RESEARCH PAPER

FORMULATION, CHARACTERIZATION AND EVALUATION OF TOPIRAMATE LOADED FAST DISSOLVING TABLETS.

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ABSTRACT

The present study was designed to formulate, optimize and evaluate the topiramate loaded fast dissolving tablets (FDTs) for better patient compliance which will ensure rapid drug release. Superdisintegrants, Crospovidone (CPV) and Sodium Starch Glycolate (SSG), were selected for the direct compression method to get fast dissolving tablets. A full-factorial experimental design with two variables (CPV and SSG) was used to explore the influence of the CPV and SSG concentration on disintegration time and percentage drug release. Pre-compression and post-compression physiochemical properties like flow properties, hardness, friability, weight variation, disintegration time and in vitro drug release of the prepared formulations were determined. Drug–excipient compatibility was studied by Fourier Transform Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC) and Powder X-ray Diffraction (PXRD) studies. All the physicochemical properties of the formulations were acceptable and within the Pharmacopeial requirements. The optimized formulation with 25 mg of Crospovidone and 12 mg of Sodium Starch Glycolate exhibited disintegration time of 26 s and cumulative drug release 96.12% in 15 min. Statistical analysis revealed a significant effect for both the superdisintegrants on the tablet properties namely disintegration time and cumulative drug release and greater effect was observed for Crospovidone. Good correlation between the predicted and experimental responses were used to validate the optimization model. The study found that the optimized Topiramate fast dissolving tablets showed excellent disintegration characteristics, as well as better dissolution characteristics, and that there is a potential for improving the adherence of patients to these tablets for the treatment of epilepsy.

Keywords: Topiramate; Fast Dissolving Tablets; Direct Compression; Crospovidone; Sodium Starch Glycolate; Response Surface Methodology; 3^2 Full Factorial Design; Drug Release; Disintegration Time; Optimization.

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1.INTRODUCTION

Convenience, low cost, ease of manufacturing and easy patient acceptance are all reasons why oral drug delivery is the most desired route of drug delivery. However, swallowing difficulties are sometimes a problem with standard tablets and capsules, particularly in children, the elderly and dysphagic patients, which can lead to poor compliance and effectiveness of drug regimes. To address these shortcomings, rapid dissolving tablets (fast dissolving tablets or fast dissolving tablets) (FDTs) have become an attractive alternative oral dosage form that rapidly disintegrates in the oral cavity without the need for water. The ability of rapid disintegration is better than conventional solid dosage forms, which in turn can increase patient adherence and contribute to more rapid drug release.[1-11]

A good super disintegrant with fast water absorbing properties is essential to make the tablets swell and disintegrate effective with the help of capillary action of the super disintegrant is essential for the efficacy of FDTs. Crospovidone, croscarmellose sodium and sodium starch glycolate have been used to a great extent as tablet disintegrating agents while maintaining an adequate tablet strength. In addition, excipients are also typically employed to improve the mouthfeel, palatability and patient acceptability of dosage forms.[10,12-16]

Topiramate is a broad-spectrum antiepileptic agent that is used in the treatment of epilepsy and for the prophylaxis of migraine. The drug has a unique multimodal mechanism of action characterized by

blockade of voltage-gated sodium channels, enhancement of the GABA-mediated neurotransmission, antagonism of glutamate receptors and inhibition of carbonic anhydrase isoenzymes. While the effectivity of the conventional topiramate tablets is established for therapeutic activity, the use of these conventional tablets may be difficult on patients with swallowing difficulties, thus the need for more patient friendly topiramate formulation.[17,18]

Some reports have now been published on the successful development of fast dissolving formulations with synthetic and natural superdisintegrants that have significantly improved the disintegration time, dissolution behavior and patient compliance. Previous investigations have shown that crospovidone frequently produces faster disintegration and superior dissolution profiles than other commonly used superdisintegrants.[17-20]

Therefore, the present study aimed to formulate, characterize, and evaluate topiramate-loaded fast dissolving tablets prepared by the direct compression method. The developed formulations were investigated for pre-compression characteristics, post-compression quality attributes, *in vitro* drug release behavior, and release kinetics to identify an optimized formulation with improved pharmaceutical performance and patient acceptability.

2. MATERIALS AND METHODS

2.1 Materials

Topiramate was obtained as a gift sample from a Yarrow Chem Products Pvt. Ltd., Mumbai, India Crospovidone (CPV), sodium starch glycolate (SSG), mannitol, microcrystalline cellulose (Avicel PH 102), polyvinylpyrrolidone K30 (PVP K30), aspartame, talc, and magnesium stearate were procured from commercial sources and used as received. All chemicals and reagents used throughout the study were of analytical grade.

2.2 Formulation Method

Topiramate fast dissolving tablets were prepared by the direct compression method according to the formulation composition shown in Table 2. Accurately weighed quantities of Topiramate, crospovidone, sodium starch glycolate, mannitol, microcrystalline cellulose (Avicel PH 102), polyvinylpyrrolidone K30 (PVP K30), and aspartame were individually passed through sieve No. 60. The drug and excipients were blended geometrically to obtain a homogeneous powder mixture. Subsequently, talc and magnesium stearate were added as glidant and lubricant, respectively, and mixed for an additional 5 min to ensure uniform distribution.

The prepared powder blends were evaluated for pre-compression parameters, including angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner's ratio. The final blends were compressed into tablets using a rotary tablet compression machine to obtain tablets of uniform weight and thickness. A total of nine formulations (F1–F9) were prepared

2.3 Experimental Design

Design-Expert® software (version 13) was used for a 3^2 full factorial design in order to optimize the formulation of Topiramate fast dissolving tablets. There were two independent formulation variables each at three levels, and the experimental design was a total of nine experimental runs. Crospovidone (CPV) concentration (X_1) and Sodium Starch Glycolate (SSG) concentration (X_2) were selected as the independent variables for investigation to evaluate the effect on the performance of the developed tablets.

The concentrations of CPV and SSG were varied between 15–25 mg and 8–12 mg, respectively. These formulation variables have been evaluated for their effects on the critical quality attributes of the tablets using Response surface methodology. The measured variables (the responses) chosen were the disintegration time (Y_1) and the percentage of drug released (Y_2).

Table 1. Independent and Dependent Variables Used in DOE

Factors	Variables	Low (-1)	Medium (0)	High (+1)
X_1	Crospovidone (CPV)	15 mg	20 mg	25 mg
X_2	Sodium Starch Glycolate (SSG)	8 mg	10 mg	12 mg

Responses	Parameters
Y_1	Disintegration Time (sec)
Y_2	Percentage Drug Release (%)

Table 2. Composition of the Topiramate fast dissolving tablet formulations prepared by the direct compression method.

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Topiramate	25	25	25	25	25	25	25	25	25
Crospovidon	20	25	25	15	15	25	20	15	20
SSG	10	12	10	10	8	8	12	12	8
Mannitol	45	45	45	45	45	45	45	45	45
PVP K30	3	3	3	3	3	3	3	3	3

Aspartame	3	3	3	3	3	3	3	3	3
Talc	1	1	1	1	1	1	1	1	1
Avicel	91	84	86	96	98	88	89	94	93
Mg stearate	2	2	2	2	2	2	2	2	2
Total	200	200	200	200	200	200	200	200	200

according to the 3^2 factorial design by varying the concentrations of crospovidone and sodium starch glycolate. The prepared tablets were subsequently evaluated for physicochemical properties, disintegration characteristics, and *in vitro* drug release performance

2.4 Pre-compression Evaluation of Powder Blend

All the batches of the formulation powder blends were subjected to an evaluation of micromeritic properties before compression into tablets, to check their suitability for direct compression. Standard procedures were used to evaluate angle of repose, bulk density, tapped density, Carr's compressibility index and Hausner's ratio. All these parameters are useful in understanding the flowability, compressibility and packing characteristics of powder blends which are essential to achieve uniform die filling and tablet quality. The results achieved indicated good flow characteristics and compressibility for all formulations.[21-23]

a) Angle of repose

The flow properties of the powder blend were tested by the fixed funnel method and angle of repose was measured. A funnel was mounted at a fixed height and an accurately measured amount of powder blend was allowed to pour freely into the funnel, thus creating a conical pile of powder. The height h and radius r of powder cone were then measured and angle of repose (θ) was obtained from the following equation:[21,22]

$$\tan\theta = \frac{h}{r}$$

If the angle of repose is θ, the height of the powder cone h (cm) and the radius of the base of the cone r (cm), then the volume of the cone is proportional to the product of h and r. The angle of repose is an important indicator of powder flowability, with lower values indicating better flow characteristics.[21-23]

b) Bulk Density

Bulk density was determined by accurately weighing a quantity of the powder blend and carefully transferring it into a graduated measuring cylinder without compacting the material. The initial volume occupied by the powder blend was recorded as the bulk volume (Vb). Bulk density was calculated using the following equation:[21]

$$\rho_b = \frac{M}{V_b}$$

where, ρb is the bulk density (g/cm³), M is the mass of the powder blend (g), and Vb is the bulk volume (mL).[21-23]

c) Tapped Density

Tapped density was determined by placing a known quantity of powder blend in a graduated measuring cylinder and subjecting it to mechanical tapping until a constant volume was obtained. The final volume after tapping was recorded as the tapped volume (Vt). Tapped density was calculated using the following equation:[21,22]

$$\rho_t = \frac{M}{V_t}$$

where, ρt is the tapped density (g/cm³), M is the mass of the powder blend (g), and Vt is the tapped volume (mL).

d) Carr's Compressibility Index

Carr's compressibility index was calculated from the bulk density and tapped density values to assess the compressibility and flow characteristics of the powder blend. Lower values indicate better flow properties.

$$\text{Carr's Index (\%)} = \frac{\rho_t - \rho_b}{\rho_t} \times 100$$

where, ρt is the tapped density and ρb is the bulk density.[22]

e) Hausner's Ratio

Hausner's ratio was determined using the ratio of tapped density to bulk density and was used as an indicator of powder flowability. A Hausner's ratio below 1.25 generally indicates good flow properties.

$$\text{Hausner's Ratio} = \frac{\rho_t}{\rho_b}$$

where, ρt is the tapped density and ρb is the bulk density.[23]

2.5 Post compression Evaluation

2.5.1 Tablet Hardness and Friability

The mechanical strength of the prepared tablets was evaluated by determining hardness and friability. Tablet hardness was measured using a Monsanto/Pfizer tablet hardness tester (Cadmach, India). Six tablets were randomly selected from each formulation batch, and the crushing strength was recorded in kg/cm². The average value was calculated and reported as mean ± standard deviation (SD).[24,25]

Friability was determined using a Roche friabilator (Electrolab). Ten tablets were accurately weighed (W_1) and placed in the friabilator, which was operated at 25 rpm for 4 min (100 revolutions). The tablets were then removed, dedusted, and reweighed (W_2). The percentage friability was calculated using the following equation:[24-26]

$$\text{Friability (\%)} = \frac{W_1 - W_2}{W_1} \times 100$$

where W_1 is the initial weight of tablets and W_2 is the final weight after the friability test.

2.5.2 Weight Variation and Tablet Thickness

Weight variation was determined according to the Indian Pharmacopoeia (IP) specifications. Twenty tablets were randomly selected from each formulation batch and individually weighed using a digital analytical balance. The average tablet weight was calculated and compared with the individual tablet weights to evaluate weight uniformity.[26,27]

Tablet thickness was measured using a digital Vernier caliper. Ten tablets were randomly selected from each batch, and the thickness of each tablet was recorded in millimeters (mm). The average thickness was expressed as mean ± standard deviation (SD).[25,26]

2.5.3 Drug Content Uniformity

Content uniformity of drugs was achieved by sampling 3 tablets from each batch of formulation. The tablets were crushed and a precise quantity of 25 mg of the drug Topiramate was weighed and transfer to 100 mL volumetric flask. Phosphate buffer (pH 6.8) was added and the solution sonicated to complete the extraction of the drug. The volume was adjusted to 100 mL with the same medium and filtered thru mouslin cloth and absorbance was measured by UV–Visible spectrophotometer at the pre-determined (λmax) of Topiramate. Three tests were done for each measurement.[28-30]

2.5.4 Fourier Transform Infrared Spectroscopy (FTIR)

Fourier Transform Infra-red Spectroscopy (FTIR) was used to check the compatibility of the drugs with the excipients. The potassium bromide (KBr) pellet method was used to record the spectra of pure Topiramate and optimized formulation in the spectral range of 4000-400 cm^{-1}. The spectra obtained were examined for any significant difference in the peaks that might have arisen due to any interactions between the drug and excipients.[31,32]

2.5.5 Differential Scanning Calorimetry (DSC)

An optimized formulation was subjected to Differential Scanning Calorimetry (DSC) analysis to study the thermal behaviour of Topiramate and optimized formulation. The sample amount (2-5 mg) was burned under controlled heating rate in a nitrogen atmosphere within an appropriate temperature range in an aluminium pan. The thermograms were analyzed with the consideration of drug–excipient interactions, melting behavior and thermal stability.[31,33]

2.5.6 Powder X-Ray Diffraction (PXRD)

Powder X-ray diffraction studies were carried out to investigate the crystalline characteristics of pure Topiramate and the optimized formulation. Diffractograms were recorded over an appropriate diffraction angle range (2θ), and the characteristic diffraction peaks were compared to evaluate changes in crystallinity following formulation development.[31,34]

2.5.7 *In Vitro* Disintegration Time

The *in vitro* disintegration time of the prepared Topiramate fast dissolving tablets was determined using a digital disintegration test apparatus (Electrolab, Mumbai, India). The test was performed in 900 mL of phosphate buffer (pH 6.8) maintained at 37 ± 0.5 °C. Six tablets from each formulation batch were randomly selected, and the time required for complete disintegration was recorded. The average disintegration time was calculated and expressed as mean ± standard deviation (SD). The study was conducted according to pharmacopeial guidelines.[35,36]

2.5.8 *In Vitro* Drug Release Study

In vitro dissolution studies were performed using USP dissolution apparatus type II (paddle method). The dissolution medium consisted of 900 mL phosphate buffer (pH 6.8) maintained at 37 ± 0.5 °C and stirred at 50 rpm. Samples were withdrawn at predetermined time intervals, filtered, and analyzed spectrophotometrically at the λ_{max} of Topiramate. The cumulative percentage drug release was calculated and plotted as a function of time.[35,36,37]

3. RESULTS AND DISCUSSION

3.1 Optimization Using 3^2 Full Factorial Design

A 3^2 full factorial design was employed to investigate the influence of Crospovidone (X_1) and Sodium Starch Glycolate (X_2) on the disintegration time (Y_1) and percentage drug release (Y_2) of Topiramate fast dissolving tablets. The experimental design facilitated systematic evaluation of the individual and combined effects of the selected formulation variables on the critical quality attributes of the tablets.

3.1.1 Effect of Formulation Variables on Disintegration Time

Table 3. ANOVA for Quadratic Model for Disintegration time

Source	Sum of Squares	dfs	Mean Square	F-value	p-value	
Model	736.67	2	368.33	70.53	< 0.0001	significant
A-CPV	640.67	1	640.67	122.68	< 0.0001	
B-SSG	96.00	1	96.00	18.38	0.0052	
Residual	31.33	6	5.22			
Cor Total	768.00	8				

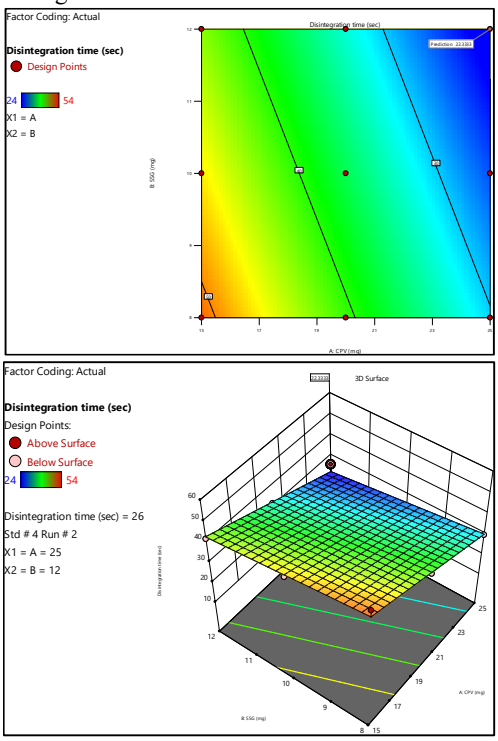
The statistical analysis results are presented in (Table 3) The linear model for disintegration time

was significant ($p < 0.05$), with both Crospovidone (CPV) and Sodium Starch Glycolate (SSG) significantly influencing disintegration time, while CPV showed a greater effect. The model demonstrated good predictive capability with R^2 = 0.9592, Adjusted R^2 = 0.9456, and Predicted R^2 = 0.8816. Furthermore, the Adequate Precision value of 21.7275 and the coefficient of variation (CV = 6.23%) confirmed the robustness, precision, and reliability of the developed model

The relationship between the independent variables and disintegration time was described by the following polynomial equation:

$Y_1 = 36.67 - 10.33A - 4.00B$

where Y_1 represents disintegration time, A represents the concentration of Crospovidone, and B represents the concentration of Sodium Starch Glycolate. The negative coefficients of both variables indicate that increasing the concentration of CPV and SSG resulted in a reduction in disintegration time, thereby promoting rapid tablet disintegration.



(A)

(B)

Figure 1. (A) 2D contour plot and (B) 3D response surface plot showing the effect of Crospovidone concentration (X_1) and Sodium Starch Glycolate concentration (X_2) on Disintegration Time (Y_1) of Topiramate Fast Dissolving Tablets.

The effect of Crospovidone (CPV), and Sodium Starch Glycolate (SSG) on disintegration time was shown in the 2D contour plot and 3D response surface plot (Fig.1). An increase in concentrations of both super disintegrants resulted in a marked reduction in disintegration time, CPV showing a greater effect than SSG. As the disintegration time was lowest for higher concentration of both the super disintegrants, which showed an effectiveness to promote rapid disintegration of the tablet by wicking and swelling action.

3.1.2 Effect of Formulation Variables on Percentage Drug Release

Table 4. ANOVA for Quadratic Model for % Drug Release

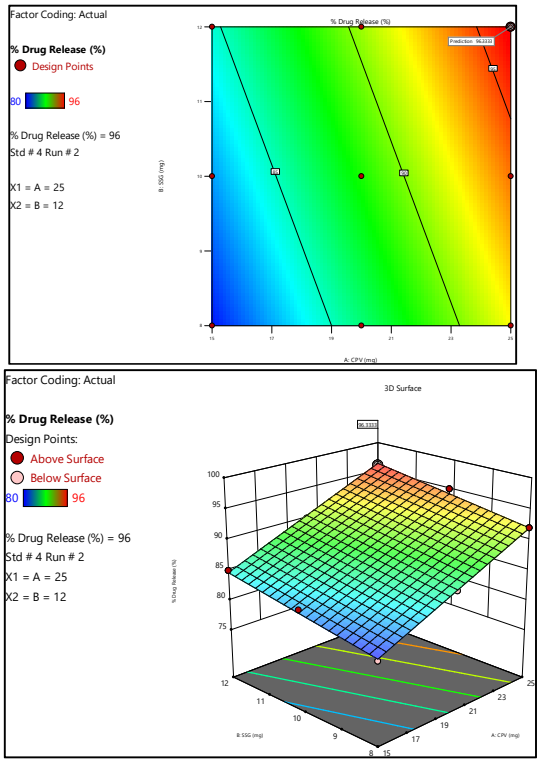
Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	232.33	2	116.17	418.20	< 0.0001	significant
A-CPV	204.17	1	204.17	735.00	< 0.0001	
B-SSG	28.17	1	28.17	101.40	< 0.0001	
Residual	1.67	6	0.2778			
Cor Total	234.00	8				

The linear model for percentage of drug released turned out to be significant ($p<0.05$) and both the Crospovidone (CPV) and Sodium Starch Glycolate (SSG) have significant effect on the drug release, with more effect of CPV. The model had a good predictive capability with R^2 = 0.9929, adjusted R^2 = 0.9905 and predicted R^2 = 0.9848. Besides, value of Adequate Precision (52.5814) and low value of coefficient of variation (CV = 0.5967%) made the developed model robust, precise and reliable.

The following polynomial equation was used to describe the relationship between the independent variables and percentage drug released:

$Y_2 = 88.33 + 5.83A + 2.17B$

Y_2 is the percentage drug released, A is the concentration of Crospovidone and B is the concentration of Sodium Starch Glycolate. Both the values of the coefficient(s) were positive indicating that the drug release increased with the increase in the concentration of CPV and SSG. This had the highest coefficient of CPV, suggesting that it had a greater effect on drug release than had SSG.



(A) (B)

Figure 2: (A) 2D contour plot and (B) 3D response surface plot showing the effect of Crospovidone concentration (X_1) and Sodium Starch Glycolate concentration (X_2) on % Drug Release (Y_2) of Topiramate Fast Dissolving Tablets.

The 2D contour and 3D response surface plots (Fig.2) showed the effect of Crospovidone (CPV) and Sodium Starch Glycolate (SSG) on the percentage drug released. As for the drug release, it increased with the increase of both concentration of superdisintegrants, CPV exhibited a higher effect compared to SSG. The concentration of both superdisintegrants is higher, the more drug released from the tablets, which indicates the effectiveness of both superdisintegrants in improving the drug release from the tablets.

3.1.3 Optimization of Formulation

Numerical optimization was performed using Design-Expert® software to minimize disintegration time and maximize drug release. The overlay plot (Fig.3) identified the optimum design space, predicting an optimized formulation containing 25 mg Crospovidone and 12 mg Sodium Starch Glycolate, with a disintegration time of 22.33 s, drug release of 96.33%, and a desirability value of 1.000, confirming the suitability of the optimized formulation

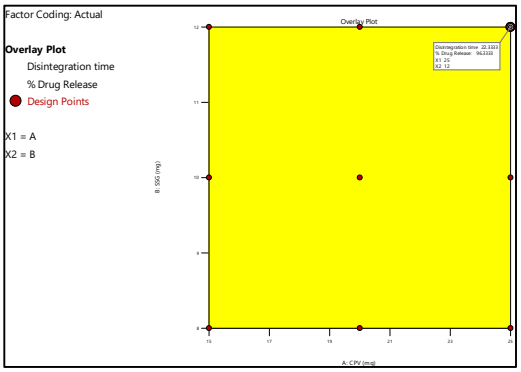


Figure 3: Overlay Plot Showing the Optimized Region for Topiramate Fast Dissolving Tablets Based on Disintegration Time (Y_1) and Percentage Drug Release (Y_2).

3.1.4 Validation of Optimized Formulation

The optimized Topiramate fast dissolving tablet formulation was prepared and evaluated to validate the predictive capability of the developed factorial design model. The predicted disintegration time and percentage drug release were 22.33 s and 96.33%, respectively, whereas the experimentally observed values were 26 s and 96%, respectively.

Table 5. Comparison of Predicted and Experimental Responses of Optimized Formulation

Response	Predicted Value	Experimental Value
Disintegration Time (s)	22.33	26
Drug Release (%)	96.33	96

The close agreement between the predicted and experimental values demonstrated the reliability and robustness of the developed model. The low prediction error confirmed the suitability of the optimization approach, indicating that the selected formulation variables successfully achieved the desired performance characteristics of the optimized formulation.

3.2 Pre-compression Evaluation of Powder Blend

The micromeritic properties of the powder blends were evaluated prior to compression, and the results are presented in (Table 6) The angle of repose values ranged from 23.8 ± 0.1° to 28.0 ± 0.2°, indicating excellent to good flow characteristics of the powder blends. Bulk density and tapped density values were found in the ranges of 0.40 ± 0.02–0.46 ± 0.01 g/cm³ and 0.49 ± 0.02–0.51 ± 0.01 g/cm³, respectively.

Table 6. Micromeritic Properties of Powder Blends (F1–F9)

Batch Code	Angle of repose (Degr	Bulk Density	Tapped Density	Compressibility Index	Hausner,s Ratio

	ees)				
F1	25.3 ± 0.2	0.43 ± 0.01	0.50 ± 0.01	14.00 ± 0.10	1.16 ± 0.01
F2	28.0 ± 0.2	0.40 ± 0.02	0.49 ± 0.02	18.36 ± 0.20	1.22 ± 0.02
F3	26.8 ± 0.2	0.41 ± 0.02	0.49 ± 0.02	16.32 ± 0.20	1.19 ± 0.02
F4	24.1 ± 0.1	0.45 ± 0.01	0.51 ± 0.01	11.76 ± 0.10	1.13 ± 0.01
F5	23.8 ± 0.1	0.46 ± 0.01	0.51 ± 0.01	9.80 ± 0.10	1.10 ± 0.01
F6	27.2 ± 0.2	0.41 ± 0.01	0.49 ± 0.01	16.32 ± 0.10	1.19 ± 0.01
F7	26.2 ± 0.2	0.42 ± 0.01	0.50 ± 0.02	16.00 ± 0.20	1.19 ± 0.02
F8	24.8 ± 0.1	0.44 ± 0.01	0.50 ± 0.01	12.00 ± 0.10	1.13 ± 0.01
F9	24.5 ± 0.1	0.44 ± 0.01	0.50 ± 0.01	12.00 ± 0.10	1.13 ± 0.01

The compressibility index of the powder blends varied between 9.80 ± 0.10% to 18.36 ± 0.20% and Hausner's ratio was between 1.10 ± 0.01 and 1.22 ± 0.02, which were good. The results indicated that all the micromeritic parameters used were within acceptable limits and thus the powder blends are suitable for direct compression tablet formulation of Topiramate fast dissolving tablets.

3.3 Post-compression Evaluation of Fast Dissolving Tablets

All the formulations were tested for different post compression parameters as shown in (Table 7) and uniformity of die filling was checked during compression, which was within the limits of Pharmacopoeia. All the batches were found to be uniform with respect to thickness of the Tablets, which means uniformity in size of Tablets.

Table 7. Post-compression Evaluation of Topiramate Fast Dissolving Tablets (F1–F9)

Batch Codes	Hardness (kg/cm2)	Thickness (mm)	Friability (%)	DT (sec)	% Drug Release	Wt. Variation
F1	3.7 ± 0.1	3.28 ± 0.03	0.55 ± 0.02	36 ± 1	88 ± 0.5	198 ± 2
F2	3.2 ± 0.1	3.25 ± 0.04	0.74 ± 0.03	26 ± 1	96 ± 0.5	200 ± 2
F3	3.4 ± 0.1	3.26 ± 0.02	0.66 ± 0.03	24 ± 1	95 ± 0.5	198± 2
F4	3.8 ± 0.1	3.30 ± 0.03	0.46 ± 0.02	46 ± 1	83 ± 0.5	202 ± 2
F5	3.9 ± 0.1	3.31 ± 0.04	0.42 ± 0.02	54 ± 1	80 ± 0.4	203 ± 2
F6	3.3 ± 0.2	3.25 ± 0.05	0.69 ± 0.02	30 ± 1	92 ± 0.4	198 ± 2
F7	3.6 ± 0.1	3.27 ± 0.02	0.58 ± 0.02	32 ± 1	90 ± 0.5	197 ± 2
F8	3.6 ± 0.1	3.29 ± 0.03	0.54 ± 0.02	42 ± 1	85 ± 0.5	199 ± 2
F9	3.7 ± 0.2	3.28 ± 0.04	0.56 ± 0.03	40 ± 1	86 ± 0.4	201 ± 2

The hardness of the tablets was adequate for handling and transportation and allowed for the desired mechanical strength. All the formulations have friability values of less than 1% which showed acceptable resistance to abrasion and mechanical stress. The drug content analysis revealed that the drug in the tablet matrix was distributed uniformly and all the formulations met the acceptable content uniformity limit stipulated by the Pharmacopoeia.

Overall, the post-compression evaluation confirmed that all formulations possessed satisfactory physical characteristics and were suitable for further evaluation of fast dissolving tablet performance.

3.4 Drug–Excipient Compatibility Studies

3.4.1 Fourier-Transform Infrared spectroscopy (FTIR) Analysis

The FTIR spectrum of pure Topiramate API is presented in (Fig.4A) Characteristic absorption peaks were observed at 3375.67 cm^{-1} (O–H stretching), 2997.00 and 2937.55 cm^{-1} (C–H stretching), 1253.34 cm^{-1} (C–O–C stretching), and 1168.89 cm^{-1} (S=O stretching). These characteristic peaks confirmed the presence of the functional groups of Topiramate. The observed spectrum was consistent with the reported FTIR profile of Topiramate, confirming the identity and purity of the drug.

The FTIR spectrum of the optimized Topiramate fast dissolving tablet formulation is presented in (Fig.4B) The spectrum showed characteristic peaks at 3374.65 cm^{-1} (O–H stretching), 2928.69 cm^{-1} (C–H stretching), 1248.76 cm^{-1} (C–O–C stretching), and 1120.08 cm^{-1} (S=O stretching). These characteristic peaks were retained without any significant shift or disappearance, indicating the absence of chemical interaction between Topiramate and the selected excipients. Thus, the

FTIR study confirmed the compatibility of Topiramate with all formulation excipients, demonstrating their suitability for the development of fast dissolving tablets

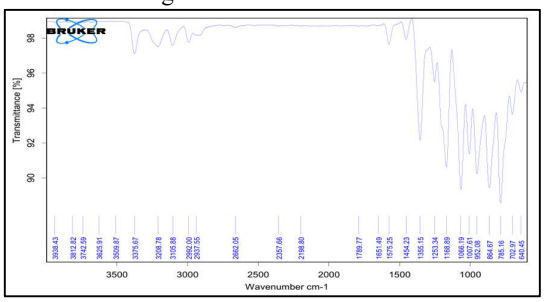


Figure 4A. FTIR spectrum of the optimized Topiramate (API)

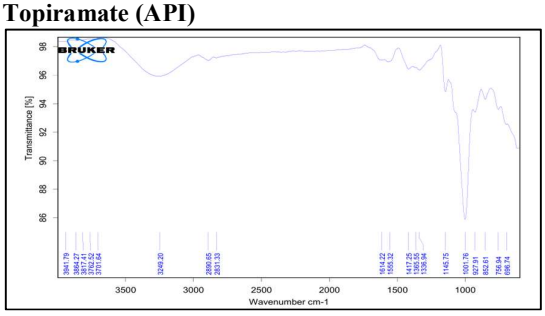


Figure 4B. FTIR spectrum of Topiramate fast dissolving tablet.

3.4.2 Differential Scanning Calorimetry (DSC) Analysis

The DSC thermograms of pure Topiramate API and the optimized formulation are presented in (Fig. 5A) and (Fig. 5B) respectively. Both thermograms exhibited a characteristic endothermic peak at 126.34°C with no significant shift in the optimized formulation. This confirmed the thermal stability of Topiramate and the absence of significant drug–excipient interactions, indicating good compatibility of the selected excipients

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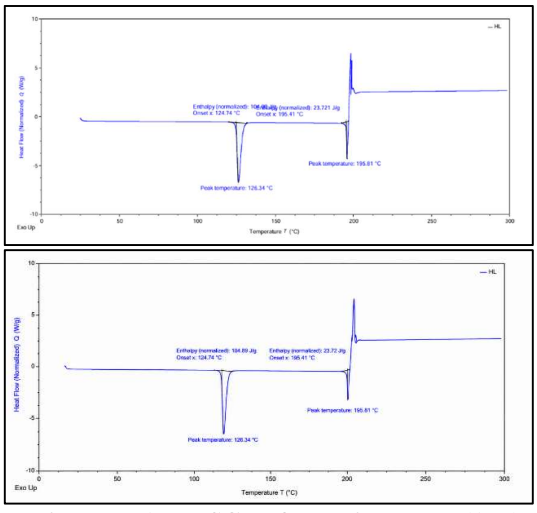


Figure 5A. DSC of Topiramate (API)
Figure 5B. DSC of Topiramate Tablet

3.4.3 X-Ray Diffraction (XRD) Analysis

The XRD pattern of pure Topiramate (Fig 6A.) exhibited sharp and intense diffraction peaks, confirming its crystalline nature. The diffractogram of the optimized formulation (Fig 6B.) also showed characteristic diffraction peaks of Topiramate, indicating retention of crystallinity after formulation development. The absence of significant changes in peak positions confirmed the physical stability and compatibility of the drug within the tablet matrix.

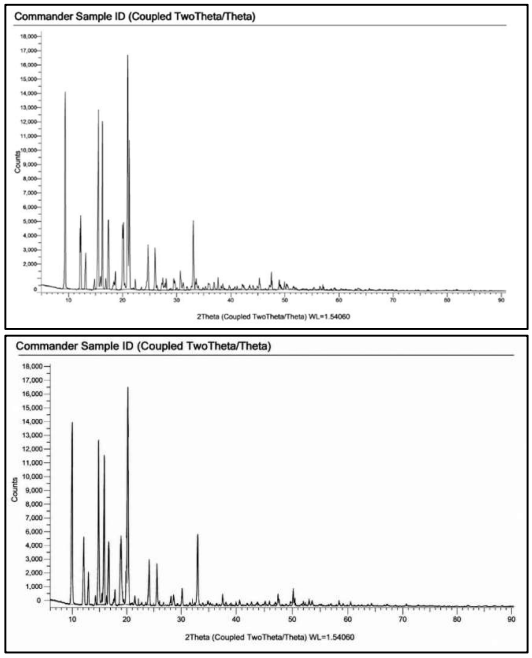


Figure 6A. XRD of Topiramate Drug
Figure 6B. XRD of Topiramate Tablet

3.5. *In Vitro* Drug Release Study

The in vitro drug release profiles of the prepared Topiramate fast dissolving tablets are presented in (Fig.7) All formulations exhibited a progressive increase in drug release with increasing dissolution time. The percentage cumulative drug release after 15 min ranged from 80.12% to 96.12%. Among all formulations, F2 showed the highest drug release (96.12%), followed by F3 and F6 (92.04% each), whereas F5 exhibited the lowest drug release (80.12%).

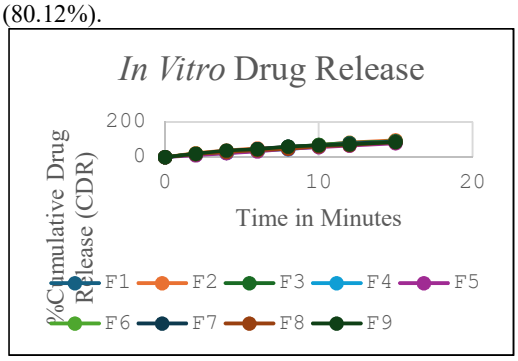


Figure 7. *In Vitro* Cumulative Drug Release Profile of Topiramate Fast Dissolving Tablets (F1–F9)

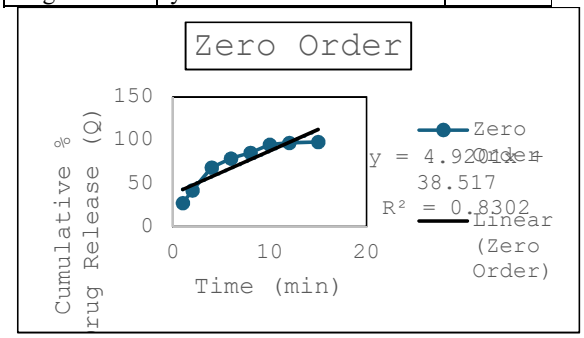
The better drug release from the optimized concentrations of Crospovidone and Sodium Starch Glycolate formulation might be due to the high tablet disintegrating rate and large surface area for dissolution in water. Incorporation of these super disintegrants greatly enhanced the dissolution characteristics of Topiramate and accelerated the drug release. Overall, F2 demonstrated superior dissolution performance and was identified as the optimized formulation based on its drug release behavior.

3.6 Drug Release Kinetic Studies

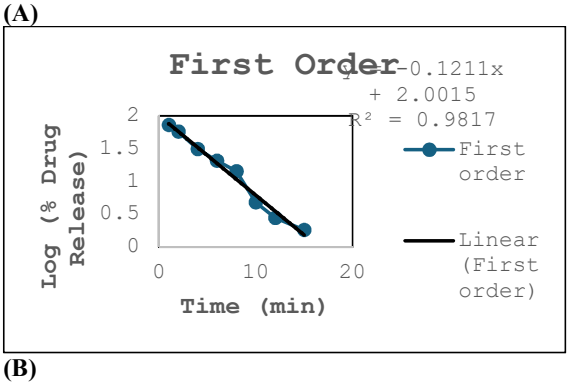
The *in vitro* drug release data of the optimized Topiramate loaded fast dissolving tablet formulation (F2) were analyzed using Zero-order, First-order, and Higuchi kinetic models. The First-order model showed the highest correlation coefficient (R^2 = 0.9817), indicating concentration-dependent drug release, while the Higuchi model (R^2 = 0.9749) suggested diffusion-mediated release. Overall, the optimized formulation predominantly followed First-order release kinetics.

Table 8. Drug release kinetic parameters of optimized formulation (F2)

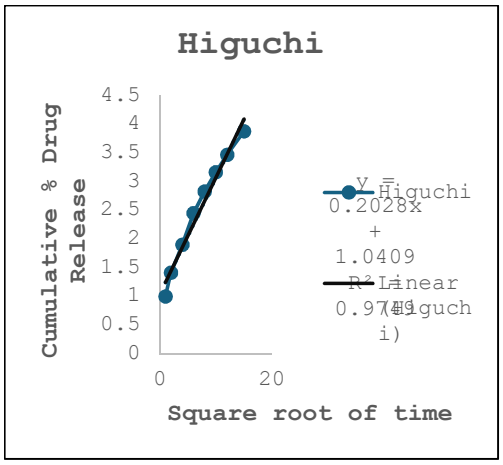
Model	Equation	R^2
Zero-order	y = 4.9201x + 38.517	0.8302
First-order	y = -0.1211x + 2.0015	0.9817
Higuchi	y = 0.2028x + 1.0409	0.9749



(A)



(B)



(C)

Figure 8. Drug release kinetic models of the optimized formulation (F2): (A) Zero-order, (B) First-order, and (C) Higuchi plots.

The optimized formulation (F2) was evaluated using zero-order, first-order, and Higuchi kinetic models. Among the investigated models, the first-order plot showed the highest correlation coefficient (R^2 = 0.9817), indicating concentration-dependent drug release, while the Higuchi model (R^2 = 0.9749) suggested diffusion-mediated release. The zero-order model showed comparatively lower linearity (R^2 = 0.8302).

4. CONCLUSION

Topiramate fast dissolving tablets were successfully formulated and optimized by direct compression using Crospovidone and Sodium Starch Glycolate as superdisintegrants. FTIR, DSC, and XRD studies confirmed the compatibility of Topiramate with the selected excipients, while all formulations exhibited satisfactory pre-compression and post-compression characteristics. The selected superdisintegrants showed their performance in improving tablet performance with their developed tablets, which exhibited good disintegration and drug release.

The optimisation using 3^2 full factorial design showed that both Crospovidone and Sodium Starch Glycolate were significant factors affecting the disintegration time and drug release. Crospovidone and Sodium Starch Glycolate formulations showed disintegration times of 26 s and cumulative release of 96.12% in 15 min, respectively, which showed the optimized formulations. The model was validated using the good agreement between the response predicted and the experimental response. The optimized formulation has desirable characteristics of rapid dissolving tablets and may be used as an oral dosage form to improve patient compliance in the treatment of epilepsy.

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