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FORMULATE AND EVALUATION OF PULSATILE DRUG DELIVERY SYSTEM OF PREGABALIN

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Abstract:

Pregabalin binds with high affinity to the alpha2-delta site (an auxiliary subunit of voltage-gated calcium channels) in central nervous system tissues. Pregabalin is a new anticonvulsant drug indicated as an add on therapy for partial onset seizures and for certain types of neuropathic pain. It was designed as a more potent successor to a related drug, gabapentin. Pregabalin binds to the alpha2-delta subunit of the voltage-gated calcium channel in the central nervous system.

Pregabalin 150 mg pulsatile release tablets were prepared by direct compression method and evaluated for thickness, hardness, weight variation, friability, drug content and in vitro release of drug. In vitro drug release was carried out using USP type II apparatus at 50 rpm in 900 ml of dissolution media for 8 hrs. Mean dissolution time is used to evaluate drug release rate from a dosage form and indicates the drug release retarding efficiency of polymer. Various kinetics models were applied to the dissolution profile to determine the drug release kinetics. All the physical characteristics evaluated for the tablets were obtained to be within the acceptable limits. Finally it was clear that core polymer Sodium Starch Glycolate and coating polymer Xanthan Gum is good candidate for preparing pulsatile tablets of Pregabalin.

Keywords: *Pregabalin , Dammar gum, Guar Gum, Xanthan Gum*

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INTRODUCTION:

In recent years, a major goal for the drug delivery research is turned towards the development of efficacious drug delivery systems with already existing active ingredients in case of new drug discovery. Many of pharmaceutical therapeutic agents are mostly effective when made available at constant rates or near to absorption sites. Much effort has been going on to develop sophisticated drug delivery systems such as osmotic devices for oral application. Oral drug delivery system is more favored on popular controlled drug delivery system in pharmaceutical research and development (R & D) business due to increase in awareness of medical and pharmaceutical community about the importance of safe and effective use of drug. This system aims to maintain plasma drug concentration within the therapeutic window for long period of time[1].

Traditionally, it is becoming increasingly more evident with the specific time that patients have to take their medication may be even more significant than was recognized in the past. The tradition of prescribing medication at evenly spaced time intervals throughout the day, in an attempt to maintain constant drug levels throughout a 24-hr period, may be changing as researcher's report that some medications may work better if their administration is coordinated with day-night patterns and biological rhythms. In the human body systems such as cardiovascular, pulmonary, hepatic and renal systems show variation in their function throughout a typical day. They are naturally followed by the internal body clocks and are controlled by the sleep wake cycle. This system focused on controlled or sustained release of drug of which has such advantages of nearly constant level of drug at site of administration, minimizing peak - valley fluctuation of drug concentration in body and avoidance of adverse effect because R eduction in dose, dosage frequency and patient efficacy and compliance by this delivery system also expected[1].

A release pattern of drug is not suitable in certain disease condition. At that time, release profile of a delivery system characterized by lag time. In other words, the drug should not release during its initial period of administration, followed by a rapid and complete release (pulse release) of drug that is called pulsatile drug delivery system. This system aims to deliver a drug via the oral route at a rate different than constant i.e., zero order release. The lag time is the time interval between the dosage forms is placed into the aqueous environment and drug get to release from its dosage form after rupturing or eroding outer layer. The lag time between 0.5 hr to 4 hr is desire for upper region of gastrointestinal tract and more than 4 hr for lower portion of small intestine[2].

"Chronopharmaceutics" consist of two words chronobiology and pharmaceutics. Chronobiology is the study of biological rhythms and their mechanisms. Mainly mechanical rhythms in our body are:

Circadian - this word comes from Latin word "circa" means about and "dies" means day and oscillation completed in 24 hr

Ultradian - oscillation of shorter duration (more than one cycle per 24 hr)

Infradian - oscillations that are longer than 24 hr (less than one cycle per day)[7]

Circadian rhythms are self-sustaining, endogenous oscillations that occur with a periodicity of about 24 hr and regulate many body functions like-metabolism, sleep pattern, hormone production etc. PDDS are widely important in such wide spread disease which is mentioned below

- Chronopharmacotherapy of diseases which shows circadian rhythms in their pathophysiology Confidential
- Extended day time or night time activity
- Avoiding the first pass metabolism e.g., protein and peptides
- Biological tolerance **(**e.g., transdermal nitroglycerin)
- For targeting specific site in intestine e.g., colon
- For time programmed administration of hormone and drugs
- Gastric irritation or drug instability in gastric fluid
- For drugs having the short half life
- Lower daily cost to patient due to fewer dosage units are required in therapy
- Reduction in dose size and dosage frequency and also side effects

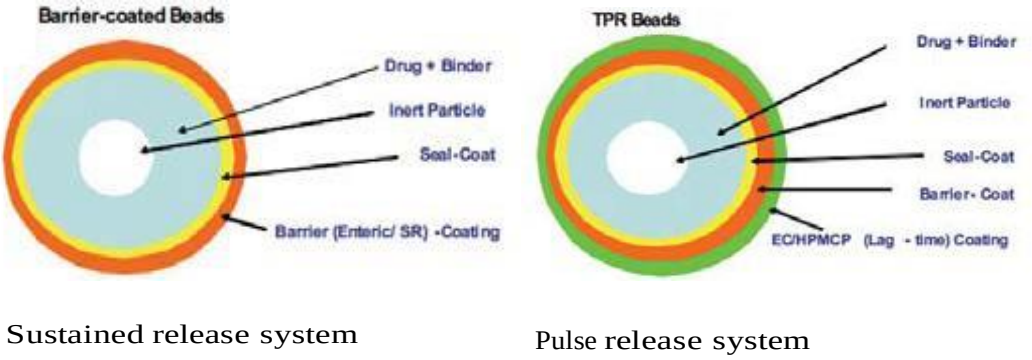

Fig1.1 A comparison between sustained and pulsatile release system

PDDS increases its attention in treatment of peak symptoms in early morning and exhibit circardian rhythm. The first pulsed delivery formulation that released the active substance at a precisely defined time point was developed in the early 1990s. The various pulsatile drug delivery systems that are reported are shown below.

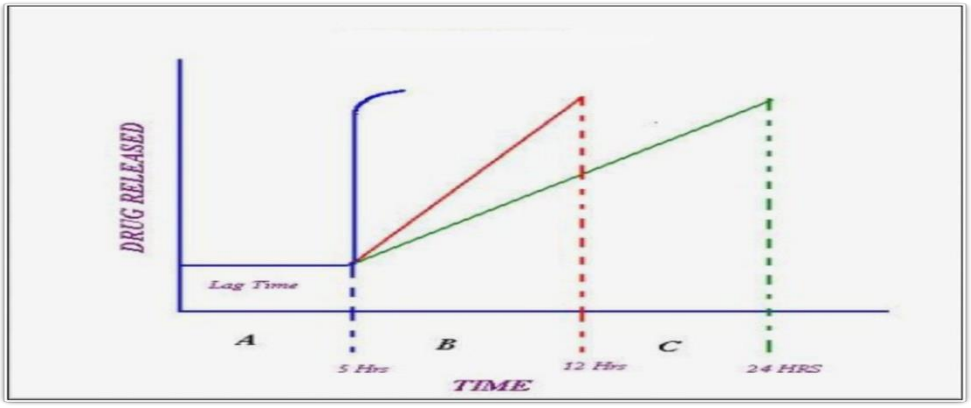

Fig1.2 Schematic diagram of different drug release profile, (a) Ideal time or sigmoidal release after lag time, (b) delayed release after initial lag time, (c) sustained release after initial lag time, (d) extended release without lag time.

Sustained release formulations are not efficient in treating the diseases especially diseases with chronological pathopysiology, for which, pulsatile drug delivery is beneficial. The different drug used for chronotherapies are shown below[2]

Table 1.1 Circadian rhythm and the manifestation of clinical diseases

SL. No	Circadian rhythmicity	Disease
1	Exacerbation more common during the sleepperiod & attacks after midnight or at early morning hr	Asthma
2	Worse in the morning/upon rising	Allergic Rhinitis
3	Growth hormone and melatonin produced at night; testosterone and cortisol in morning hr	Hormone Secretion

4	Even with constant heparin infusion rate,thromboplastin time and risk of bleeding vary significantly during the day	Blood Coagulation
5	Morning pain and more in night	Rheumatoid Arthritis
6	Symptoms worse in the middle/later portion of the day	Osteoarthritis
7	Chest pain and ECG changes more common in early morning	Angina Pectoris
8	Increased blood sugar level after meal	Diabetes mellitus
9	Incidence higher in the early morning	Myocardial Infraction
10	Incidence higher in the morning	Stroke
11	Cholesterol synthesis is generally higher during night than day time	Hypercholesterolemia
12	Incidence higher in the morning after Awakening	Sudden cardiac death
13	Acid secretion high in afternoon and at night	Peptic ulcer disease
14	Increase Dopa level in afternoon	Attention deficit syndrome

The lag time is essential for those drugs that undergo degradation in gastric acidic medium like- peptide drugs irritate the gastric mucosa or which induce nausea and vomiting. Like these conditions enteric coating providing satisfactory results and also enteric coating can be considered as a pulsatile drug delivery system.

The comparison between conventional sustained release and pulsatile drug delivery system is shown in**.** Sustained release approach which shift to modern pulsatile drug delivery having certain advantages:

Table 1.2 Drugs developed or under development as chronotherapies

SLNo.	Class	Examples of drugs
1	Cardiovascular Drugs	Verapamil, Felodipine, Propranolol, Captopril,Metoprolol, Diltiazem, Nifedipine, Enalapril, Nitrogycerine, Dofetilide.
2	Antiasthmatic Drugs	Methylprednisolone, Prednisolone, Albuterol, Terbutaline, Theophylline, Montelukast sodium, Budesonide
3	Anticancer Drugs	Cisplatine, Oxaliplatine, Doxorubicin, 5- fluorouracil, Folinic acid, Methotrexate, Mercaptopurine
4	Non Steroidal Anti- Inflammatory Drugs	Diclofenac sodium, Ibuprofen, ketoprofen, oxymorphone, Indomethacine, Tenoxicam, Acetylsalicylic acid,
5	Diabetes Mellitus	Sulphonylurea, insulin
6	Anti Angina Drug	Nitroglycerine
7	Anti Ulcer Drugs	Cimetidine, Ranitidine, Famotidine, Pirenzipine, Omeprazole
8	Anti Cholesterolemic Drugs	Simvastatin, Lovastatin
9	In Irritable Bowel Disease	5-amino salicylic acid
10	Others	Amoxycilline, Vitamin D3, Dizepam, Haloperidol, Methylphenidate,

METHODOLOGY:

6.1. Analytical method development:

a) Preparation of calibration curve in 0.1N HCL:

10mg of Pregabalin pure drug was dissolved in 10 ml of methanol (stock solution 1). 1ml of solution was taken and makes up with10 ml of 0.1N HCL (100µg/ml) stock-2. From this 1ml was taken and make up with 10 ml of 0.1N HCL (10µg/ml) stock-3. The above stock-II solution was subsequently diluted with 0.1N HCL to obtain series of dilutions containing and 2,4,6,8 and 10µg/ml of solution. The absorbance of the above dilutions was measured at 276 nm for 0.1 N HCL by using UV-Spectrophotometer taking 0.1N HCL as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis. The Same procedure repeated in pH 6.8 phosphate buffer.

6.2. Drug – Excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy:

The compatibility between the pure drug and excipients was detected by FTIR spectra obtained on Bruker FTIR Germany (Alpha T). The solid powder sample directly place on yellow crystal which was made up of ZnSe. The spectra were recorded over the wave number of 4000 cm^{-1} to 550 cm^{-1}.

6.3. Formulation development of Tablets:

Formulation of core tablets by direct compression: The inner core tablets were prepared by using direct compression method as shown in the Table. Powder mixtures of Pregabalin, microcrystalline cellulose, Sodium Starch Glycolate, Aerosil ingredients were dry blended for 20 min. followed by addition of Sodium Stearyl Fumerate. The mixtures were then further blended for 10 min., 300 mg of resultant powder blend was manually compressed using , Lab press Limited, India with a 9 mm punch and die to obtain the core tablet.

Formulation of mixed blend for barrier layer: The various formulation compositions containing Ethyl cellulose and HPMC K100M, Sodium Stearyl Fumerate, Aerosil And Microcrystalline Cellulose. Different compositions were weighed dry blended at about 10 min. and used as press coating material to prepare press-coated pulsatile tablets respectively by direct compression method.

Preparation of press-coated tablets: The core tablets were press-coated with 150 mg of mixed blend as given in Table.No. 150 mg of barrier layer material was weighed and transferred into a 10 mm die then the core tablet was placed manually at the center. The remaining of the barrier layer materiel was added into the die and compressed by using Lab press Limited, India

Table 6.1: Formulation development of core tablets

Ingredients	C1	C2	C3
Pregabalin	150	150	150
Sodium Starch Glycolate	25	50	75
Mannitol	101	76	51
PVP K 30	15	15	15
Sodium Stearyl Fumerate	6	6	6
Aerosil	3	3	3
Total weight	300	300	300

Table 6.2: Formulations for press coated tablets

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Core Tablet	300	300	300	300	300	300	300	300	300
Dammar gum	50	75	100	-	-	-	-	-	-
Guar Gum	-	-	-	50	75	100	-	-	-
Xanthan Gum	-	-	-	-	-	-	50	75	100
Sodium Stearyl Fumerate	3	3	3	3	3	3	3	3	3
Mannitol	95	70	45	95	70	45	95	70	45
Aerosil	2	2	2	2	2	2	2	2	2
Total weight	450	450	450	450	450	450	450	450	450

RESULTS AND DISCUSSION:

Present study was done on pulsatile tablets with different formulations F1 to F9. Formulations had weight ratio of polymers like Dammar gum, Guar Gum, Xanthan Gum along with various excipients. This section gives detailed description of the results and discussion on pulsatile Pregabalin tablets.

7.1 Preformulation Studies

Standardization method for estimation of Pregabalin

Standard curves of Pregabalin were prepared in 0.1N HCL and phosphate buffer (pH 6.8).

Standard graph of Pregabalin in 0.1N HCL

Pregabalin showed maximum absorbance in 0.1N HCL at 276 nm. The solution obeyed Beer-Lambert's law for concentration range of 0 µg / mL to 10 µg / mL with regression coefficient of 0.998. Standard curve of Pregabalin prepared in 0.1N HCL is shown below in **Table 7.1** and **Figure 7.1**.

Table 7.1: Calibration data of Pregabalin in 0.1N HCL

Concentration [µg/ml]	Absorbance
0	0
2	0.177
4	0.369
6	0.557
8	0.743
10	0.934

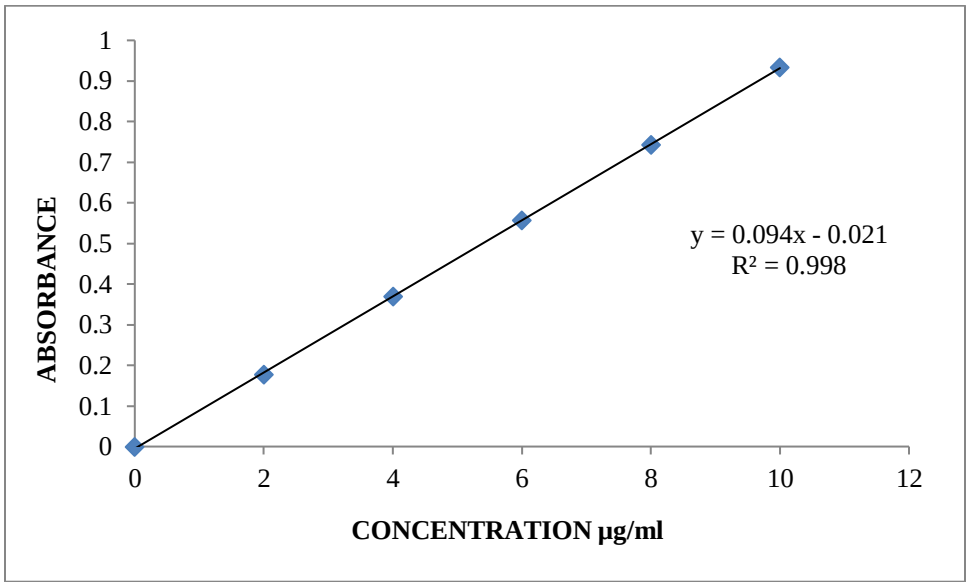

Fig:7.1: Standard Graph of Pregabalin in 0.1N HCL

Standard graph of Pregabalin in phosphate buffer (pH 6.8)

Pregabalin showed maximum absorbance in phosphate buffer (pH 6.8) at 276 nm. The solution obeyed Beer-Lambert's law for concentration range of 0 to 10 µg / mL with regression coefficient of 0.999. Standard curve of prepared Pregabalin in phosphate buffer pH 6.8 is shown below.

Table : Calibration data of Pregabalin in pH 6.8 phosphate buffer

Conc [µg/ml]	Abs
0	0
2	0.176
4	0.354
6	0.527
8	0.714
10	0.838

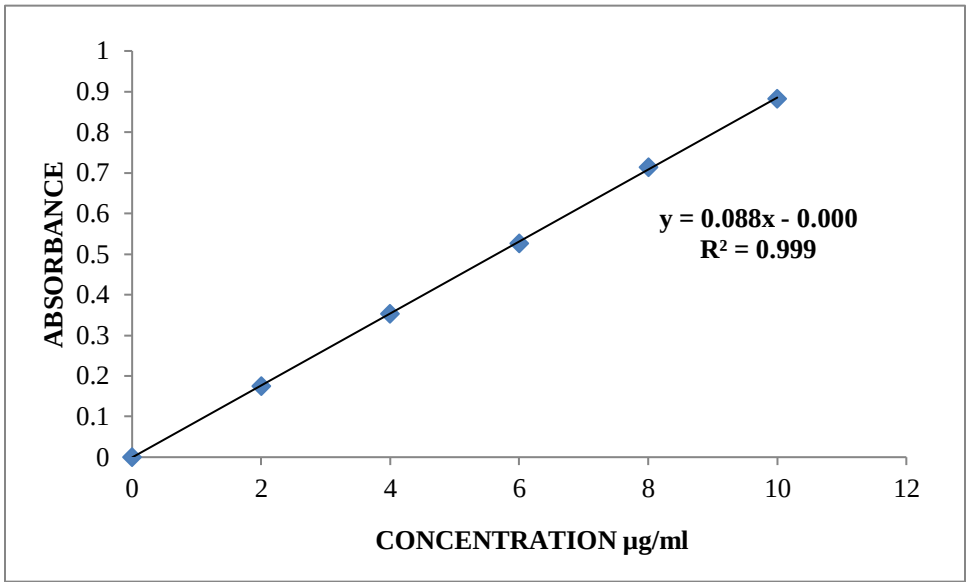

Fig: 7.2: Standard Graph of Pregabalin in pH 6.8 phosphate buffer

7.3: FT-IR (Fourier Transform Infrared Spectrophotometry)

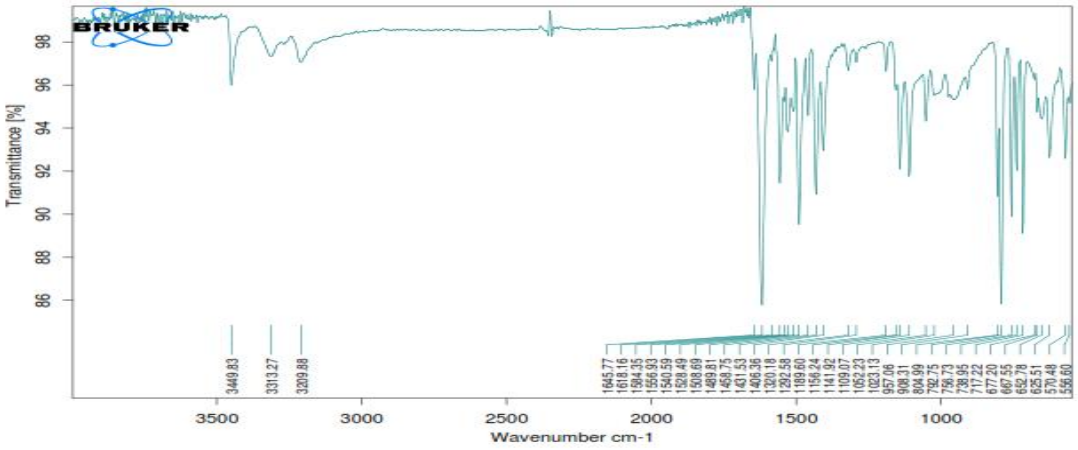

Fig.:7.3. FTIR spectra of Pregabalin pure drug

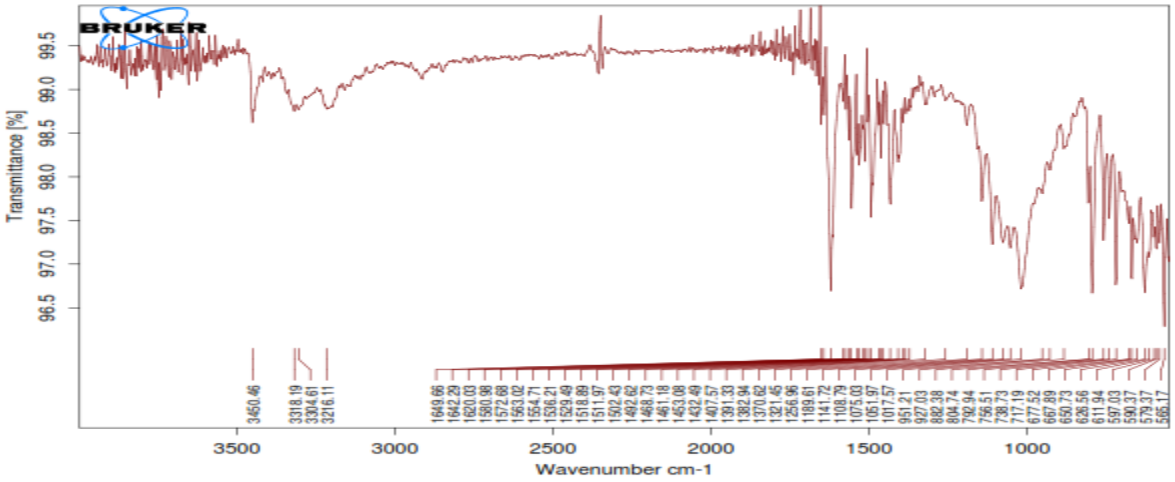

Fig:7. 4. FTIR spectra of Optimized Formula

The spectra for pure Pregabalin and for the physical mixture of Pregabalin and all the polymers were determined to check the intactness of the drug in the polymer mixture using FTIR Spectrophotometer.

The comparative FTIR studies of Drug and excipients combination had shown negligible variation in the values as compared with that of only pure form of Drug. Therefore it implies good compatibility of drug and excipients.

From the above table, the wave number of mixture of drug with excipients is within the range of wave number of pure drug. This implies that the excipients are compatible with the drug since their combination did not alter the functional groups of pure drug

Table 7.3: Pre compression parameters of Cap core tablets

Formulation Code	Angle of repose (^{0}) *	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
C1	26.29	0.34	0.38	10.52	1.11
C2	27.29	0.33	0.38	13.15	1.15
C3	28.29	0.34	0.38	13.14	1.14

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.33 to 0.34 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.38 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging from 10.52 to 13.14 which were showed that the powder has good flow properties. All the formulations has shown the hausner ratio ranging from 0 to 1.15 indicating the powder has good flow properties.

Table 7.4: Post compression parameters of Core tablet:

Formulation code	Average Weight (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)	*In vitro* disintegration time (min)
C1	299.12	1.13	0.24	0.345	99.18	10
C2	300.28	1.25	0.18	0.287	98.27	15
C3	300.77	1.34	0.22	0.321	99.33	18

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits

Weight variation and thickness: All the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown in table 7.4. The average tablet weight of all the formulations was found to be between 59.12 to 60.77. The maximum allowed percentage weight variation for tablets weighing <80 mg is 10% and no formulations are not exceeding this limit. Thus all the formulations were found to comply with the standards given in I.P. And thickness of all the formulations was also complying with the standards that were found to be between 0.287 to 0.345.

Hardness and friability: All the formulations were evaluated for their hardness, using monsanto hardness tester and the results are shown in table 7.4. The average hardness for all the formulations was found to be between (1.13– 1.34) Kg/cm^2 which was found to be acceptable.

Friability was determined to estimate the ability of the tablets to withstand the abrasion during packing, handling and transporting. All the formulations were evaluated for their percentage friability using roche friabilator and the results were shown in table 7.4. The average percentage friability for all the formulations was between 0.18-0.24 which was found to be within the limit.

Drug content: All the formulations were evaluated for drug content according to the procedure described in methodology section and the results were shown in table 7.4. The drug content values for all the formulations were found to be in the range of 98.27 **to** 99.33. According to IP standards the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the formulations comply with the standards given in IP.

***In vitro* disintegrating time:** All the formulations were evaluated for *in vitro* disintegration time according to the procedure described in methodology section and the results were shown in table 7.4. The *in vitro* disintegration time values for all the formulations were found to be in the range of 10 to 18.

Table 7.5: Pre compression Parameters of Pregabalin **coated Tablets**

Formulation code	Angle of repose (^{0}) *	Bulk density (gm/ml)	Tapped dens (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	17.10	0.318	0.38	16.31	1.19
F2	28.97	0.342	0.4	15.0	1.176
F3	18.19	0.34	0.43	20.93	1.26
F4	22.61	0.36	0.42	14.28	1.16
F5	26.56	0.33	0.41	19.06	1.24
F6	23.10	0.33	0.42	22.35	1.28
F7	19.85	0.33	0.41	19.51	1.24
F8	21.80	0.32	0.42	24.70	1.32
F9	17.74	0.33	0.4	17.5	1.21

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.32 – 0.342 (gm/cm3) showing that the powder has good flow

properties. The tapped density of all the formulations was found to be in the range of 0.4- 0.43 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging from 14 to 24 which show that the powder has good flow properties. All the formulations has shown the hausner ratio ranging between 0.16 to 0.176 indicating the powder has good flow properties.

Table 7.6: Post compression parameters of Coated tablet:

Formulation code	Average Weight (mg)	Hardness (kg/cm2)	Thickness	Friability (%loss)	Drug content (%)
F1	451.28±0.12	5.82±0.22	4.12±0.78	0.54±0.28	99.28
F2	448.36±0.95	5.66±0.51	4.67±0.64	0.23±0.34	98.12
F3	449.98±0.74	5.09±0.95	4.85±0.48	0.47±0.94	99.73
F4	450.57±0.64	5.16±0.46	4.45±0.32	0.61±0.47	100.01
F5	449.48±0.37	5.77±0.37	4.98±0.17	0.44±0.85	97.42
F6	448.61±0.56	5.62±0.55	4.12±0. 95	0.50±0.24	99.35
F7	447.38±0.33	5.94±0.48	4.44±0. 81	0.38±0.95	98.75
F8	450.73±0.76	5.81±0.72	4.89±0.99	0.31±0.81	99.41
F9	449.68±0.84	5.19±0.22	4.18±0.75	0.45±0.76	99.27

7.5 Post compression parameters for tablets

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

Weight variation and thickness: All the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown in table 7.6. The average tablet weight of all the formulations was found to be between 447.38±0.33 to 450.73±0.76. The maximum allowed percentage weight variation for tablets weighing >250 mg is 5% and no formulations are not exceeding this limit. Thus all the formulations were found to comply with the standards given in I.P. And thickness of all the formulations was also complying with the standards that were found to be between 4.12±0.78 to 4.98±0.17.

Hardness and friability: All the formulations were evaluated for their hardness, using monsanto hardness tester and the results are shown in table. The average hardness for all the formulations was found to be from 5.09±0.95 to 5.94±0.48 Kg/cm^2 which were found to be acceptable.

Friability was determined to estimate the ability of the tablets to withstand the abrasion during packing, handling and transporting. All the formulations were evaluated for their percentage friability using roche friabilator and the results were shown in table. The average percentage friability for all the formulations was between 0.23±0.34 - 0.61±0.47 which was found to be within the limit.

Drug content: All the formulations were evaluated for drug content according to the procedure described in methodology section and the results were shown in table 7.6. The drug content values for all the formulations were found to be in the range of **(**98.12 **to** 100.01**).** According to IP standards the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the formulations comply with the standards given in IP.

***In Vitro* Drug Release Studies of Pregabalin core tablet:**

In vitro dissolution studies of Pregabalin core tablets were performed using USP XXIII Type II rotating paddle dissolution apparatus by using phosphate buffer (pH 6.8) as a dissolution medium. From formulation C1-C3 Pregabalin core tablets, C2 showed faster drug release than the other formulations. Faster drug release can be correlated with the high disintegration time. So, C2 formulation was selected as best formulation for further press coating and enteric coating formulations. *In vitro* drug release profiles of all Pregabalin core tablets were shown in **Table 7.7** and

Figure.7.5.

Table 7.7.Drug release of Pregabalin core tablets

Time (min)	C1	C2	C3
0	0	0	0
5	12.82	18.98	7.98
10	22.08	35.48	10.14
15	37.41	55.58	36.98
20	67.66	82.31	58.9
30	91.2	96.88	92.53
45	94.6	98.86	96.66
60	96.92	99.76	98.27

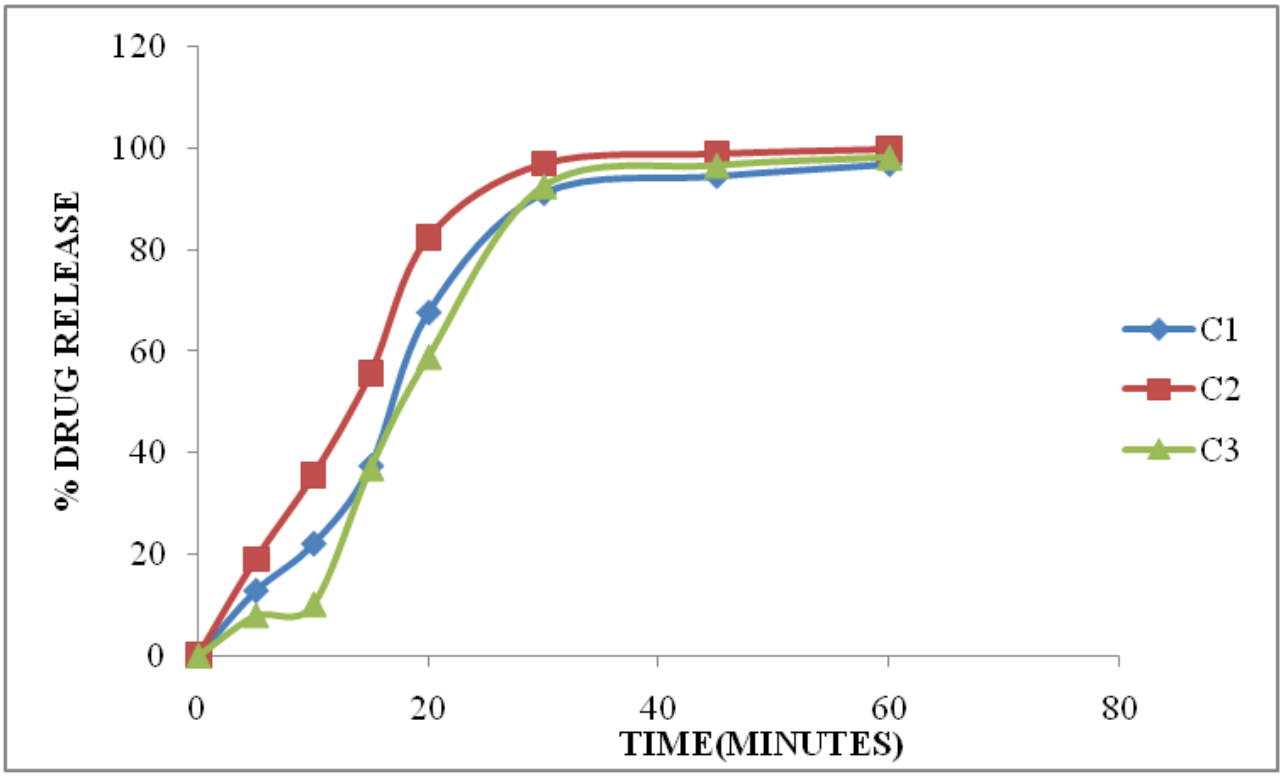

Fig 7.5 Cumulative % drug released of Pregabalin core tablets

***In vitro* drug release study of Pregabalin pulsatile tablets**

Based on the above characters formulation C2 was selected as best formulation and that c2 formulation were used for the further study i.e., delayed release using press coated method. The time dependent pulsatile tablets were prepared by using different concentrations of Dammar gum. The formulations C1, C2, and C3 showed maximum drug release at immediately.

Table 7.8: Cumulative % drug Release of Coated Pregabalin Tablets containing Dammar gum

Time (hr)	F1	F2	F3
0	0	0	0
0.5	0.14	0.13	0.12
1	0.18	0.19	0.22
2	0.25	0.21	5.43
3	28.54	25.29	15.68
4	50.34	30.18	24.32
5	98.37	41.72	30.62
6		51.31	39.57
7		60.34	44.28
8		72.48	50.02
9		88.68	61.25
10		100.64	77.31
11			84.92
12			95.45

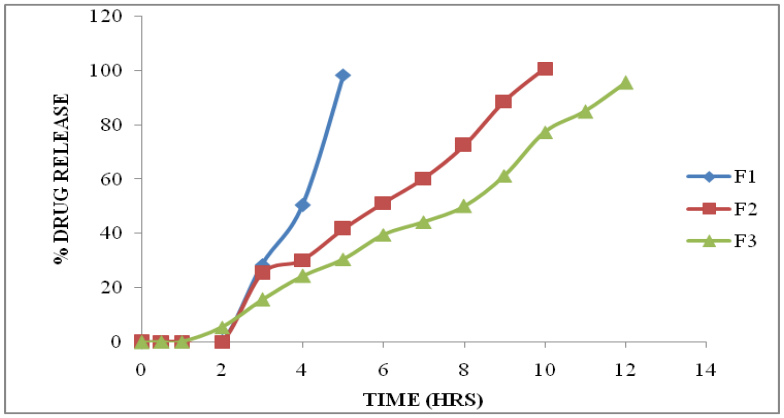

Fig: 7.6: Cumulative % drug release study of Pregabalin pulsatile tablets (F1, F2 & F3)

The formulations F1 to F3 were containing Dammar gum. At low concentration such as 50, 75, 100 mg of Dammar gum was unable to delay the drug release hence that formulations were not considered. Then the coating polymer concentration was increased to 60%, it was showed maximum % drug release 100.64 % at 10 hours and lag phase was 6 hours. Among 3 formulations F2 was showed good result and consider as optimized.

Table 7.9: Cumulative % drug Release of Coated Pregabalin Tablets containing Guar Gum

Time (Hr)	F4	F5	F6
0	0	0	0
0.5	0.28	0.12	0.11
1	12.56	0.19	0.17
2	28.18	1.95	1.35
3	50.34	10.12	9.38
4	85.17	21.23	20.38
5	90.61	30.22	28.39
6	99.76	39.15	35.59
7		43.52	40.38
8		49.06	52.12
9		55.79	64.21
10		75.34	74.86
11		94.25	80.67
12			94.76

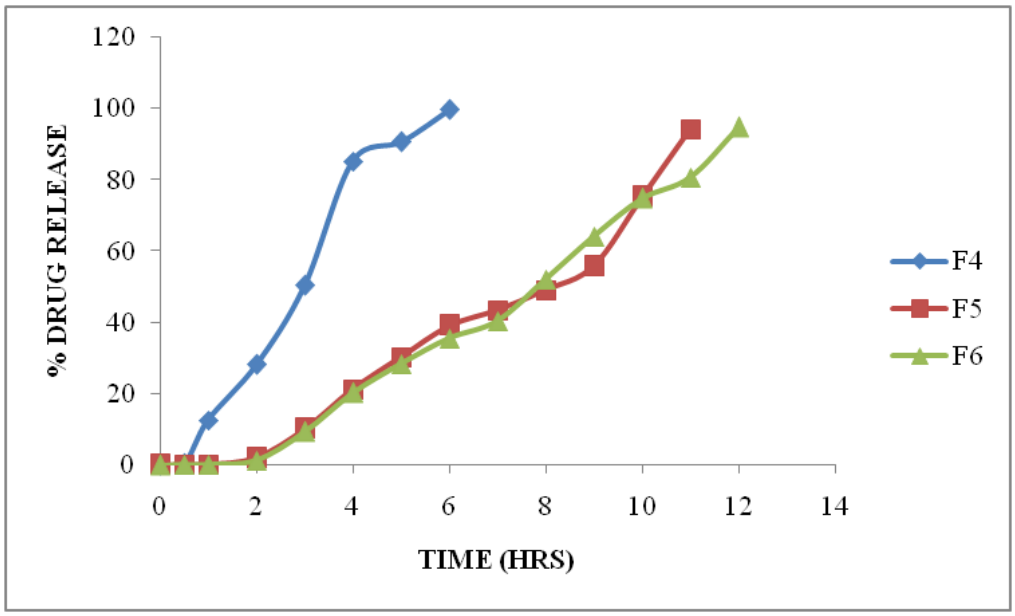

Fig: 7.6: Cumulative % drug release study of Pregabalin pulsatile tablets (F4, F5 & F6)

The formulations F4 to F6 containing different concentrations of Guar Gum, at low concentration of coating material it was not delayed up to desired time the core tablet immediately release at 2 hr. whenever the coating material concentration was increased to 75 mg the maximum % drug release of core tablet from coated tablet at 11 hrs. So F5 formulation also was not good formulation. Then the coating material concentration was increased to 100 mg it was delayed up to 12 hours then core tablet released up to desired time period i.e., 94.76% at 12 hours.

Table 7.9: Cumulative % drug Release of Coated Pregabalin Tablets containing Xanthan Gum

e (hr)	F7	F8	F9
0	0	0	0
0.5	0.19	0.16	0.12
1	0.65	0.54	0.54
2	1.95	1.84	0.59
3	5.39	14.74	19.74
4	13.73	20.38	25.38
5	27.37	38.48	36.48
6	41.38	47.48	45.48
7	63.83	50.29	52.29
8	80.29	61.27	66.27
9	96.38	79.38	71.38
10		86.39	78.39
11		96.28	86.28
12			99.58

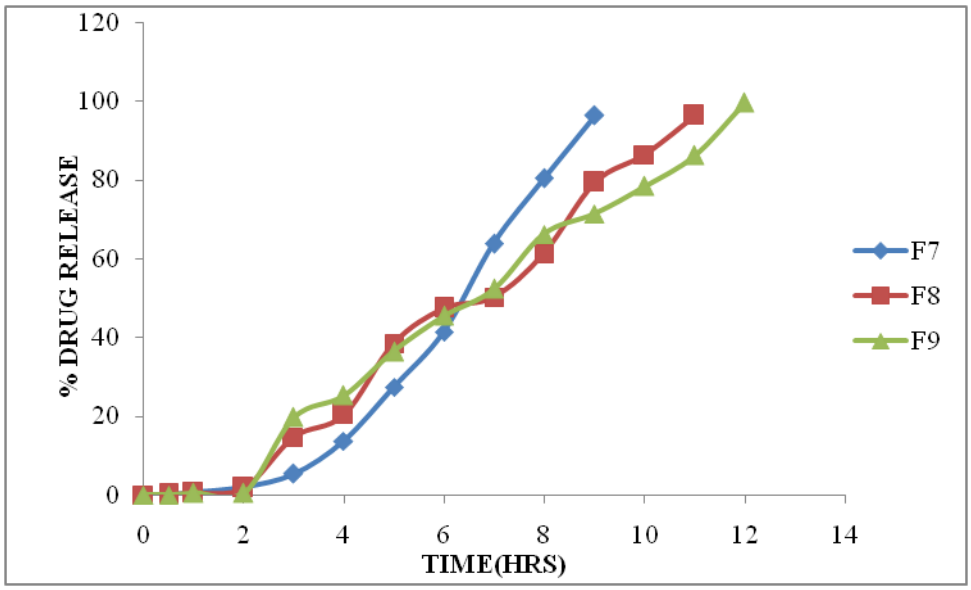

Fig 7.7: Cumulative % drug release study of Pregabalin pulsatile tablets (F7, F8, F9)

The formulations F7 to F9 were containing Xanthan Gum. At low concentration such as 50, 75 mg of Xanthan Gum was unable to delay the drug release up to desired time hence that formulations were not considered. Then the coating polymer concentration was increased to 100 mg F9 was showed maximum % drug release 99.58% at 12 hours and lag phase was 2 hours. Hence F9 Formulation was considered as optimized Formulation.

CONCLUSION:

Pregabalin Pulsatile dosage form was formulated by press coating technique. The lag time and time-controlled release behavior of Pregabalin from press coated tablets could be modulated by varying the concentration of polymer in outer coating layer and thickness if compression coating. From formulation C1-C3 Pregabalin core tablets, C2 showed faster drug release than the other formulations. Faster drug release can be correlated with the high disintegration time. So, C2 formulation was selected as best formulation for further press coating and enteric coating formulations. Among All Formulations F9 was showed maximum % drug release 99.58% at 12 hours. Hence F9 Formulation was considered as optimized Formulation.

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