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Research Article

Formulation and *Invitro* Evaluation of Sustained Release Tablets of Pregabalin

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ABSTRACT

The main aim of proposed work was to develop Pregabalin sustained release matrix tablets. Sustained release formulation is the drug delivery system that is designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of single dose. The sustained release tablets were prepared by direct compression method using HydroxyPropylMethylCellulose (HPMC K4M, K15M), Dicalcium phosphate, Metalose (60SH-50). Tablets blends were evaluated for loose bulk density, tapped bulk density, compressibility index and angle of repose, shows satisfactory results. The compressed tablets were then evaluated for various physical tests like diameter, thickness, uniformity of weight, hardness, friability, and drug content. The results of all these tests were found to be satisfactory. The *Invitro* dissolution studies was carried out in 0.1N HCl (pH 1.2) for first 2 hours and remaining 10 hours was carried out in Phosphate buffer (pH 6.8) by using paddle method as dissolution medium. F1 to F12 formulations were prepared by using direct compression method. Among all the formulations, F12 formulation was comparatively releases 100% drug over 12hrs. F12 performed similar to the Marketed product therapeutically. Kinetic models were applied to the Optimized formulation and observed that formulation (F12) followed First order kinetic model and it was complied with (reference sample). The best linearity was found in Korsmeyer-Peppas model (where n=0.583 is release exponent) indicating non-Fickian mechanism of drug release. FTIR compatibility studies reveal no incompatibility in the formulations.

Keywords: HPMC K4M, HPMC K15M, Di calcium phosphate, Metalose 60SH-50, Mg. stearate.

INTRODUCTION

Sustained release dosage forms: Are designed to release their medication at a predetermined rate, duration and location to achieve and maintain optimum therapeutic blood levels. **Eg:** prolonged-release, controlled-release, controlled-delivery, slow-release and sustained-release.

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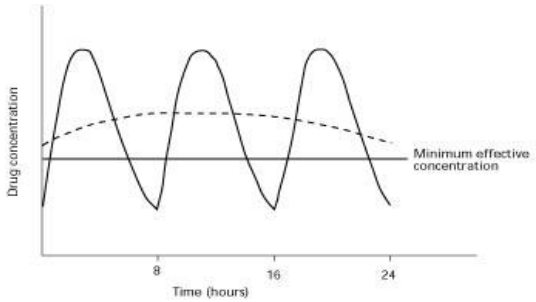

Fig 1: Theoretical drug concentration profile following multiple dosing of a drug as an immediate-release form every 8 hours (–) and as an sustained-release form once every 24(--) hours.

Advantages: sustained blood levels, attenuation of adverse effects, Improved patient compliance.

Sustained blood levels

The size and frequency of dosing is determined by the pharmacodynamic and pharmacokinetic properties of the drug. The slower the rate of absorption, the less the blood concentrations fluctuate within a dosing interval. This enables higher doses to be given less frequently. For drugs with relatively short half-lives, the use of sustained-release products may maintain therapeutic concentrations over prolonged periods.

Attenuation of adverse effects

With conventional dosage forms, high peak blood concentrations may be reached soon after administration with possible adverse effects related to the transiently high concentration.

Improved patient compliance

Drugs with short half-lives often need to be given at frequent intervals to maintain blood concentrations within the therapeutic range. There is an inverse correlation between the frequency of dosing and patient compliance. A reduction in the number of daily doses offered by sustained-release products has the potential to improve compliance. However, this advantage probably only occurs when conventional formulations need to be given 3 or more times a day.

Design of sustained release products:

Principle behind SR drug release:

Dissolution and diffusion-controlled systems have classically been of primary importance in oral delivery of medication because of their relative ease of production and cost compared with other methods of sustained or controlled delivery [4]. Most of these systems are solids, although a few liquids and suspension have been recently introduced. The classifications of such systems are as follows:

1.Dissolution-controlled release system,
2.Osmotic pump system,
3.Erosion controlled release systems.

Dissolution controlled release systems:

In dissolution controlled sustained release systems the rate of dissolution of drug or other Ingredients in the intestinal juice are the release controlling process. Reduced drug solubility can be accomplished by preparing poorly soluble salts or derivatives of the drug. An alternative means to achieve sustained release based on dissolution is to incorporate the drug in a slowly dissolving carrier. Dissolution controlled sustained release systems can also be obtained by covering drug particles with a slowly dissolving coating.

Diffusion Controlled Release:

Diffusion-controlled release system involves two types they are 1. Réservoir devices and 2. Matrix devices.

Osmotic pump system:

The rate of drug release in these products is determined by the constant inflow of water across semipermeable membrane into a reservoir, which contains an osmotic agent. The drug is either mixed with the agent or is located in a reservoir. The dosage form contains a small hole from which dissolved drug is pumped at a rate determined by the rate of entrance of water due to osmotic pressure. The advantage of this type of product is that the constant release is unaltered by the environment of the gastrointestinal tract. The rate of release can modified by altering the osmotic agent and the size of the hole.

MATERIALS AND METHODS

Pregabalin was obtained as gift sample from Spectrum Labs Hyderabad. Di Calcium Phosphate, Metalose 60SH50, HPMC K4M, HPMC K15M, Aerosil, Magnesium Stearate was procured from Spectrum Labs Hyderabad.

FORMULATION DEVELOPMENT:

Composition of Pregabalin drug formulations done by direct compression method.

Table 1: Composition of Pregabalin formulations (F1-F12)

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Pregabalin	50	50	50	50	50	50	50	50	50	50	50	50
DCP	88	82	77	72	88	82	77	72	88	82	77	72
HPMC K4M	10	15	20	25	_	_	_	_	_	_	_	_
HPMC K15M	_	_	_	_	10	15	20	25	_	_	_	_
Metalose 60SH-50	_	_	_	_	_	_	_	_	10	15	20	25
Aerosil	1	1	1	1	1	1	1	1	1	1	1	1
Mag.stearate	2	2	2	2	2	2	2	2	2	2	2	2
Total(mg)	150	150	150	150	150	150	150	150	150	150	150	150

Pre-Compression Parameters:

1.Organoleptic evaluation:

The color, odor and taste of the drug were evaluated and tabulated using descriptive terminology.

2.Particle size distribution:

10.35 grams of sample was taken and added to an assembly consisting sieve numbers # 30, 40, 60, 80,100,120 base plates. Then assembly was closed and kept on sieve shaker and started analysis. Weights retained were checked for every 5 min and process was continued until variation in weights retained was not more than 5% or 0.1 gram. 20 min was set as end point based on the observation.

3. Bulk density:

Bulk density is very important in the size of containers needed for handling, shipping and storage of raw material and blend. It is also important in size blending equipment

$$\text{Bulk density} = \frac{\text{weight of blend}}{\text{Bulk volume of blend}}$$

4. Tapped density:

It is the ratio of total mass of the blend to the tapped volume of blend.

$$\text{Tapped density} = \frac{\text{weight of blend}}{\text{Tapped volume of blend}}$$

Determination of Bulk & Tap Density: An accurately weighed quantity of the blend (W), was carefully poured into the graduated cylinder and the volume (V_o) was measured. Then the graduated cylinder was closed with lid and set into the density determination apparatus. The density apparatus was set for 500 taps and after that, the volume (V_f) was measured and continued operation till the two consecutive readings were equal.

The bulk density, and tapped density were calculated using the following Formulas:

Bulk density $= W / V_o$

Tapped density $= W / V_f$

Where,

W = weight of the powder, $\mathbf{V_o}$ = bulk volume, $\mathbf{V_f}$ = tapped volume

5. Compressibility Index:

Carr's Index is measured using the values of bulk density and tapped density. The following equation is used to find the Carr's index.

$$\text{Compressibility Index} = \frac{\text{(Tapped Density-Bulk Density)}}{\text{Tapped Density}} \times 100$$

6. Hausner's Ratio:

It indicates the flow properties of the blend. And it is the ratio of Tapped density to the Bulk density of the powder or granules.

Hausner's Ratio = Tapped density/Bulk density

7.Angle of Repose:

Angle of repose was measured by passing Drug through a funnel on graph paper until the pile touches the tip of the funnel. The funnel was kept at a fixed height of 2cm, from the horizontal surface to the tip of funnel. The radius 'r' of the cone base formed was determined. The angle of repose (θ) was calculated as follows:

$$\theta = \tan^{-1}(h/r)$$

Where h = height of heap the pile, r = radius of base of the pile, and θ = angle of repose.

SELECTION OF FORMULATION METHOD:

Sustained release tablets of Pregabalin were formulated by using Direct compression method.

DIRECT COMPRESSION:

In this process the tablets are compressed directly from powder blends of active ingredient and suitable excipients, which will flow uniformly in to the die cavity and forms a firm compact.

Brief manufacturing procedure for the preparation of tablets:

Step 1- Weighed all the ingredients separately.

Step 2- The Pregabalin and the other excipients were passed through 40# sieve together and blended for 10 minutes.

Step 3- The magnesium stearate was passed through 60# sieve and added to the blend of step2 and blended for 5 minutes.

Step 4- Compressed the blend of step 3 in to tablets by using 8.5mm, round punches.

Post Compression Parameters:

1. Physical appearance:

The surface of the formulated tablets was evaluated to ensure that there was no capping, lamination, sticking or other defects during compression.

2. Uniformity of weight (Weight variation test):

This is an important In-process quality control test to be checked frequently (every half an hour). Corrections were made during the compression of tablets. Any variation in the weight of tablet (for any reason) leads to either under medication or overdose. So, every tablet in each batch should have a uniform weight. 20 tablets were weighed individually. Average weight was calculated from the total weight of all tablets. The individual weights were compared with the average weight.

Table 2: Acceptance criteria for tablet weight variation (I.P Limits)

Average weight of tablet(mg)	Maximum % difference allowed
130 or Less than	± 10
130-324	± 7.5
More than 324	± 5

Twenty tablets were taken randomly and weighed accurately. The average weight is calculated by

$$\text{Average weight} = \frac{\text{weight of 20 tablets}}{20}$$

3. Hardness:

Hardness (diametric crushing strength) is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength. The hardness of tablet of each formulation was checked by using Dr.Schleuniger Hardness tester in terms of Kilo ponds (KP).

4. Thickness:

Thickness was measured using Vernier caliper. It was determined by checking ten tablets from each formulation.

5. Friability:

Friability is the loss of weight of tablet in the container/package, due to removal of fine particles from the surface. This In-process quality control test is performed to ensure the ability of tablets to withstand the shocks during processing, handling, transportation, and shipment. Roche friabilator was used to measure the friability of the tablets. It was rotated at a rate of 25 rpm.

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

Where, W_1= weight of tablets before test

W_2 = weight of tablets after test

6. Dissolution studies:

Dissolution Parameters: The *Invitro* drug release studies for the prepared formulation were conducted for a period of 12 hrs using an Electro lab model dissolution tester USP Type-2 apparatus (rotating paddle) set at 100 rpm and a temperature of 37± 0.5°C. Formulation was placed in the 900ml of 0.1N HCl (pH 1.2) for first 2 hours, remaining 10 hours in Phosphate buffer (pH 6.8) of the medium. At specified intervals 10ml samples were withdrawn from each of dissolution medium and replaced with fresh respective medium which is maintained at 37± 0.5°C to keep the volume constant. The absorbance of the sample solution was analyzed at 210 nm for the presence of drug, using a UV-visible spectrophotometer.

KINETIC STUDIES:

In this study, data from *Invitro* release were fitted to different equations and kinetic models to explain the release kinetics of Pregabalin sustained release matrix tablets. The kinetic models used were Zero order equation, First order, Higuchi release and Korsmeyer-Peppas models. were applied to interpret the release rate of the drug from matrix systems for the optimized formulation. The best fit with higher correlation (r2) was calculated.

Zero-Order model: The equation represents

$$Qt = Q0 + K0t$$

Where Qt is the amount of drug dissolved in time t, Q0 is the initial amount of drug in the solution (most times, Q0 = 0) and K0 is the zero-order release constant. To study the release kinetics, data obtained from *Invitro* drug release studies were plotted as cumulative amount of drug released versus time.

First -Order model: The equation represents

$$\text{Log } C = \text{Log } Co - kt/2.303$$

Where C is the amount of drug dissolved at time t, Co is the amount of drug dissolved at t=0 and k is the first order rate constant. A graph of log cumulative of % drug remaining vs time yields a straight line.

Higuchi model: The first example of a mathematical model aimed to describe drug release from a system was proposed by Higuchi in 1961. This model is based on the hypothesis that: - initial drug concentration is much higher than drug solubility; swelling and dissolution are negligible; Perfect sink conditions are always attained in the release environment.

The equation expressed by

$$Q = KH - t1/2$$

Where, KH is the Higuchi dissolution constant. The data obtained were plotted as cumulative % drug release versus square root of time.

Korsmeyer-Peppas model: Korsmeyer *et al*. (1983) derived a simple relationship which describe d drug release from a polymeric system equation. To find out the mechanism of drug release, first 60% drug release data were fitted in Korsmeyer-Peppas model equation,

$$Mt / M\infty = Ktn$$

where Mt / M∞ is a fraction of drug released at time t, k is the release rate constant and 'n' is the release exponent. The 'n' value is used to characterize different release mechanism of drug as described in the following table.

Table 3: Drug transport mechanisms suggested based on 'n' value.

S. No	Release exponent	Drug transport mechanism	Rate as a function of time
1	0.5	Fickian diffusion	$t^{-0.5}$
2	0.45 < n = 0.89	Non -Fickian transport	t^{n-1}
3	0.89	Case II transport	Zero order release
4	Higher than 0.89	Super case II transport	t^{n-1}

To find out the exponent of *n* the portion of the release curve, where Mt / M∞ < 0.6 should only be used. To study the release kinetics, data obtained from *Invitro* drug release studies were plotted as log cumulative percentage drug release *versus* log time.

Comparison of dissolution profiles:

The similarity factor (f2) was employed to evaluate the release profiles of various formulations compared with the ideal release profile.

$$f_2 = 50 \log \left\{ \left[1 + \left(\frac{1}{n} \right) \sum_{t=1}^{n} (R_t - T_t)^2 \right]^{-0.5} X\, 100 \right\}$$

Where 'n' is the number of dissolution time points, R and T are references and test dissolution values at time t. The similarity factor (f2) is a logarithmic transformation of the sum-squared error of differences between the experimental drug release Tt and the ideal drug release Rt for over all time points 'n'.

The similarity factor fit the result between 0 and 100. It is approached 0 as the dissimilarity of the test and the reference profile increased, whereas, it attained 100 when the test and the reference profile was identical.

FT-IR SPECTROSCOPY STUDY:

In this study FT-IR data of drug and excipient was compared with standard spectrum of pure Pregabalin drug. The characteristics peak associated with specific functional groups and bonds of the molecule and their presence/ absence in the polymer carrier formulation noted. The IR spectra showed that there is no significant evidence for interaction between the drug and the excipients (HPMC K4M, HPMC K15M, Di calcium phosphate, Aerosil, Metalose 60SH-50, Mg. stearate).

RESULTS AND DISCUSSION

1. Formulation Development:

The formulation of tablets were prepared as discussed in the Materials and Methods and results are noted in (Table 1).

2. Pre-Compression Parameters:

i. Organoleptic properties of drug:

The Organoleptic properties of drug was observed and tabulated in (Table 4).

Table 4: Organoleptic properties

S. No	Properties	Observation
1	Description	Crystalline powder
2	Color	White to light yellow
3	Taste	Characteristic

iii. Particle size distribution of drug:

Particle size distribution study was found around 99.8% were below 250 microns and recorded in (Table 5).

Table 5: Particle Size Distribution

Sieve Mesh Number	Sieve Size Opening (µm)	Mass of Sample Retained	Percentage of Sample Retained	Cumulative Percentage of Sample (%)
30	841	0.08	0.77	0.8
40	425	0.06	0.57	1.4
60	250	0.05	0.48	1.9
80	180	0.41	3.96	5.9
100	150	1.55	14.97	20.9
120	130	2.62	25.31	46.2
Pan	-	5.55	53.62	99.8

ii. Flow properties of drug:

The flow properties of drug observations recorded in the Table 6. It was found that Carr's index and Hausner's ratio have Fair Flow properties. Angle of repose have Excellent flow properties.

Table 6: Flow properties

Test	Result
Bulk density	0.33
Tapped density	0.42
Carr's index	20.09
Hausner's ratio	1.15
Angle of repose (θ)	20

iv. Characterization of Blend:

The powder blend were evaluated for different formulations as discussed in the procedure of pre-compression parameters under Materials and Methods. The results are mentioned in (Table 7).

Table 7: Characterization of Blend

Formulation Code	Derived properties		Flow properties		
	BD (mean±SD)	TD (mean±SD)	Angle of repose (mean±SD)	Carr's index (mean±SD)	Hausner's ratio (mean±SD)
F1	0.436±0.01	0.492±0.015	26.48±0.30	11.47±1.97	1.128±0.02
F2	0.449±0.015	0.505±0.02	27.24±0.39	11.21±1.96	1.129±0.03
F3	0.491±0.015	0.58±0.01	24.98±0.68	11.88±3.97	1.137±0.05
F4	0.478±0.015	0.527±0.015	23.23±0.96	9.46±1.81	1.108±0.02
F5	0.432±0.02	0.499±0.03	25.97±0.73	12.68±2.25	1.148±0.03
F6	0.44±0.01	0.467±0.006	24.27±0.36	9.34±3.16	1.105±0.04
F7	0.451±0.025	0.538±0.025	28.23±0.29	15.53±1.19	1.186±0.02
F8	0.43±0.01	0.53±0.017	23.89±0.40	11.67±3.61	1.128±0.05
F9	0.42±0.01	0.459±0.025	25.19±0.34	10.86±2.84	1.115±0.04
F10	0.444±0.015	0.518±0.032	26.76±0.63	14.22±1.11	1.167±0.01
F11	0.408±0.02	0.49±0.01	23.95±0.46	13.49±2.48	1.158±0.03
F12	0.415±0.02	0.475±0.015	28.23±0.27	14.21±3.22	1.152±0.02

Inference: The angle of repose for various formulations was 28.24, indicating that the material had acceptable flow characteristics. Bulk density ranged from 0.408 g/cm3 to 0.492 g/cm3. The tapped density ranged from 0.465 g/cm3 to 0.6 g/cm3. These values indicate that the blends had good flow property. Carr's index was found between 9.27-15.0 for all formulations, while Hausner's ratio was found to be between 1.105-1.19, indicating that the blends had good flow character.

3.Direct Compression Method:

The Pregabalin tablets were prepared by direct compression method as discussed in the above procedure.

4. Post Compression Parameters:

All the batches of tablet formulations were characterized for official evaluation parameters like Weight variation, Hardness, Friability, Tablet thickness and Drug content and results are shown in the (Table 8).

Table 8: Characterization of Pregabalin matrix tablets

Formulation	Weight variation (mg)	Thicknes (mm)	Hardness (kp)	Friability (%)
F1	100±1.55	2.04±0.03	3.2±0.15	0.17±0.03
F2	99±0.94	2.08±0.02	3.2±0.25	0.14±0.02
F3	101±0.59	2.03±0.03	3.1±0.31	0.15±0.01
F4	100±1.81	2.06±0.05	3.8±0.21	0.31±0.02
F5	100±1.41	2.09±0.03	3.1±0.2	0.13±0.01
F6	101±1.57	2.07±0.04	3.3±0.26	0.24±0.02
F7	100±0.49	2.05±0.07	3.	0.16±0.05
F8	100±1.46	2.08±0.02	3.3±0.25	0.14±0.03
F9	100±0.84	2.02±0.02	3.1±0.45	0.19±0.08
F10	99±1.65	2.04±0.02	3.1±0.41	0.23±0.02
F11	100±0.43	2.10±0.03	3.3±0.21	0.14±0.02
F12	100±1.23	2.06±0.03	3.2±0.15	0.26±0.01

Hardness of the tablet was acceptable and uniform from batch-to-batch variation, which was found to be 3 - 4 kg/cm^2. All the formulations passed the weight variation test as the % weight variation was within the pharmacopoeial limits of the tablet weight. Friability values were found to be less than 1% in all the formulations F1 – F12 and considered to be satisfactory ensuring that all the formulations are mechanically stable.

5. *Invitro* dissolution studies:

The *Invitro* dissolution studies were conducted for the prepared formulations as discussed in the above procedure (Dissolution parameters).

(I)Dissolution profile for Pregabalin sustained release tablets:(Pregabalin Reference)

Table 9: % CDR of Marketed product

Time(hr)	Mean % drug release MP
1	18.67±0.36
2	26.26±0.43
4	39.24±0.28
6	49.19±0.65
8	62.23±0.37
10	74.52±0.81
12	96.41±0.31

The dissolution study was performed with Marketed product and the mean% cumulative drug release was calculated and noted in (Table 9).
Reference graph was also plotted can be seen in (Figure 2).

Reference *Invitro* drug release graph

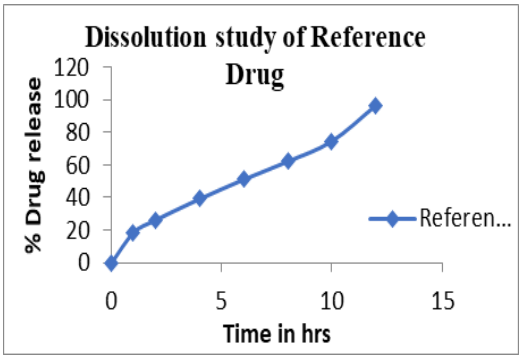

Figure 2: Dissolution study of Reference Drug

(II) Dissolution studies: % Cumulative drug release for formulations from F1-F12 were performed.

Table 10: % Cumulative drug release of formulations F1-F4

Time (hr)	% drug release			
	F1	F2	F3	F4
1	28.15±0.6	28.28±0.8	25.32±0.2	22.25±0.5
2	44.33±0.4	41.55±0.5	33.71±0.4	31.89±0.6
4	61.21±0.5	58.33±0.5	52.65±0.9	46.48±0.5
6	78.82±0.8	78.28±0.5	67.28±0.5	58.57±0.4
8	98.18±0.4	89.69±0.6	83.126±0.5	69.36±0.2
10	_	100.39±0.2	98.23±0.2	83.66±0.6
12	_	_	_	100.23±0.2

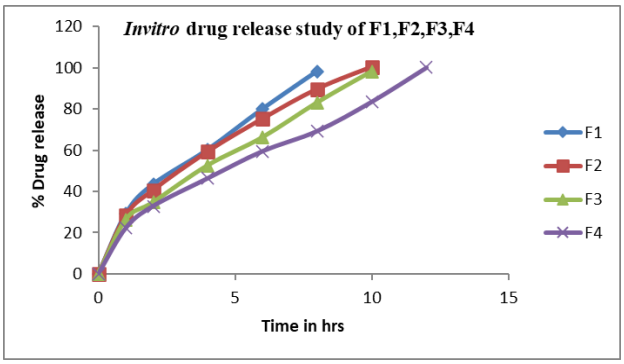

Figure 3: *Invitro* drug release study of F1, F2, F3, F4

Table 11: % Cumulative drug release of formulations F5-F8

Time (hr)	% drug release			
	F5	F6	F7	F8
1	28.16±0.6	24.29±0.8	24.39±0.2	20.34±0.5
2	42.36±0.4	38.58±0.5	32.76±0.4	26.26±0.6
4	60.25±0.5	57.37±0.5	48.68±0.9	42.6±0.5
6	78.87±0.8	73.29±0.5	67.25±0.5	58.26±0.4
8	96.28±0.4	87.68±0.6	77.126±0.5	66.64±0.2
10	_	99.34±0.2	91.26±0.2	78.34±0.6
12	_	_	100.82±0.4	97.75±0.2

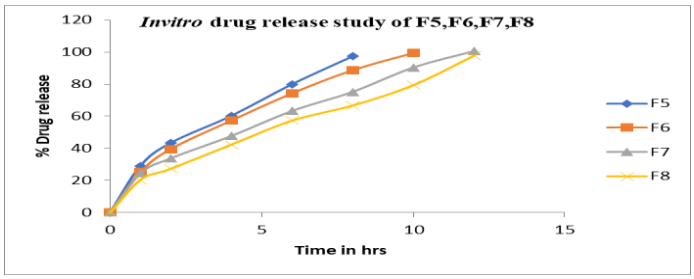

Figure 4: *Invitro* drug release study of F5, F6, F7, F8

Table 12: % Cumulative drug release of formulations F9-F12

Time (hr)	% drug release			
	F9	F10	F11	F12
1	34.16±0.6	35.26±0.24	31.44±0.48	31.26±0.32
2	61.39±0.4	56.65±0.46	53.86±0.56	49.39±0.12
4	88.26±0.5	86.29±0.61	73.74±1.20	61.89±1.1
6	101.86±0.8	97.55±0.17	85.29±0.51	74.54±0.7
8	_	_	92.36±0.65	87.26±0.4
10	_	_	97.48±0.23	94.65±0.2
12	_	_	_	100.04±0.9

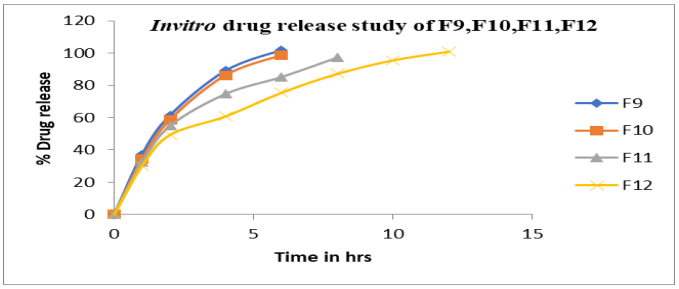

Figure 5: *Invitro* drug release study of F9, F10, F11, F12

Inference: From the above dissolution studies for (Table 10,11,12) formulations FI, F2, F3 containing (10%,15%,20% concentrations of HPMC K4M); F5 & F6 with (10%,15% concentrations of HPMC K15M); F9, F10, F11 containing (10%,15%,20% concentrations of Metalose 60SH-50) showed within 8-10 hrs can be seen in (Figure 3,4,5). For F4 containing (25% HPMC K4M); F7, F8 containing (20%,25% HPMC K15M) and F12 containing (25% Metalose 60SH-50) extended drug released up to 12 hrs can be seen in (Figure 3,4,5).

Comparison of *Invitro* drug release of Reference product and Optimized formulation(F12):

The Reference product and Optimized formulation (F12) had been compared and showed the extended drug release up to 12 hours. It can be seen (Figure 6).

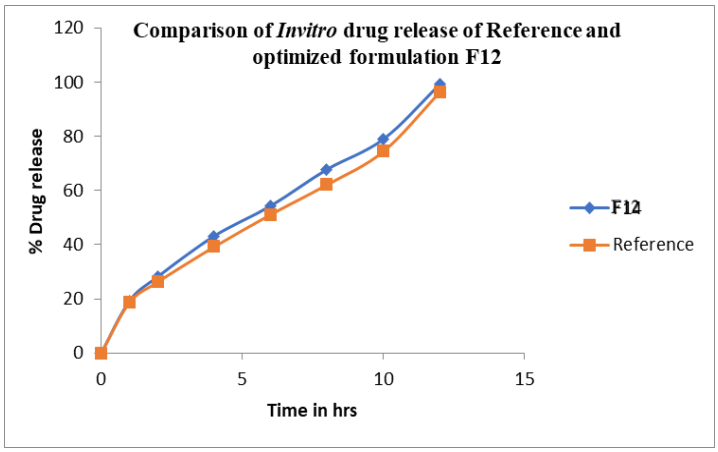

Figure 6: Comparison of *Invitro* drug release of Reference and Optimized (F12)

6. Kinetics:

The kinetic release data from *Invitro* release was computed in (Table 13) with different kinetic models (such as Zero order, First order, Higuchi model, Korsmeyer-Peppas model) and the 'n' value was characterized different release mechanism of drug as described in the (Table 3) as discussed in the procedure. The graphs were plotted accordingly can be observed in (Figure 7,8,9,10).

Table 13: *Invitro* drug release kinetics for Optimized formulation (F12)

R^2 values					n values
Formulation	Zero order	First order	Higuchi	Korsmeyer - Peppas	Korsmeyer-Peppas (n)
Reference	0.9702	0.9852	0.9847	0.9964	0.579
F-12	0.9686	0.9858	0.9947	0.9995	0.583

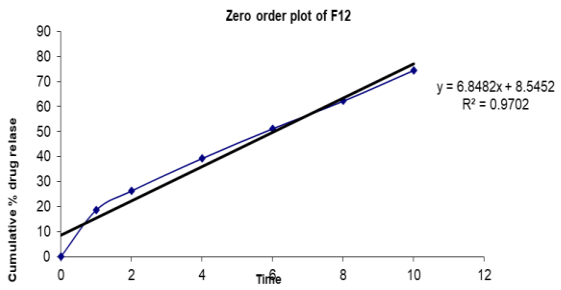

Figure 7: Zero order plot of F12

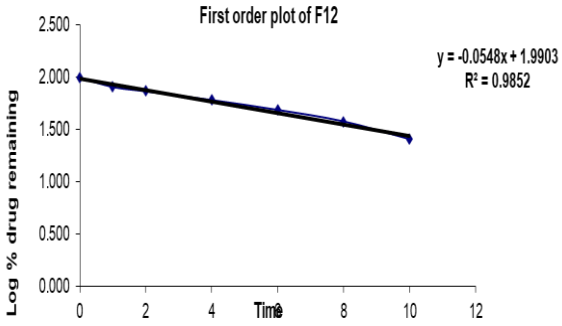

Figure 8: First order plot F12

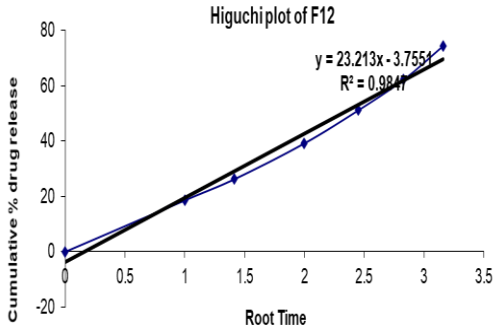

Figure 9: Higuchi plot of F12

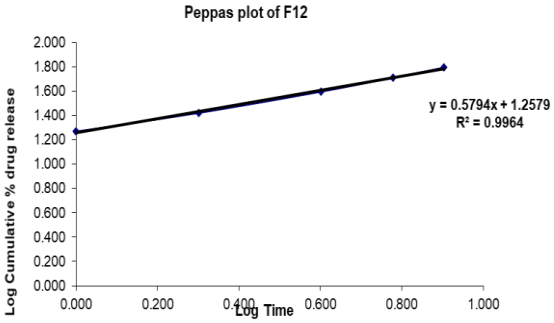

Figure 10: Peppas plot of F12

7. FT-IR spectroscopy studies:

In the study drug and excipient was compared with standard spectrum of pure Pregabalin drug. The IR spectra showed that there is no significant evidence for interaction between the drug and the excipients as discussed in the procedure and observed in (Figure 11 & 12).

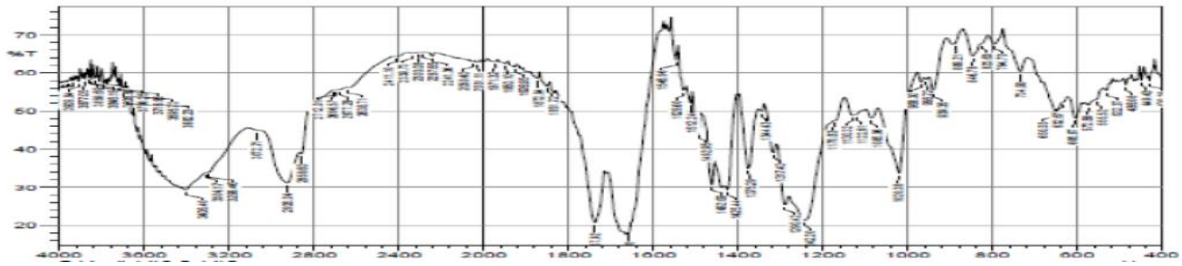

Figure 11: FT-IR spectra of Pregabalin

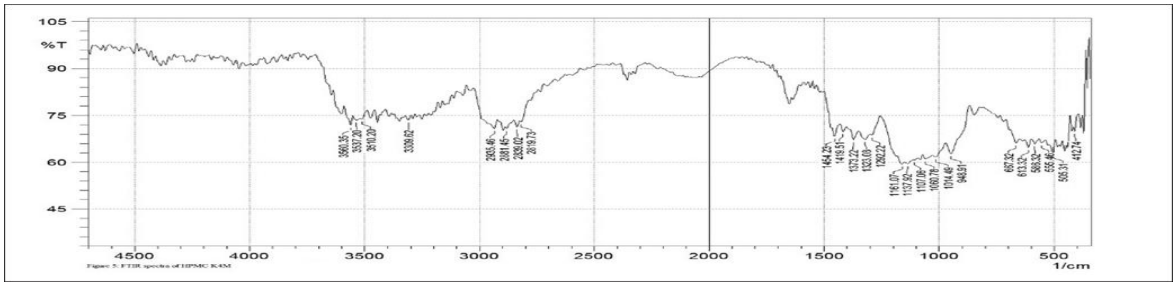

Figure 12: FT-IR spectra of Optimized formulation

CONCLUSION

The study involves preformulation, formulation & evaluation studies for prepared Pregabalin sustained release matrix tablets. The physical evaluation of API along with excipients has shown compatibility supporting the choice of excipients. FTIR studies reveal no incompatibility between drug, polymer and various excipients used in the formulations.

Formulations were prepared by using direct compression. Sustained release tablets of Pregabalin were formulated and evaluated with different polymers. Formulations with HPMC K4M and HPMC K15M polymers has successfully sustained the Pregabalin release up to 12 hours and they were formulated (F4&F8) in (25% concentration) 0.75:1 ratio with Metalaose 60SH-50 as the polymer has sustained the drug release up to 12 hours in 0.45:1 ratio (25% concentration) with drug.

The *Invitro* dissolution studies was compared with the Marketed Product to Optimized (F12) formulation for drug release pattern and was matched using similarity(F12) which showed that formulation (F12) performed similar to the Marketed Product therapeutically. The dissolution profiles and kinetic studies (Zero-order, First-order, Higuchi's equation and Korsmeyer-peppas equation) indicate that the release of Pregabalin can

be effectively controlled by use of hydrophilic matrix systems. Different kinetic models were applied to the formulation Optimized and observed that Formulation (F12) followed First Order Kinetic Model and it was complied with (Reference Sample). The best Linearity was found in Korsmeyer-peppas Model (where N=0.583 is the Release Exponent). Applicability of data indicating Non Fickian Diffusion (or) Anomalous Transport as mechanism of drug release. Non Fickian Diffusional Release occurs by the usual Molecular Diffusion of the drug due to a chemical potential gradient. FTIR studies reveal no incompatibility between drug, polymer and various excipients used in the formulations.

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