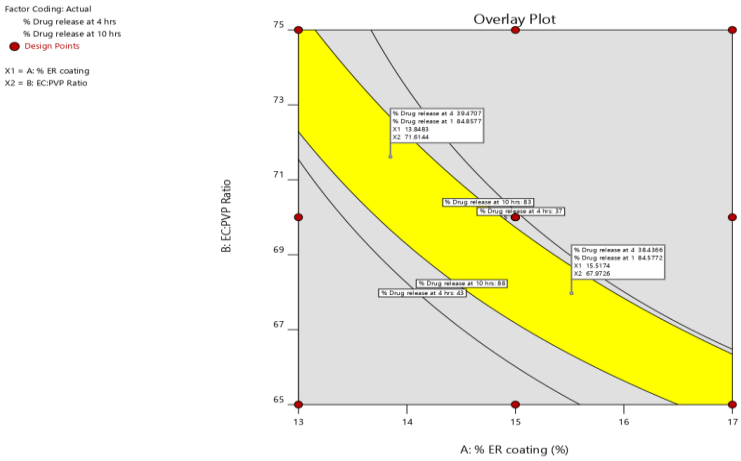

Figure 10: Overlay plot for optimized formulation

Table 16: Overlay plot for optimized formulation

Batch no.	Parameters	Predicted value	Observed value	% Error
CP1	% Drug release at 4 hrs	39.4707	38.5	2.45
CP2	% Drug release at 10 hrs	84.8577	82.9	2.30
CP1	% Drug release at 4 hrs	38.4366	37.8	1.65
CP2	% Drug release at 10 hrs	84.5772	83.3	1.51

3.5 Stability study

Table 17: Stability study of optimized batch (B3)

Physical properties	Initial	At 40 ±2 °C/75±5% RH for 1 month	
		HDPE bottle + 2 gm Silica gel	Alu Alu blister pack
Assay (%w/w)	99.8±0.082	99.5±0.081	99.7±0.047
Water content (%)	0.77±0.008	0.78±0.004	0.77±0.012
Related substance			
Test-AD (-) fructose	ND	ND	ND
Test-B related compound A	ND	ND	ND
Unknown impurity	ND	ND	ND
Total degradation product	ND	ND	ND

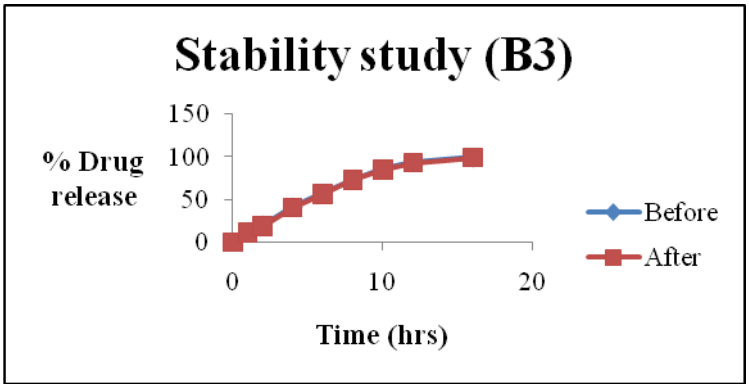

Figure 11: In-vitro drug release of optimized batch (B3)

4. CONCLUSION

In present invention, attempt was made to prepare extended release pellets of topiramate with different polymer and its different concentration by using Wurster technology.Once daily extended release pellets of topiramate are designed to achieve steadier plasma drug concentration by minimizing several side effects.Different binders and pore former were used for preparing preliminary batches of extended release pellets were HPMC K-15, PVP K-90, PVP K-30, HPC-L. During the experiment there were four critical process parameters which were optimized before the preliminary batches. The prepared extended release pellets was evaluated for assay, water content, related substance and *In-vitro* drug release.From the *In – vitro* drug release study, it was concluded that there was not that much effect of binder and its concentration on release of drug.From the experiment, it was concluded that there were two factors which affect the release study of the drug. So, extended release pellet was optimized by using 3^2 factorial design.Further optimized batch was evaluated for assay, water content, related substance, *In-vitro* drug release. From the results of above evaluated studies, formulation B3 was optimized and kept for stability studies carried out at 40 ºC ± 2 ºC and 75 % ± 5 % RH for 1 month in order to know the influence of temperature and relative humidity on assay, water content, related substance and *In-vitro* drug release.According to results of stability studies, it was concluded that optimized formulation (B3) is stable at respective temperature and humidity.The study conclusively demonstrated that topiramate can be successfully formulated into pellets by wurster technology using ethyl cellulose to obtain extended release of drug. Assay and Water content of optimized formulation (B3) was found to be 99.8±0.082 % w/w and 0.77±0.008 % respectively. From the results it was observed that the drug release decreases with increasing the % ER coating and EC:PVP ratio.

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