CODEN (USA): IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.167095

Available online at: http://www.iajps.com *Research Article*

FORMULATION AND EVALUATION OF PREGABALIN SUSTAINED RELEASE TABLETS

Hitesh N. Jain*, Parth P. Patel, Millin R. Gohel, Umesh M. Upadhyay
Sigma Institute of Pharmacy, Bakrol, Ajwa-Nimeta Road, Dist.: Vadodara -390019.

Abstract:

Objectives:

The objective of the present study is to formulate the sustained release matrix tablet of Pregabalin using various matrix polymers which release the drug up to 24 hours. As the dose of Pregabalin is 50mg thrice a day so to reduce the dosage frequency and to increase patient compliance.

Experimental Work:

The sustained release tablets of Pregabalin were prepared by direct compression method. For this, various polymers like HPMC K_4M, Ethocel, Polyox WSR 301 and Polyox WSR 303 were used in various concentrations. The formulations were evaluated for hardness, friability, weight variation and % drug release etc.

Result and Discussion:

From the result obtained, showed that all the pre-compression and post compression parameters are within limit for the batch and out of all the batch containing Polyox WSR 301 and Polyox WSR 303 (i.e. F9 and F10) was able to release drug for desirable time period. F9 shows release up to 20 hours and % drug release is 101.44±0.47 while F10 shows release up to 24 hours and % drug release is 100.67±0.57.

Conclusion:

From the results obtained, it was concluded that the formulation containing Polyox WSR 303 and Polyox WSR 301 shows desired drug release properties. Hence Polyox WSR 303 and Polyox WSR 301 is a potential polymer candidate for formulation of sustained release matrix tablets.

Keywords: *Pregabalin, PEO WSR 303, PEO WSR 301, sustained release, anti-neuropathic.*

Corresponding Author:
Hitesh N. Jain,
Sigma Institute of Pharmacy,
Bakrol, Ajwa-Nimeta Road,
Dist.: Vadodara -390019.
hitesh_hitachi@rediffmail.com
09924469131

QR code

Please cite this article in press as Hitesh N. Jain et al, ***Formulation and Evaluation of Pregabalin Sustained Release Tablets****, Indo Am. J. P. Sci, 2016; 3(11).*

INTRODUCTION:

Oral route of drug administration is the most important method of administering drugs for systemic effects. Nevertheless, it is probable that at least 90% of all drugs used to produce systemic effects are administered by the oral route [1]. Sustained release constitutes any dosage form that provides medication over an extended time or denotes that the system is able to provide some actual therapeutic control whether this is of a temporal nature, spatial nature or both. [2] [3]. Pregabalin (S) - 3 - amino methyl hexanoic acid, is a structural analogues of γ-amino butyric acid (GABA). They constitute an important group of compounds that are used in the treatment of epilepsy and neuropathic pain. It is a white crystalline solid. It is soluble in water and in both basic and acidic aqueous solutions. Pregabalin has been studied for use in a variety of disorders, including monotherapy in refractory partial seizures, diabetic neuropathy, surgical dental pain and other pain syndromes, post herpetic neuralgia, and social anxiety disorders. Pregabalin innovator is Pfizer-Global and appears world-wide under the brand name Lyrica. The half-life of Pregabalin is also short (5-6.5 hrs) which makes it suitable candidate for sustained release formulation, moreover it reducing side effects, decreasing frequency and improve patient compliance [4-9].

MATERIALS & METHODS:

Pregabalin was obtained as a gift sample from DANA Pharmaceuticals Pvt. Ltd, Ambarnath, India and all other excipients were used of analytical grade.

Preparation of tablets:

All ingredients was collected and weighed accurately. Sifted Pregabalin and polymers through sieve no. 60# and then rinsed with remaining excipients. Sifted talc and magnesium stearate separately, through sieve no. 60#.Preblending of all ingredients (except lubricant magnesium stearate) in blended for 15 minutes. Blend then again blended for 5-6 min then added magnesium stearate blended 5 min. Lubricated powder was compressed by rotary machine with pressure of 7-8 tons. Compressed tablets were examined as per official standards and unofficial tests. Prior to the compression the drug and polymers were evaluated for several tests. The composition of different formulation of Pregabalin was given in table 1.

Formulation

Table 1: Formulation composition of Pregabalin tablet

Materials (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
Pregabalin	150	150	150	150	150	150	150	150	150	150	150	150
PEO WSR 301	60	-	-	-	90	-	-	-	120	-	-	-
PEO WSR 303	-	60	-	-	-	90	-	-	-	120	-	-
HPMC K4M	-	-	60	-	-	-	90	-	-	-	120	-
Ethocel	-	-	-	60	-	-	-	90	-	-	-	120
MCC	158	158	158	158	158	158	128	128	98	98	98	98
PVP K30	20	20	20	20	20	20	20	20	20	20	20	20
Mg-Stearate	8	8	8	8	8	8	8	8	8	8	8	8
Talc	4	4	4	4	4	4	4	4	4	4	4	4
Total Wt. (mg)	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**

Evaluation

Pre-compression parameters:

All the formulations were evaluated for their pre-compression parameters like bulk density, tapped density, compressibility index, Hausner's ratio and angle of repose [10-12].

Angle of repose:

The fixed funnel and free standing cone methods employ a funnel that is secured with its tip at a given height, h, which was kept 2 cm above graph paper that is placed on a flat horizontal surface. With r being the radius, of base of conical pile, angle of repose can be determined by following equation:

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

Where, θ is the angle of repose

h is height of pile

r is radius of base of the pile

Bulk density and tapped density:

Both loose bulk density and tapped bulk density were determined. A quantity of 2gm of granules from each formula, previously light Shaken for the break of any agglomerates formed, was introduced into the 10ml of measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall down its own weight from the hard surface from a height of 2.5cm at 2 sec Intervals.

Hausner's Ratio:

A similar index has been defined by Hausner

Hausner's ratio = Tapped density / Poured Density

Post compression parameters:

Hardness:

The hardness of the tablets was determined using Monsanto hardness tester in terms of kg/cm^2. Average hardness of three tablets was taken to study the reproducibility [13].

Friability:

Six tablets from each were exposed to Roche friability test apparatus for 100 rotations and percentage loss in weight was measured against initial weight [14].

% Friability (F) = {1-(W/W0)} X 100

Where, W0= Initial weight of tablet

W = Weight of tablets after the test

Uniformity of weight:

20 tablets were selected at random from each formulated batch to check the uniformity of weight using electronic balance. Average weight and maximum percent deviation (Positive and negative) were determined [15].

Drug Content:

Ten Tablets were weighed and average weight was calculated. All the 10 tablets were crushed in a mortar. The powder equivalent to 10 mg was accurately weighed, dissolved in 0.1 N hydrochloric acid & made up to 100ml of 0.1 N hydrochloric acid. The volumetric flask was then shaken for approximately 20 minutes. The solution was filtered and 1 ml of filtrate was diluted to 10ml using 0.1 N hydrochloric acid. Absorbance was measured at 210 nm using 0.1 N hydrochloric acid as a blank. The amount of drug present in one tablet was calculated.

***In-Vitro* Drug Release Study:**

The test was performed on the prepared Pregabalin tablets using the USP dissolution apparatus II. Six individual tablets from each formula were tested. Test was performed in 900 ml of 0.1 N hydrochloric acid for two hours and then in phosphate buffer 6.8 for remaining hours. In all studies, the temperature of the dissolution medium was maintained at 37+ 0. 50ºc.The Aliquots of 5 ml were withdrawn at regular intervals, filtered and analysed spectrophotometrically at 210 nm [16-18].

RESULTS:

Table 2: Pre-compression parameter of batches F1-F12

Formulation	Bulk Density(gm/cm^3) (n=3)	Tapped density(g/cm^3) (n=3)	Carr's Index (%)(n=3)	Hausner's Ratio (n=3)	Angle of Repose(θ) (n=3)
F1	0.28±0.0024	0.35±0.0033	20.0±0.12	1.25±0.011	32.15±0.26
F2	0.28±0.0019	0.36±0.0023	22.0± 0.17	1.28±0.025	34.31±0.31
F3	0.26±0.0021	0.32±0.0025	18.7± 0.09	1.23±0.009	34.24±0.31
F4	0.28±0.0022	0.37±0.0019	24.3± 0.22	1.32±0.005	28.44±0.22
F5	0.26±0.0016	0.33±0.0023	21.2± 0.07	1.26±0.008	31.25±0.12
F6	0.33±0.0030	0.38±0.0037	13.1± 0.11	1.15±0.006	33.56±0.25
F7	0.31±0.0028	0.38±0.0014	13.2± 0.11	1.22±0.011	33.42±0.31
F8	0.33±0.0019	0.40±0.0026	17.5± 0.17	1.21±0.011	27.39±0.25
F9	0.29±0.0022	0.37±0.0011	21.6± 0.20	1.27±0.010	33.36±0.30
F10	0.30±0.0010	0.35±0.0060	14.2± 0.12	1.16±0.012	32.41±0.29
F11	0.31±0.0030	0.38±0.0015	18.4± 0.15	1.22±0.010	34.71±0.31
F12	0.32±0.0012	0.37±0.0023	13.1± 0.09	1.15±0.009	33.59±0.32

Table 3: Post-compression parameters of batches F1-F12

Formulation	Hardness(kg/cm^2) Mean (n=3)	Weight variation (mg) (n=20)	Friability (%)	Drug Content (%) (n=10)
F1	5.5 ±0.025	401.42 ± 1.3	0.56	97.56±0.44
F2	5.8 ± 0.019	398.96 ±1.8	0.51	101.67±0.57
F3	5.8 ±0.021	403.14 ± 3.6	0.49	99.85±0.81
F4	6.3 ±0.012	402.99± 0.8	0.56	97.99±0.52
F5	6.1 ±0.010	400.61± 2.1	0.61	102.47±0.67
F6	5.9 ±0.036	399.56± 0.9	0.52	97.99±0.66
F7	5.3±0.016	404.19±2.2	0.48	97.86±0.44
F8	5.9±0.028	402.47±1.1	0.53	99.84±0.48
F9	5.4±0.012	398.88±1.7	0.44	101.44±0.47
F10	5.7±0.045	397.75±3.6	0.36	100.67±0.57
F11	6.2±0.032	401.52±2.0	0.21	101.85±0.64
F12	6.4±0.039	399.94±1.8	0.29	98.46±0.29

***In vitro* dissolution study**

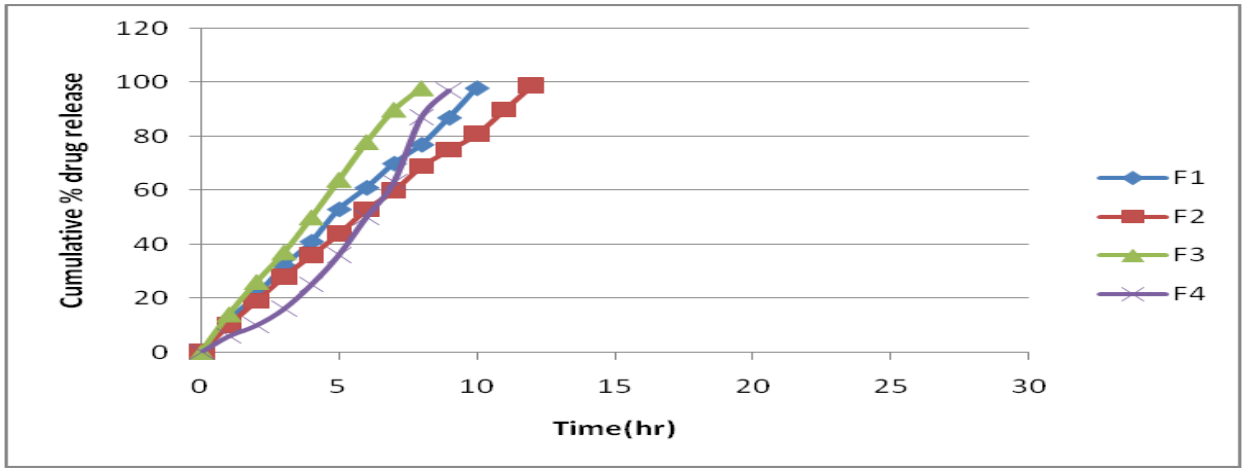

Fig. 1: % Drug release of formulation (F1-F4)

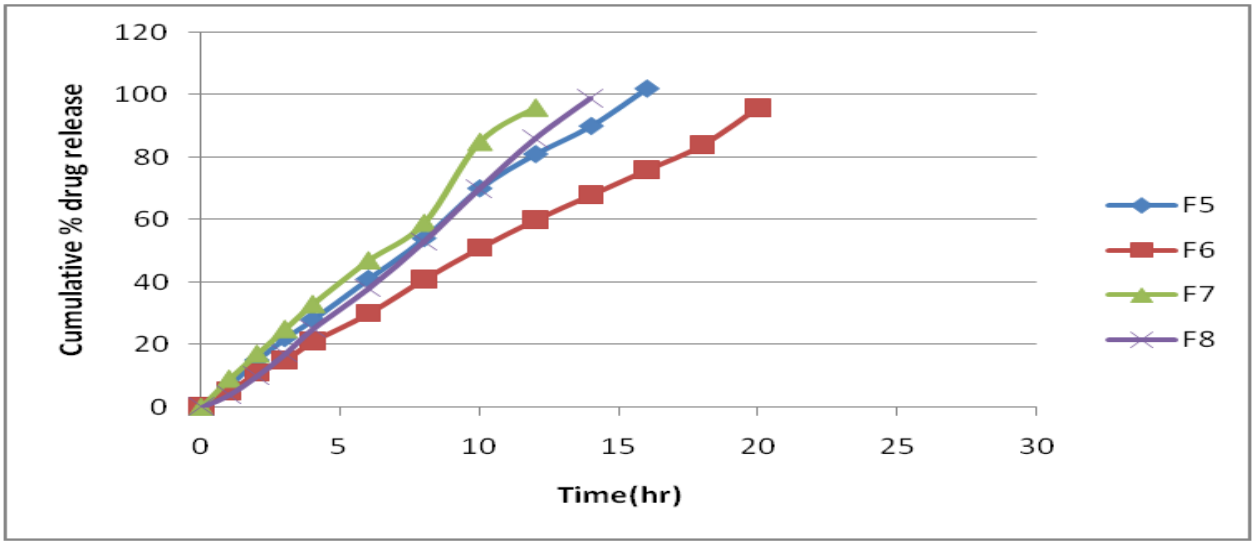

Fig. 2: % Drug release of formulation (F5-F8)

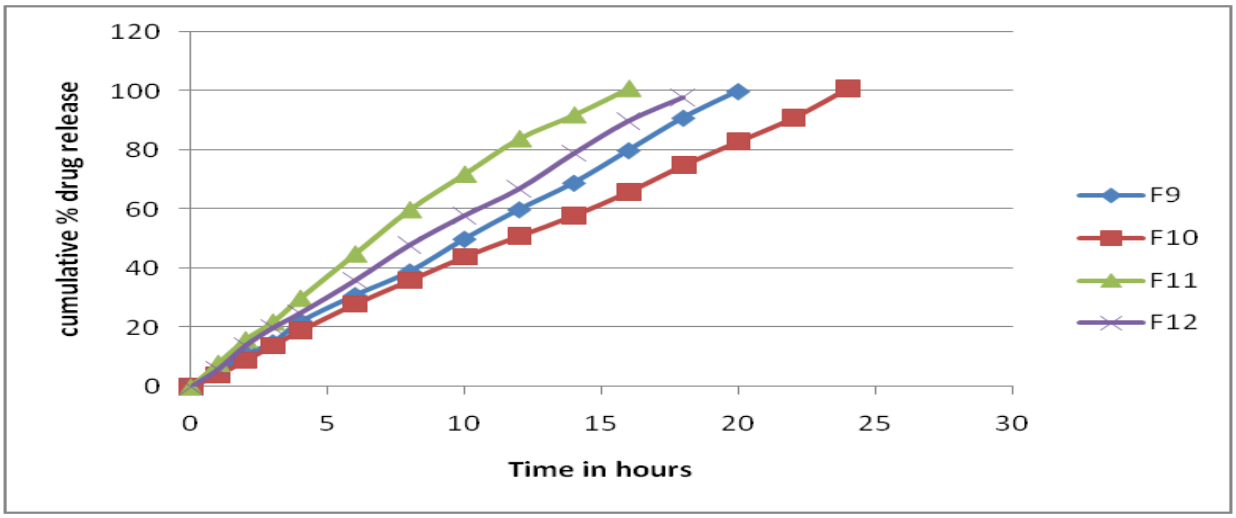

Fig. 3: % Drug release of formulation (F9-F12)

DISCUSSION:

Preformulation studies Drug excipient compatibility studies were performed by force degradation and Fourier transform infrared spectroscopy. Results showed that drug and excipients were compatible with each other. Evaluation of pre-compression parameters. The present investigation was undertaken to design, formulate and evaluate Pregabalin tablets for sustained release dosage form. The blends of different formulations were evaluated for angle of repose, bulkdensity, tapped bulk density, compressibility index and hausner‟s ratio. The results of bulk density, tapped bulk density, compressibility index and hausner‟s ratio are mentioned in (Table .No.2). The bulk density of the tablet blend was in the range of 0.26± 0.05 to 0.33± 0.03 g/ml; the tapped density was in the range of 0.32± 0.02 to 0.40± 0.04 g/ml, which indicates that the powder was not bulky. The blend indicated good flow properties for all the formulation with the angle of repose values 27° 39‟±0.55 to 34° 91‟±0.39 according to fixed funnel and free standing cone method. The results of compressibility index lies between range from 13.1±1.17 to 24.30±1.21, while hausner‟s ratio lies between 1.15±0.06 and 1.32±0.05 indicating good to excellent flow properties. Physicochemical evaluation of Pregabalin sustained release tablets. The tablets of different batches formulated were evaluated for test such as hardness, friability, uniformity of weight and drug content. The results obtained from all formulations were within the range. The weight variation test indicates that all the tablets were uniform with low standard deviation values and hence all formulation passed the test for uniformity of weight. The hardness of all the tablets was within the range of 5.3±0.03 to 6.4±0.08 kg/cm2 .The loss in friability test was in a range of 0.21 to 0.61%. The percentage drug content for different tablet formulations were discrete from 97.86% to 101.65%, were found to be within range (table.No.3). In vitro drug release studies In vitro dissolution studies (Table No 4 & Figure No 3) of all the formulations of sustained release tablets of Pregabalin were performed in 900 ml of 0.1 N hydrochloric acid for two hours and then in phosphate buffer 6.8 for remaining hours. In all studies, the temperature of the dissolution medium was maintained at 37+ 0. 50ºc.The Aliquots of 5 ml were withdrawn at regular intervals, filtered and analysed spectrophotometrically at 210 nm. From the result obtained, showed that all the pre-compression and post compression parameters are within limit for the batch and out of all the batch containing Polyox WSR 301 and Polyox WSR 303 (i.e. F9 and F10) was able to release drug for desirable time period. F9 shows release up to 20 hours and % drug release is 101.44±0.47 while F10 shows release up to 24 hours and % drug release is 100.67±0.57

CONCLUSION:

In the present study the attempt was made to formulate the sustained release matrix tablet of pregabalin using various sustained release polymers. The tablets were formulated using the direct compression technique and the compressed tablets were evaluated for their pre-compression and post compression parameters. The *In-vitro* dissolution study of the batch containing PEO WSR 301 (F9) and PEO WSR 303 (F10) showed a good sustaining effect on the release of drug.

REFERENCES:

1.Lachman L, Lieberman HA, Kanig JL. 1987. The Theory and Practice of Industrial Pharmacy. Bombay: Varghese Publishing House.

2.Patel N, Chaudhary A, Soni T, Sambyal M, Jain H. Controlled Drug Delivery System: A Review, Indo Am J Pharm Sci, 2016; 3(3): 227-233

3.John C, Morten C. 2002. The Science of Dosage Form Design Aulton: Modified release peroral dosage forms. Churchill Livingstone

4.Gujral R.S., Haque S.M., S. Kumar. African J of Pharm and Pharmacology 2009, 3(6):327-334.

5.Chaturvedi S, Singh S. Floating drug delivery systems: an approach to increase the gastric residence

time. A Review, Asian J. Pharm. Clin. Res., 2013; 6:1-9.
6.Siepmann J, Peppas N. Modelling of drug release from delivery systems based on hydroxypropyl methylcellulose. adv. Drug Deliv. Rev. 2001; 48:139–157.
7.Wilson CG, Washington N. 1989.In Physiological Pharmaceutical. UK; Ellis Horwood Chichester.
8.Shaikh R, Wolfson. A Mucoadhesive Drug Delivery System. J Pharm Bio Sci, 2011; 3:89-100.
9.Jain N. In Progress in controlled and novel drug delivery systems; 1st Ed; CBS Publishers and Distributors, New Delhi, Bangalore, pp 84-85.
10.Nagar B, Sheorey S, Agrawal V, Shah N, Shah J. Formulation and Evaluation of Oro dispersible Labetalol Tablet for Hypertensive Crisis. J of Drug Delivery & Therapeutics, 2013; 3(6):106-112.
11.Mohd A H, Lokeswara B V, Narottam P, Srinivasa R A. Formulation and evaluation of Sustained Release Matrix tablets of Montelukast Sodium. Int J of Pharm, 2012; 2(3):574-582.
12.Prabakaran P, Singh P, Kanaujia KS, Jaganathan A. Int J of Pharm, 2004; 284:95-108.
13.Sonar GS, Jain DK. Preparation and in vitro evaluation of bilayer and floating bioadhesive tablets of rosiglitazone meleate. J Pharma Sci, 2007; 2: 161-169.
14.Smith AA, KottaiMuthu A, Manavalan R. Formulation development and evaluation of ondansetron hydrochloride sustain release matrix tablet. J pharma Sci Res, 2009; 1(4): 48-54.
15.Patel K, Patel N, Jain H, Upadhyay U. Formulation and evaluation of floating tablet of ketorolac tromethamine. J Sci, 2015; 5(5): 339-342.
16.Gohel MC, Parikh RK, Nagori SA, Jena DG. Fabrication of Modified Release Tablet Formulation of Metoprolol Succinate Using Hydroxypropyl Methylcellulose and Xanthan Gum. AAPS Pharm Sci Tech, 2009;10:62-68.
17.Shabaraya AR, Aiswarya K, Azharuddin M. Formulation and Evaluation of Muco adhesive Bi-Layer Buccal Tablets of Labetalol HCl Using Natural Polymer. Int J of Advances in Pharm Biology and Chemistry,2012; 1(3):305-314.
18.Meka S, Rao N, Songa AS. Statistical Design and Evaluation of Propranolol HCl Gastric Floating Tablet. Acta Pharmaceutica Sinica B,2012; 2(1): 60-69