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# FORMULATION DEVELOPMENT AND EVALUATION OF FAST DISSOLVING TABLETS OF PREGABALIN

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## ABSTRACT

Pregabalin (PRE) is a structural analogue of γ-amino butyric acid, which is used to treat refractory partial seizures, diabetic neuropathy, post-therapeutic neuralgia, and social anxiety disorders. Its main site of action appears to be the $\alpha_2$-δ subunit of the voltage-dependent calcium channels that are widely distributed throughout the peripheral and central nervous system. The concept of formulating fast dissolving tablets containing PRE offers a suitable and practical approach in serving desired objective of faster disintegration and dissolution characteristics with increased bioavailability. Fast dissolving tablets of PRE were prepared by direct compression methods and blend was evaluated for the pre-compression parameters such as bulk density, compressibility, angle of repose etc. The tablets were prepared by using Croscarmellose sodium, Crospovidone and sodium starch glycolate, as superdisintegrants in different concentration along with microcrystalline cellulose. Total six formulations were prepared and evaluated for hardness, friability, weight variation, content uniformity, wetting time, water absorption ratio, disintegration time and *invitro* drug release. *In-vitro* dissolution studies are performed by using phosphate buffer pH 6.8 at 75 rpm by paddle method. Overall, the formulation F4containing of Croscarmellose sodium was found to be promising and has shown a disintegration time 45 sec. The stability studies were performed for two months (accelerated studies) as per ICH guidelines. The optimized formulation (F4) showed no significant variations for the tablets parameters and it was stable for the specified time period. Thus results conclusively demonstrated successful masking of taste and fastest disintegration of the formulated tablets in oral cavity.

## INTRODUCTION

Rapidly dissolving or quick dissolving dosage forms have acquired great importance in the pharmaceutical industry due to their unique properties and advantages [1, 2]. Of all the dosage forms administered orally, the tablet is one of the most preferred dosage forms. Disintegrates are agents integrated to tablet and some encapsulated formulations to promote the breakup of the tablet and capsule slugs into more small fragments in an aqueous environment thereby incrementing the available surface area and promoting a more rapid release of the drug substance.

They promote moisture penetration and dispersion of the tablet matrix. Tablet disintegration has received considerable attention as an essential step in obtaining fast drug release. The accentuation on the availability of drug highlights the importance of the relatively rapid disintegration of a tablet as a criterion for ascertaining uninhibited drug dissolution behavior. Number of factors affects the disintegration replace of tablets. The disintegrants have the major function to oppose the efficiency of the tablet binder and the physical forces that act under compression to compose the tablet. The stronger the binder, the more efficacious must be the disintegrating agents in order for the tablet to release its medication. Ideally, it should cause the tablet to disrupt, not only into the granules from which it was compressed, but additionally into powder particles from which the granulation was yare. Disintegrant are an essential component to tablet formulations. The ability to interact strongly with water is essential to disintegrate function. Combination of swelling and/or wicking and/or deformation is the mechanisms of disintegrant action.

A Disintegrant utilized in granulated formulation processes can be more efficacious if utilized both intra granularly and extra granularly thereby acting to break the tablet up into granules and having the granules further disintegrate to release the drug substance into solution. However, the portion of Disintegrant integrated intra granularly (in wet granulation processes) is conventionally not as efficacious as that integrated extra granularly due to the fact that it is exposed to wetting and drying (as a component of the granulation process), which reduces the activity of the disintegrant. Since a compaction process does not involve its exposure to wetting and

drying, the disintegrant used intragranularly inclines to retain good disintegration activity [3, 4]. Pregabalin (PRE; S-(3)-amino methyl hexanoic acid) is a structural analogue of γ -aminobutyric acid, which is used to treat refractory partial seizures, diabetic neuropathy, post-therapeutic neuralgia, and social anxiety disorders. Its main site of action appears to be the $\alpha_2$-δ subunit of the voltage-dependent calcium channels that are widely distributed throughout the peripheral and central nervous system [5-7].

PRE is a highly soluble and highly permeable drug, categorized according to the bio pharmaceutics classification system (BCS) as a class 1 compound. PRE has an oral bioavailability of more than 90% with an average elimination half-life of 6.3 h, and it is excreted unchanged in the urine [8]. The absorption of PRE is limited to the upper small intestine, where l-amino transporters that govern PRE absorption exclusively exist [9, 10]. In 2004, Pfizer introduced PRE to the market under the brand name Lyrica as a conventional, immediate release (IR)-type capsule with a recommended dosage regimen of 150-600 mg per day divided into 2 or 3 doses [11,12]. Therefore, modified release type dosage forms would be useful to reduce dosing frequency and improve patient compliance. In present study an attempt has been made to formulate the orally disintegrating tablets by direct compression method using sodium starch glycolate, Croscarmellose sodium and Crospovidone as the superdisintegrants for rapid dissolution of drug and absorption, which may produce the rapid onset of action.

## MATERIALS AND METHODS

Pregabalin was purchased from Sun Pharmaceutical Industries Limited, Mumbai, India. Crospovidone, Croscarmellose sodium and sodium starch glycolate was obtained from Hi-Media Laboratories Pvt. Ltd., Mumbai, India. Micro crystalline cellulose, mannitol, talc and magnesium stearate was procured from Central Drug House (P) Ltd. New Delhi. All other solvents and chemicals used were of analytical grade.

### PREFORMULATION STUDIES

#### *Determination of $\lambda_{max}$ of Pregabalin*

Accurately weighed 10 mg of drug was dissolved in 10 ml of 0.1N HCL solutions in 10 ml of volumetric flask. The resulted solution 1000µg/ml and from this solution 1 ml pipette out and transfer into 10 ml

volumetric flask and volume make up with 0.1N HCL solution. Prepare suitable dilution to make it to a concentration range of 10-50µg/ml Pregabalin from that take 2 ml of sample react with methyl orange and separate with chloroform. The spectrum of this solution was run in 400-800 nm range in U.V. spectrophotometer (Labindia-3000+).

***Drug-excipient compatibility study***

FTIR spectra of pure drugs, polymers used and blends were recorded on KBr disk method using Brukers Alpha Spectrophotometer with IR solution software to confirm the compatibility between drug and excipients.

Sample powder was thoroughly mixed by triturating with potassium bromide in a glass mortar with pestle and compressed into disks in a hydraulic press (Techno search Instruments, India). FTIR spectra of all the samples were recorded over a spectral region from 4700 to 400 cm-1 using 20 scans with 4 cm-1 resolution.

**Preparation of tablets of PRE**

Fast dissolving tablets of PRE were prepared by direct compression [13] according to the formulae given in Table 1. All the ingredients were passed through # 60 mesh separately. Then the ingredients were weighed and mixed in geometrical order and compressed into tablets of 200 mg using 8 mm round flat punches on on a Rimek mini press 16 station rotary compression machine.

**Table 1 Composition of PRE fast dissolving tablets**

| Ingredients (mg) | Formulation code | | | | | |
|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 |
| Pregabalin | 50 | 50 | 50 | 50 | 50 | 50 |
| Sodium starch glycolate | 15 | 30 | - | - | - | - |
| Croscarmellose sodium | _ | _ | 15 | 30 | - | - |
| Crospovidone | - | - | - | - | 15 | 30 |
| Mannitol | 10 | 10 | 10 | 10 | 10 | 10 |
| Microcrystalline cellulose | 114 | 99 | 114 | 99 | 114 | 99 |
| Talc | 5 | 5 | 5 | 5 | 5 | 5 |
| Magnesium stearate | 6 | 6 | 6 | 6 | 6 | 6 |
| Total weight | 200 | 200 | 200 | 200 | 200 | 200 |

**EVALUATION OF FAST DISSOLVING TABLETS**

***Pre-compression parameters***

***Angle of repose (θ)***

The frictional forces in a loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane.

$$\text{Tan } \theta = h/r$$

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

Where, θ is the angle of repose, h is the height, r is the radius.

The granules were allowed to flow through the funnel fixed to a stand at definite height. The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

***Bulk density***

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. Accurately weighed amount of granules taken in a 50 ml capacity measuring cylinder was tapped for 100 times on a plane hard wooden surface and estimated the LBD and TBD, calculated by using following formulas.

LBD (Loose Bulk Density) = Mass of Powder/Volume of Packing

TBD (Tapped Bulk Density) = Mass of Powder/Tapped Volume of Packing

***Compressibility index***

The compressibility index of the granules was determined by Carr's compressibility index**.**

Carr's index (%) = [(TBD – LBD)/TBD] × 100.

***Hausner's ratio***

Hausner's ratio is an indirect index of ease of measuring the powder flow. It was calculated by the following formula [14].

Hausner's ratio = Tapped density/Bulk density.

**EVALUATION OF TABLETS**

**Shape and color of tablets**

Uncoated tablets were examined under a lens for the shape of the tablet and colour was observed by keeping the tablets in light.

**Thickness**

Twenty tablets from the representative sample were randomly taken and individual tablet thickness was measured by using digital vernier caliper [15].

**Hardness**

Tablet hardness was measured by using Pfizer hardness tester. From each batch six tablets were measured for the hardness and average of six values was noted along with standard deviations and results were expressed in $Kg/cm^2$.

**Friability Test**

From each batch, ten tablets were accurately weighed and placed in the friability test apparatus (Roche friabilator). Apparatus was operated at 25 rpm for 4 minutes and tablets were observed while rotating. The tablets were then taken after 100 rotations, de dusted and reweighed. The friability was calculated as the percentage weight loss.

% friability was calculated as follows

% Friability = (W1 – W2) x 100/W1

Where W1 = Initial weight of the 10 tablets, W2 = Final weight of the 10 tablets after testing.

Friability values below 0.5-1% are generally acceptable.

**Weight Variation Test**

To study weight variation individual weights (WI) of 20 tablets from each formulation were noted using electronic balance. Their average weight (WA) was calculated. Percent weight variation was calculated as follows. Average weights of the tablets along with standard deviation values were calculated.

**Drug content**

The test is mandatory for tablets with 10 mg or less weight of active ingredient. Ten randomly selected tablets from each formulation (F1 to F6) were finely powdered and Drug equivalent to 10 mg of drug dissolved in 10 ml phosphate buffer pH 6.8 sonicate it for 20 minutes, till the entire drug leached out from complex, then the solution was filtered through whatman filter paper No. 41. From this solution take 1 ml and diluted up to 100 ml with phosphate buffer pH 6.8 and the drug content was determined spectrophotometrically at 408 nm.

**In vitro disintegration time**

The disintegration test was performed using an USP disintegration apparatus, with distilled water at 24±0.50C. The time reported to obtain complete disintegration of six tablets were recorded and average was reported.

**Dissolution rate studies**

The prepared tablets were evaluated for *in vitro* drug release. The drug release studies were carried out using USP XXII paddle type Dissolution test apparatus. A tablet placed in dissolution media (900 ml) which was stirred at 75 rpm maintained at 37±0.2°C.

Samples were withdrawn at different time interval and compensated with same amount of fresh dissolution medium. Volume of sample withdrawn was made up to 10ml Phosphate buffer pH 6.8. The samples withdrawn were assayed spectrophotometrically at 408 nm using UV visible spectrophotometer. The release of drug was calculated with the help of standard curve of PRE [16, 17].

**Mathematical treatment of *in-vitro* release data**

The quantitative analysis of the values obtained in dissolution/release tests is easier when mathematical formulas that express the dissolution results as a function of some of the dosage forms characteristics are used.

**Zero-order kinetics**

The pharmaceutical dosage forms following this profile release the same amount of drug

by unit of time and it is the ideal method of drug release in order to achieve a pharmacological prolonged action. The following relation can, in a simple way, express this model:

$$Q_t = Q_o + K_o t$$

Where $Q_t$ is the amount of drug dissolved in time t, $Q_o$ is the initial amount of drug in the solution (most times, $Q_o$=0) and $K_o$ is the zero order release constant.

**First-order kinetics**

The following relation expresses this model:

$$\log Q_t = \log Q_o + \frac{K_1 t}{2.303}$$

Where $Q_t$ is the amount of drug dissolved in time t, $Q_o$ is the initial amount of drug in the solution and $K_1$ is the zero order release constant.

In this way a graphic of the decimal logarithm of the released amount of drug versus time will be linear. The pharmaceutical dosage forms following this dissolution profile, such as those containing water-soluble drugs in porous matrices, release drug in a way that is proportional to the amount of drug remaining in its interior, in such way, that the amount of drug released by unit of time diminish.

**Higuchi model**

Higuchi developed several theoretical models to study the release of water-soluble and low soluble drugs in semi-solid and/or solid matrixes. Mathematical expressions were obtained for drug particles dispersed in a uniform matrix behaving as the diffusion media.

The simplified Higuchi model is expressed as:

$$Q = K_H \cdot t^{1/2}$$

Where Q is the amount of drug released in time t and $K_H$ is the Higuchi dissolution constant. Higuchi model describes drug release as a diffusion process based in the Fick's law, square root time dependent. This relation can be used to describe the drug dissolution from several types of modified release pharmaceutical dosage forms such as transdermal systems and matrix tablets with water-soluble drugs.

**Korsmeyer-Peppas model**

Korsmeyer *et al.* used a simple empirical equation to describe general solute release behaviour from controlled release polymer matrices:

$$\frac{M_t}{M_\infty} = a\, t^n$$

Where $M_t/M_\infty$ is fraction of drug released, a is kinetic constant, t is release time and n is the diffusional exponent for drug release. 'n' is the slope value of log $M_t/M_\infty$ versus log time curve. Peppas stated that the above equation could adequately describe the

release of solutes from slabs, spheres, cylinders and discs, regardless of the release mechanism. Peppas used this n value in order to characterize different release mechanisms, concluding for values for a slab, of *n* =0.5 for fickian diffusion and higher values of *n*, between 0.5 and 1.0, or *n* =1.0, for mass transfer following a non-fickian model. In case of a cylinder *n* =0.45 instead of 0.5, and 0.89 instead of 1.0. This equation can only be used in systems with a drug diffusion coefficient fairly concentration independent.

To the determination of the exponent *n* the portion of the release curve where $M_t/M_\infty$ < 0.6 should only be used. To use this equation it is also necessary that release occurs in a one-dimensional way and that the system width-thickness or length-thickness relation be at least 10. A modified form of this equation was developed to accommodate the lag time (*l*) in the beginning of the drug release from the pharmaceutical dosage form.

$$\frac{M_{t-l}}{M_\infty} = a\,(t-l)^n$$

When there is the possibility of a burst effect, b, this equation becomes:

$$\frac{M_t}{M_\infty} = at^n + b$$

In the absence of lag time or burst effect, l and b value would be zero and only $at^n$ is used. This mathematical model, also known as Power Law, has been used very frequently to describe release from several different pharmaceutical modified release dosage forms [18-20].

## RESULTS AND DISCUSSION

The $\lambda_{max}$ of PRE was found to be 408 nm by using U.V. spectrophotometer (Labindia-3000+) in linearity range 10-50µg/ml Fig 1. Tablet powder blend was subjected to various pre-compression parameters Table 2. The angle of repose values indicates that the powder blend has good flow properties. The bulk density, tapped density, compressibility index and Hauser's ratio of all the formulations was found to be within the range and showing that the powder has well flow properties.

The results of post-compression parameters such as the uniformity of weight, hardness, thickness, friability and drug content of the tablets are given in Table 3. All the tablets of different batches complied with the official requirements of uniformity of weight. The hardness of the tablets ranged from 3.6 to3.9 kg/cm$^2$ and the friability values were less than 0.8% indicating that the tablets were compact and hard. The

thickness of the tablets ranged from 2.2 to 2.4 mm. All the formulations satisfied the content of the drug as they contained 98.89 to 99.45 % of PRE and good uniformity in drug content was observed.

Thus all the physical attributes of the prepared tablets were found be practically within control. The result in vitro disintegration were within the prescribe limit and comply with the criteria for orally disintegrating tablets. The tablets were evaluated for in vitro dissolution studies in phosphate buffer pH 6.8 for 10 min. The results of the optimized formulation F4 showed maximum drug release i.e. 98.21 % at the end of 10 min. The results of release studies of formulations F4 was shown in Table 4.

The *in vitro* drug release data of the optimized formulation F4 was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic equation, Higuchi's and Korsmeyer's models in order to determine the mechanism of drug release. When the regression coefficient values of were compared, it was observed that 'r' values of Korsmeyer's models was maximum i.e. 0.996 hence indicating drug release from formulations was found to follow Korsmeyer's models kinetics Table 5 & Fig. 2-5.

**Figure 1 Determination of $\lambda_{max}$ of Pregabalin at 408.0 nm**

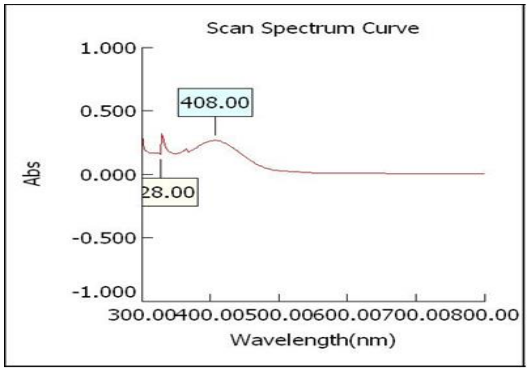



**Table 2 Results of pre-compression parameters of Pregabalin**

| Formula | Parameters | | | |
|---|---|---|---|---|
| | Bulk density (gm/ml) | Tapped bulk density (gm/ml) | Carr's Index (%) | Hausner's Ratio |
| F1 | 0.325 | 0.426 | 23.709 | 1.311 |
| F2 | 0.335 | 0.448 | 25.223 | 1.337 |
| F3 | 0.326 | 0.431 | 24.362 | 1.322 |
| F4 | 0.328 | 0.429 | 23.543 | 1.308 |
| F5 | 0.329 | 0.432 | 23.843 | 1.313 |
| F6 | 0.331 | 0.432 | 23.380 | 1.305 |

**Table 3 Results of post-compression parameters of all formulations**

| F. Code | Hardness (kg/cm$^2$)* | Friability (%)* | Weight variation (%)* | Thickness (mm)* | Drug content (%)* | Disintegration Time (sec.)* Mean ± SD |
|---|---|---|---|---|---|---|
| F1 | 3.8 | 0.785 | 200 | 2.3 | 98.89 | 65 |
| F2 | 3.9 | 0.658 | 205 | 2.2 | 99.12 | 80 |
| F3 | 3.8 | 0.789 | 206 | 2.4 | 98.98 | 72 |
| F4 | 3.7 | 0.658 | 198 | 2.4 | 99.45 | 45 |
| F5 | 3.6 | 0.754 | 196 | 2.3 | 98.98 | 62 |
| F6 | 3.7 | 0.658 | 204 | 2.4 | 99.32 | 32 |

***Average of three determinations (n=3)**

**Table 4 *In-vitro* drug release data for optimized formulation F4**

| Time (min) | Square Root of Time(h)$^{1/2}$ | Log Time | Cumulative* % Drug Release | Log Cumulative % Drug Release | Cumulative % Drug Remaining | Log Cumulative % Drug Remaining |
|---|---|---|---|---|---|---|
| 2 | 1.414 | 0.301 | 45.23 | 1.655 | 54.77 | 1.739 |
| 5 | 2.236 | 0.699 | 73.32 | 1.865 | 26.68 | 1.426 |
| 10 | 3.162 | 1 | 98.21 | 1.992 | 1.79 | 0.253 |

**Table 5 Regression analysis data**

| Batch | Zero Order | First Order | Higuchi | Korsmeyer-Peppas |
|---|---|---|---|---|
| | $R^2$ | $R^2$ | $R^2$ | $R^2$ |
| **F4** | 0.968 | 0.968 | 0.995 | 0.996 |

**Figure 2 Zero order release Kinetics**

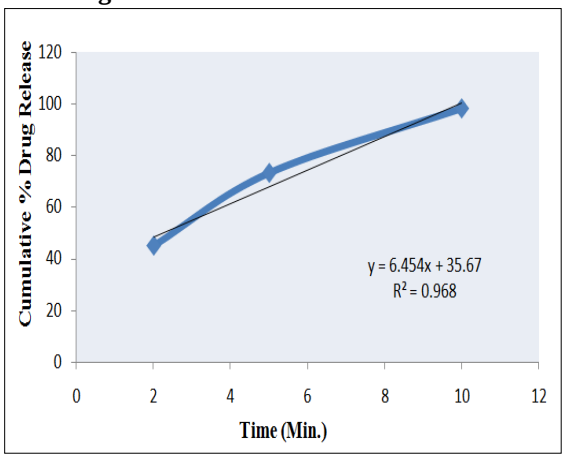



**Figure 3 first order release kinetics**

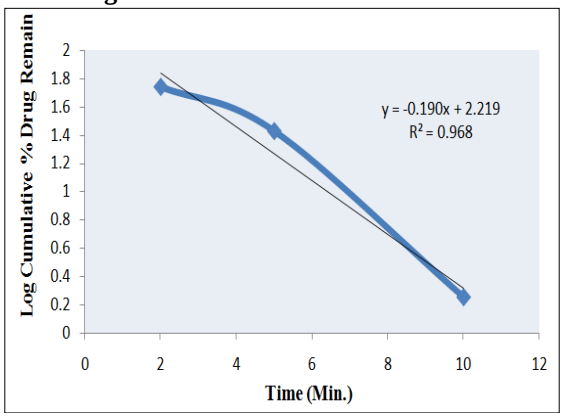



**Figure 4 Higuchi release kinetics**

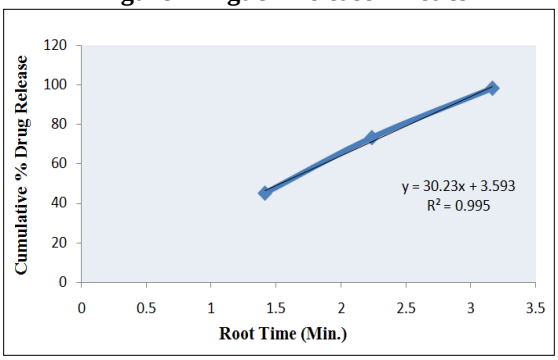
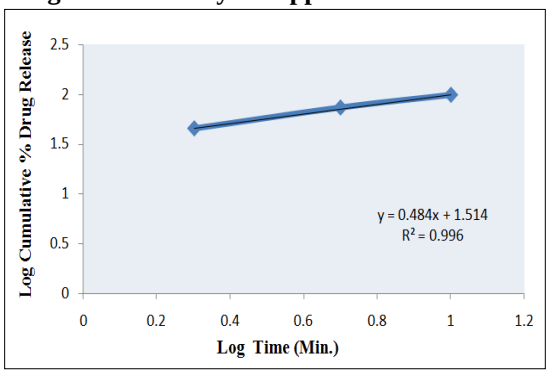



**Figure 5 Korsmeyer-Peppas release kinetics**




## CONCLUSION

Thus from the whole research work it can be concluded that, the oral fast dissolving tablet of PRE were formulated and evaluated for various parameters. From the compatibility studies by IR of drug it was found to be compatible with other formulation excipients. All evaluation parameter were within specification. The Croscarmellose sodium shown faster drug release than sodium starch glycolate and Crospovidone. Formulation F4 release maximum drug within the 10mins.ie. 98.21 % and shown minimum disintegration time i.e. 45sec than

other formulation and hence considered best formulation.

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## REFERENCES

1. Liang AC, Chen LH, 2001. Fast-dissolving intraoral drug delivery systems. Exp Opin Ther Patents; 11:981–6.
2. Borsadia S, O'Halloran D, Osborne JL, 2003. Quick dissolving films a novel approach to drug delivery. Drug Deliv Technol; 3:63-6.
3. H C Ansel, N G Popvich, L V Allen, 1998. Pharmaceutical Dosage Forms and Drug Delivery System, 1st edition, 1998.
4. N K Jain, S N Sharma, 1998. A Text Book of Professional Pharmacy, 4th edition, 1998.
5. Gee NS, Brown JP, Dissanayake VU, Offord J, Thurlow R, Woodruff GN, 1996. The novel anticonvulsant drug, gabapentin (Neurontin), binds to the alpha 2 delta subunit of a calcium channel. J. Biol. Chem. 271, 5768-5776.
6. Bryans JS, Wustrow DJ, 1999. 3-substituted GABA analogs with central nervous system activity: a review. Med. Res. Rev. 19, 149-177.
7. Bian F, Li Z, Offord J, Davis MD, McCormick J, Taylor CP, Walker LC, 2006. Calcium channel alpha 2 delta type 1 subunit is the major binding protein for pregabalin in neocortex, hippocampus, amygdala, and spinal cord an ex vivo auto radiographic study in alpha 2 delta type 1 genetically modified mice. Brain Res. 1075, 68-80.
8. French JA, Kugler AR, Robbins JL, Knapp LE, Garofalo EA, 2003. Dose response trial of pregabalin adjunctive therapy in patients with partial seizures. Neurology 60, 1631-1637.
9. Su TZ, Feng MR, Weber ML, 2005. Mediation of highly concentrative uptake of pregabalin by L-type amino acid transport in Chinese hamster ovary and Caco 2 cells. J. Pharmacol. Exp. Ther. 313, 1406-1415.
10. Cundy KC, Branch R, Chernov Rogan, T, Dias T, Estrada T, Hold K, Koller K, Liu X, Mann A, Panuwat M, Raillard SP, Upadhyay S, Wu QQ, Xiang JN, Yan H, Zerangue N, Zhou CX, Barrett

RW, Gallop MA, 2004. XP13512 (+/-) 1-(alpha iso butanoyl oxyethoxy) carbonyl] amino methyl) 1-cyclohexane acetic acid], a novel gabapentin prodrug: I. Design, synthesis, enzymatic conversion to gabapentin, and transport by intestinal solute transporters. J. Pharmacol. Exp. Ther. 311, 315-323.

11. NDA 2004. Lyrica (Pregabalin) Capsules Clinical Pharmacology Bio-pharmaceutics Review(s). CDER, U.S. Food and Drug Administration, December 30.
12. Dworkin RH, Kirkpatrick P, 2005. Pregabalin. Nat. Rev. Drug Discov. 4, 455-456.
13. Kuchekar BS, Badhan AC, Mahajan HS, 2004. Mouth dissolving tablets of salbutamol sulphate: A novel drug delivery system. Indian Drugs; 41:592-8.
14. Subramanyam CVS. 2001. Textbook of Physical Pharmaceutics. 3rd ed. Vallabh Prakashan: Delhi 181-234.
15. T Salsa, F Veiga ME, 1997. Pina Oral controlled-release dosage forms. Cellulose ether polymers in hydrophilic matrices Drug Dev Ind Pharm; 23:929-938.
16. Mohd. Adil Khan, Girijesh Kumar Pandey, Amit Joshi, BK Dubey, Amit Kumar Jain, Prabhat Jain. 2019. Formulation development and evaluation of fast dissolving oral film of a lipid-lowering drug. Asian Journal of Pharmaceutical Education and Research, Vol 8, Issue 1 (12-22)
17. Surya Prakash Gautam, Janki Prasad Rai, Uma Billshaiya, Nilesh Jain, Pradeep Vikram, Deepak Kumar Jain, 2013. Formulation and evaluation of mouth dissolving tablet of loperamide. International Journal of Pharmaceutical Sciences and Research; Vol. 4(5): 1782-1788.
18. Brahamankar DM, Jaiswal SB, 2009. Bio-pharmaceutics and pharmaco-kinetics treatise, pharmacokinetics: basic consideration. 2nd ed. Vallabh Prakashan; pp. 240e3.
19. Higuchi T, 1963. Mechanism of sustained action medication, theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J Pharm Sci; 52:1145-9.
20. Korsmeyer RW, Gumy R, Doelker E, Buri P, Peppas NA, 1983. Mechanism of solute release from porous hydrophilic polymer. Int J Pharm; 15:25-35.