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# Formulation and Evaluation of Bilayer Tablets of Sustained Release Pregabalin and Immediate Release Methylcobalamin

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## ABSTRACT

Neuropathic pain is intense in nature and difficult to maintain. The main aim of this study is to provide maximum relief from pain. The objective was to prepare bilayer tablet comprising of pregabalin and methylcobalamin for effective treatment of neuropathic pain. Methylcobalamin was formulated as immediate release (IR) layer using super-disintegrant sodium starch glycolate (SSG) whereas pregabalin was formulated as sustained release (SR) layer using polymers hydroxypropyl methyl cellulose (HPMCK4M, K100M) to deliver the drug at sustained manner effective for the treatment of neuropathic pain. The SR layer of pregabalin is prepared by wet granulation method and IR layer of methylcobalamin is prepared by direct compression method. Tablet blends were evaluated through various pre-compression and post-compression tests. Super disintegrant, SSG at 20% concentration produced excellent results for immediate release of methylcobalamin to exert its action and other additional beneficial effects. The K100M and K4M grade of HPMC produced excellent SR efficiency. Optimum formulation released methylcobalamin and pregabalin at 98.92% in 45 min and 97.81% in 12 h from respective layers. Pre-compression and post-compression parameters of optimized IR layer comprising Methylcobalamin and SR layer comprising pregabalin exhibit satisfactory results. Bilayer tablet of Methylcobalamin and pregabalin prove to be effective as a combination therapy for the treatment of neuropathic pain by sequential release of the drug.

**Keywords:** Pregabalin,Methylcobalamin,bilayer tablet,hydroxypropyl methyl cellulose,sodium starch glycolate, superdisintegrant.

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## INTRODUCTION

Bilayer tablets is an innovative technique developed by pharmaceutical researchers whereby two drugs or two different drug release profiles can be given as a single dosage form. The use of this innovative technique has been widely accepted in the industry for its versatile application[1]. The use of this bilayer technology has reduced the shortcomings of conventional tablets. Bilayer tablet is an improved technology to overcome the shortcomings of the single layered tablets[2]. Combination products, also known as fixed dose combinations are combination of two or more active drugs produced in a single-dosage form. They provide the advantages of combination therapy while reducing the number of prescriptions and the attendant administrative costs and improving patient compliance[3].

Neuropathic pain (NP) is intense in nature and difficult to manage. Thus, the main goal in the treatment regimen is to provide maximum relief from pain. Neuropathic pain caused by various central and peripheral nerve disorders is especially problematic because of its severity, chronicity and resistance to simple analgesics. The condition affects 2% – 3% of the population, is costly to the health care system and is personally devastating to the people who experience it. The management of NP is difficult due to the inadequacies of the existing therapeutic options. Even the well-established drugs used in the management of peripheral neuropathy have limitations with respect to dosing regimen, unpredictable effectiveness, delay in the onset of the analgesic effects and tolerability[4].

Pregabalin (PB), a member of the gamma aminobutyric acid class, is considered as one of the first-line drugs for the treatment of NP. It has a high affinity for the auxiliary α2δ subunits of the voltage-gated calcium channel and thus blocks $Ca^{2+}$ influx into nerve terminals, which leads to reduced transmitter release. It has been reported that pregabalin is effective for both central and peripheral NP. After commencement of treatment, pain relief is seen in the first week, with improvement that is dose related from 150 to 600 mg/day. Pregabalin has also been shown to have beneficial effects on sleep and mood disturbances[5]. It is freely soluble in water both in acid and basic aqueous solution. It is well absorbed after oral administration and largely excreted by renal excretion[6].

Methylcobalamin (MC) is an essential element in the synthesis of the myelin sheath and in the maintenance of nerve function. The myelin sheath provides insulation to the nerve and aids in the proper and rapid conduction of impulses along the nerve. The damage to the myelin sheath is due to deficiency of vitamin B12. Methylcobalamin has an important role in the regeneration of myelin sheath and helps to restore the function of the nerve in neuropathy[7-8].

This is novel type of smart and advanced drug delivery system in the form of bilayer tablet used for oral administration of methylcobalamin as immediate release (IR) and Pregabalin as sustained release (SR) for effective treatment of neuropathy by combination therapy.

## MATERIALS AND METHOD

### Materials

Pregabalin and methylcobalamin were obtained as a gift sample from Sai Mirra Innopharm Pvt. Ltd., Chennai. Hydroxypropyl methylcellulose (HPMC) K100M, K4M, lactose, poly vinyl pyrrolidone K30 (PVP K30), isopropyl alcohol was purchased from Sigma-Aldrich Chemicals Pvt. Ltd., All other solvents and chemicals used were of analytical standard.

### Drug-excipients compatibility studies

The compatibility of drug and polymer under the experimental conditions is an important pre-requisite and it is, therefore, necessary to confirm that the drug does not react with excipients.

The interaction study of drug and excipients was performed by FTIR spectroscopic analysis. FTIR spectra of drug and the physical mixture of drug and excipients were recorded on a Fourier-transform infrared spectrophotometer (FTIR-8400 S, Shimadzu, Japan) in the range 4000– 400 $cm^{-1}$ and observed for the interaction between drug and excipients. The scanning was performed at scanning speed 2 mm/sec with resolution of 4 $cm^{-1}$over the region 4000-400 cm−1.The scans were evaluated for presence of principle peaks of drug, shifting and masking of drug peaks, and appearance of new peaks due to polymer interaction.

### Construction of Calibration Curve of pregabalin and Methylcobalamin:[9]

Standard dilutions were prepared in the range of 30-150 $\mu$g/mL using distilled water for pregabalin and absorbance was determined at $\lambda$max (222 nm) in UV spectrophotometer (UV-1700, Shimadzu). Similarly standard dilutions were prepared in the range of 0.6-3$\mu$g/mL using distilled water for methylcobalamin and absorbance was determined at $\lambda$max (219 nm) in UV spectrophotometer. From the values obtained, standard graph was plotted between concentration and absorbance values.The simultaneous equation method for simultaneous estimation of pregabalin and methylcobalamin in bilayer tablet was used[9].

### Formulation of bilayer tablets:

Bilayer tablet is prepared in two stages as following

Formulation of Methylcobalamin immediate release layer

Formulation of Pregabalin sustained release layer

### Formulation of Methylcobalamin (MC) immediate release layer[10]:

The composition for all batches are represented in Table 1. Drug and excipients were accurately weighed and shifted through sieve No.40 and mixed in a polybag. The sifted powders were thoroughly mixed for approximately 5 min and again passed through sieve No.40 to get uniform particle size. Magnesium stearate and talc was added into the powder mixture for lubrication after passing through sieve No.40 and 0.125%w/w of iron oxide red previously sifted to sieve No.100 was added to the above mixed mixture and blended thoroughly to ensure uniform colour.

**Table 1 : Composition of methylcobalamin IR layer**

| Sr No. | Ingredients (mg) | F1 | F2 | F | F4 |
|---|---|---|---|---|---|
| 1 | Methylcobalamin | 1 | 1 | 1 | 1 |
| 2 | Lactose | 28 | 22 | 26.5 | 31.25 |
| 3 | MCC | 32 | 33 | 30 | 31.25 |
| 4 | Magnesium stearate | 1 | 1 | 1 | 1 |
| 5 | Talc | 3 | 3 | 3 | 3 |
| 6 | Sodium starch glycolate | 10 | 15 | 13.5 | 7.5 |
| | Total weight | 75 | 75 | 75 | 75 |

**Formulation of sustained release layer of pregabalin (PB)[11]:**

The SR granules were prepared by wet granulation technique. The composition of all formulations are given in Table 2. Required quantity of pregabalin, lactose and polymers (HPMC K100M and K4M) was weighed and passed through sieve No.40 and were mixed homogenously in a polybag for about 5-10 min and was taken in a mortar.To the mortar 5% PVPK30 in isopropyl alcohol was added as granulating agent.The wet mass was passed through sieve No.10 and dried in hot air oven at 50$^{o}$C for 30 min. Dried granules were screened through sieve No.14. Finally 10% fine was added and granules were lubricated with magnesium stearate and colloidal silicon dioxide and mixed for 5 min.

The granules were processed for compression using 10 mm round flat faced punches of 8 punch tablet machine (Cadmach).

**Table 2 : Composition of pregabalin SR layer**

| Sr.No | Ingredients(mg) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Pregabalin | 75 | 75 | 75 | 75 | 75 | 75 | 75 | 75 | 75 |
| 2 | HPMC K4M | 67.5 | 67.5 | 67.5 | 22.5 | 45 | 45 | 45 | 22.5 | 22.5 |
| 3 | HPMC K100 M | 90 | 45 | 135 | 45 | 45 | 90 | 135 | 135 | 90 |
| 4 | PVP K-30 | 45 | 45 | 45 | 90 | 90 | 90 | 45 | 67.5 | 90 |
| 5 | IPA | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. |
| 6 | Lactose | 157 | 202 | 112 | 202 | 179.5 | 134.5 | 134.5 | 134.5 | 157 |
| 7 | Colloidal silicon dioxide | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 |
| 8 | Magnesium stearate | 7.5 | 7.5 | 7.5 | 7.5 | 7.5 | 7.5 | 7.5 | 7.5 | 7.5 |
| | Total weight | 450 | 450 | 450 | 450 | 450 | 450 | 450 | 450 | 450 |

**Pre-compression parameters:**

Before the compression process, both blends of granules were evaluated for angle of repose, density, compressibility index and Hausner's ratio as per reported methods[12].

**Evaluation of MC immediate release (IR) tablets and PB sustained release (SR) tablets:**

The following tests were done for the MC IR tablets and PB SR tablets separately before compression of the bilayer tablets.

**Weight variation:**

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets were calculated.

**Hardness:**

The tablet-crushing load is the force required to break a tablet by compression. Hardness was measured by using hardness tester (Monsanto hardness tester). For each batch, six tablets were selected randomly and evaluated. Hardness of about 4-6 $kg/cm^2$ is considered to be minimum for uncoated tablets and for mechanical stability.

**Friability:**

Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the purpose. Preweighed sample of ten tablets were placed in the friabilator, which was then operated for 100 revolutions. After 100 revolutions, the tablets were dusted and reweighed. Compressed tablets should not lose more than 1% of their weight.

Percentage friability = initial weight-final weight/ Final weight X 100

**Drug content:**

20 tablets were weighed and powdered and equivalent weight of MC and PB was accurately weighed, transferred into a 100 ml volumetric flask and dissolved in water. It was suitably diluted to obtain concentration of 100 µg/ml of PB and 3 µg/ml of MC and assayed for drug content using a double-beam UV/VIS spectrophotometer (Shimadzu 1700) at 222 and 219 nm respectively.

***In Vitro* Drug Dissolution Test:**

Dissolution study of MC tablets was performed in 0.1 N Hcl as dissolution medium using USP dissolution test apparatus II at 50 rpm and 37°C ± 0.5°C temperature. Test sample (5 ml) was withdrawn at a specific time interval (5, 10, 15, 30 and 45 min) and replaced with fresh dissolution media maintained at 37°C ±0.5°C. The test sample was filtered and the concentration of dissolved drug was determined using UV-Vis spectrophotometer (Shimadzu 1700) λ max 219 nm.

*In vitro* release profile of PB sustained release tablets were performed in pH 6.8 phosphate buffer as dissolution medium using USP dissolution test apparatus II at 50 rpm and 37°C ± 0.5°C temperature. Test sample (5 ml) was withdrawn at a specific time interval (2,4,6,8,10, and 12 h) and replaced with fresh dissolution media maintained at 37°C ±0.5°C. The test sample was filtered and the concentration of dissolved drug was determined using UV-Vis spectrophotometer (Shimadzu 1700) at λ max 222 nm[13].

**Compression of bilayer tablets:**

Optimized batch of MC (F2) and PB (F1) was selected for formulation of bilayer tablet and was compressed using 12 mm round flat faced punch of the 8 station Cadmach compression machine. Development of bilayer tablets was carried in two different stages. Blends of IR layer of methylcobalamin and SR layer of pregabain were prepared separately and after optimization of individual layer the bilayer tablets were prepared using selected formulas. First, the granules of SR layer were poured in the die cavity and compressed with moderate force. Then, the upper punch was lifted and the IR granules were poured in the die cavity, containing initially compressed SR layer and compressed with full force to form bilayer tablet with hardness of 5-8 kg / $cm^2$.

**Evaluation of Bilayer tablets of MC and PB:**

Bilayer tablets were evaluated for weight variation, friability, hardness as per the procedure previously mentioned.

**Drug content:**

20 tablets were weighed and powdered and equivalent weight of MC and PB was accurately weighed, transferred into a 100 ml volumetric flask and dissolved in water. It was suitably diluted to obtain concentration of 100 µg/ml of PB and 3 µg/ml of MC and assayed for drug content using a double-beam UV/VIS spectrophotometer (Shimadzu 1700) at 222 and 219 nm using simultaneous equation[9].

**Dissolution test:**

The *in vitro* dissolution studies were carried out in two phases using USP type II apparatus at 50 rpm. The dissolution medium (900mL) consisting of 0.1 N Hcl for the was used for the first 2 h and then replaced with phosphate buffer pH 6.8 (900mL) for intestinal phase, maintained at 37°C ± 0.5°C. The drug release at different time intervals was determined by simultaneous equation method by measurement of absorbance at two wavelengths 219 nm (λ max of methylcobalamin) and 222 nm (λ max of pregabalin) and calculation of absorptivity values at both wavelengths[9].

**Kinetic Data Analysis:**

In order to investigate the kinetics of drug release from SR layer of bilayer tablets, the data of *in vitro* release of pregabalin were fitted to various kinetic models. *In vitro* release data was fitted to a zero-order ($m_0$–m = Kt), first order (log m = log $m_0$–Kt/2.303) and Higuchi model ($m_0$–m = $Kt^{1/2}$) where m is the amount of the drug remaining in the formulation at time t and m0 is the initial amount of the drug in the formulation. The regression coefficient values ($r^2$) were calculated for all the models. Korsmeyer–Peppas equation ($M_t/M_0 = Kt^n$) was used to study the diffusion mechanism by analyzing the diffusion exponent ‘‘n”. If $n \leq 0.45$, the release follows fickian mechanism, if $0.5 \leq n \leq 0.8$, the release follows non fickian mechanism[10].

**Stability Study:**

The optimized bilayer tablets were packed in HDPE (high density poly ethylene) containers and kept in stability chamber at 40°C/75% RH. After specific period of storage for stability, the tablets were evaluated for physical parameters, in-vitro drug release and assay.

## RESULTS AND DISCUSSION

**Drug-Excipient Compatibility Studies by FTIR:**

As part of compatibility studies, FT-IR studies were performed as shown in Figure 1-4 for both drugs along with the excipients to detect any major interference between drug and excipients. There was no significant shift in the positions of wave numbers when compared to that of the pure drugs. As there is no interaction observed between the drugs and excipients of the formulations, these excipients were chosen for the formulations

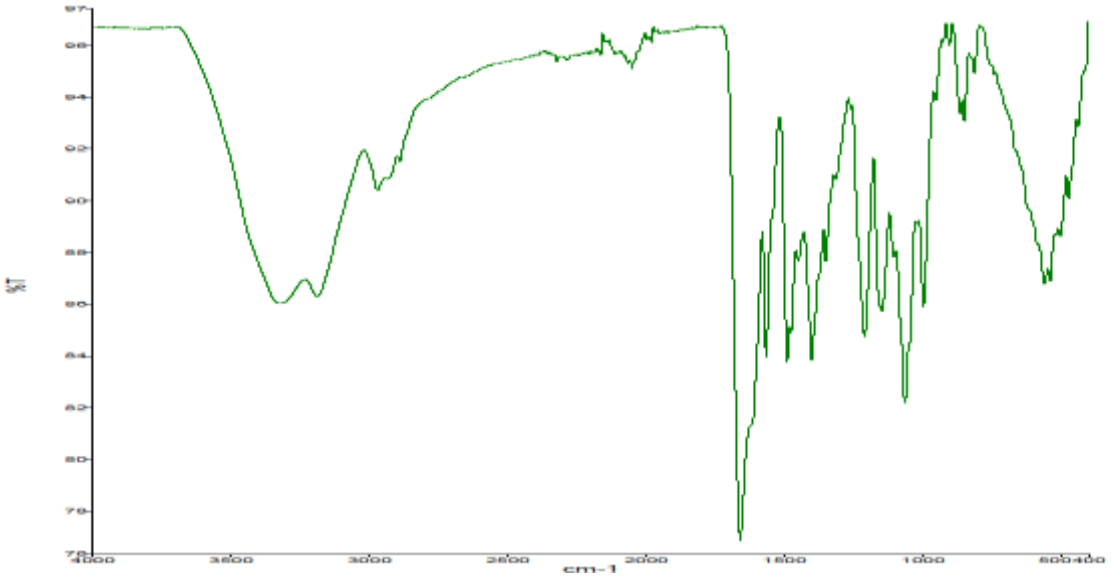


**Figure 1: FTIR spectrum of methylcobalamin**

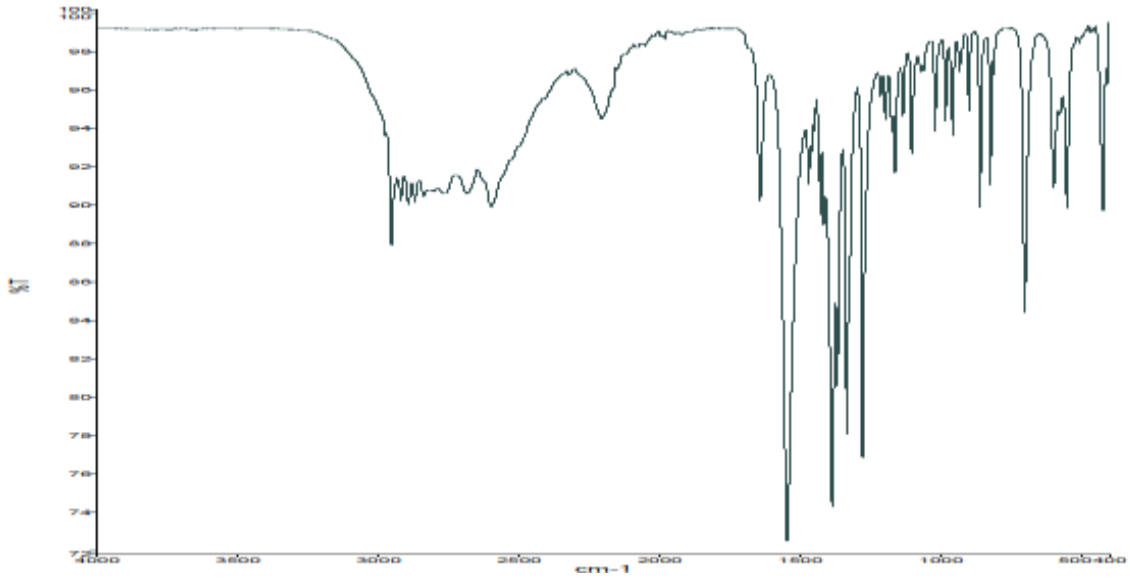

**Figure 2: FTIR spectrum pregabalin**

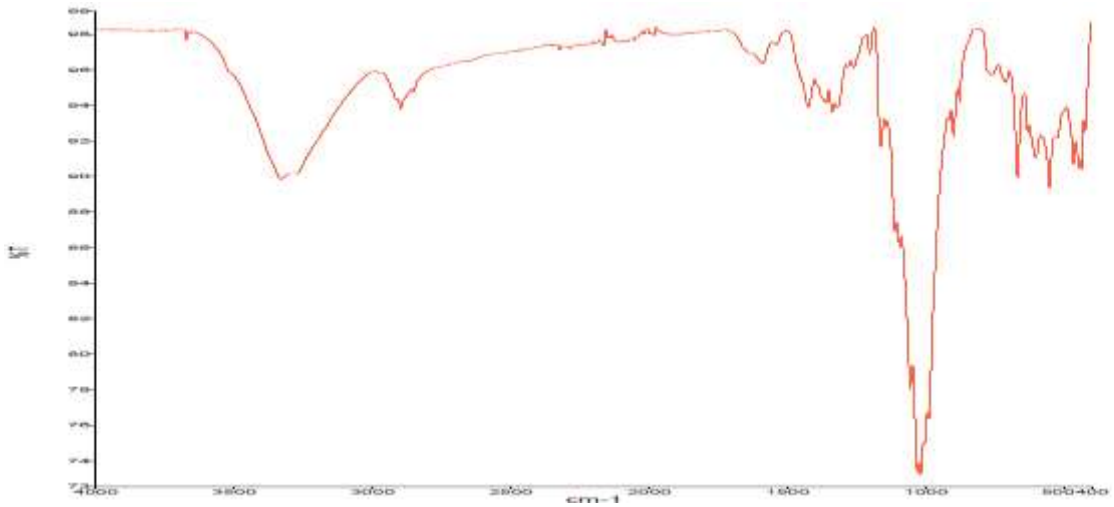

**Figure 3: FTIR spectrum of IR layer of methylcobalamain**

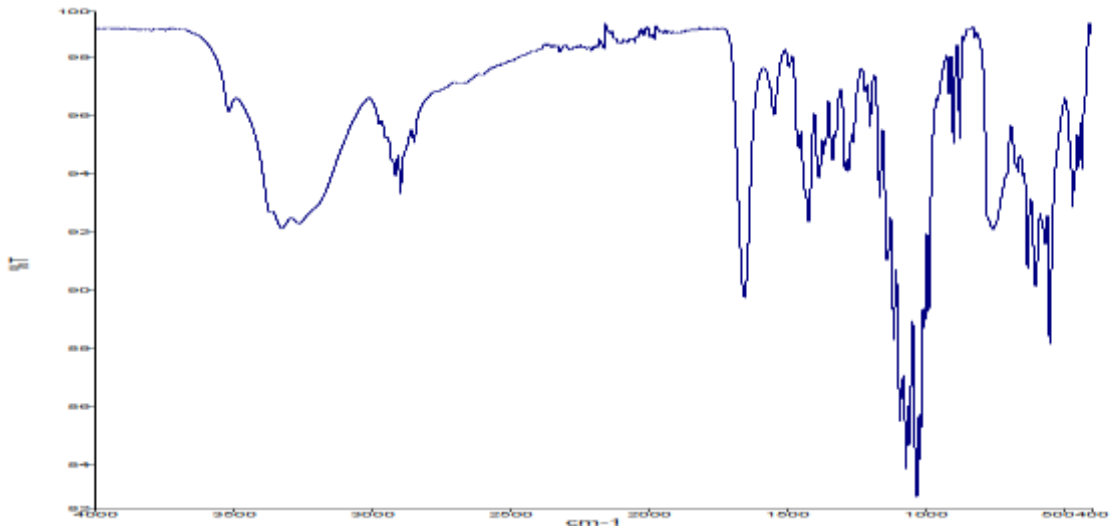

**Figure 4: FTIR spectrum of SR layer of pregabalin**

**Micromeritics studies on granulation blends:**

The compressibility index of the IR blends ranged from 13.5 to 14.7 and Hausner's ratio ranged from1.13 to 1.15. The angle of repose of IR blends ranged from 26.42 to 28.44°. The formulated IR blends showed good flow property.

The compressibility index and Hausner's ration of SR blend ranged from 11.7 to 14.7 and 1.13 to 1.16 respectively which indicates good flow. The angle of repose was found to be between 26.56 to 28.61°. Hence the blends belong to good flow. The results are tabulated in Table 3 and 4.

**Table 3: Precompression parameters of powder blend for methylcobalamin IR layer**

| Formulation | Carr′s index | Hausner′s Ratio | Angle of repose (θ) |
|---|---|---|---|
| F1 | 14.1±0.14 | 1.14±0.010 | 28.44±0.24 |
| F2 | 14.7±0.0011 | 1.15±0.011 | 27.39±0.19 |
| F3 | 13.6±0.004 | 1.14±0.004 | 26.71±0.24 |
| F4 | 13.5±0.010 | 1.13±0.010 | 26.42±0.27 |

**Table 4: Precompression parameters of powder blend for pregabalin SR layer**

| Formulation | Carr′s index | Hausner′s Ratio | Angle of repose (θ) |
|---|---|---|---|
| F1 | 14.1±0.14 | 1.16±0.010 | 28.44±0.24 |
| F2 | 14.7±0.0011 | 1.15±0.011 | 27.39±0.19 |
| F3 | 13.6±0.004 | 1.13±0.004 | 27.71±0.24 |
| F4 | 13.5±0.010 | 1.15±0.010 | 28.61±0.27 |
| F5 | 13.8±0.011 | 1.14±0.011 | 28.59±0.18 |
| F6 | 13.7±0.009 | 1.14±0.009 | 28.58±0.15 |
| F7 | 14.1±0.005 | 1.13±0.005 | 28.14±0.26 |
| F8 | 11.7±0.010 | 1.13±0.010 | 27.55±0.21 |
| F9 | 13.8±0.007 | 1.15±0.007 | 26.56±0.31 |

**Tablet evaluation:**

Tablet properties such as weight variation, hardness, friability, and drug content of each batch are represented in Table 5-6. All batches pass the weight variation test and found to be within range. Friability of all batches was found <1%, indicates that tablet surfaces are strong enough to withstand mechanical shock and attrition during transportation or storage until they are used. The hardness of tablet increase as polymer concentration increases and friability also decreases as polymer amount increases. Drug content of all batches was found within limit (90- 110%).

**Table 5: Post compression parameters for methylcobalamin tablet layer**

| Formulation | Hardness ($kg/cm^2$) | Weight variation (mg) | Friability (%) | Drug content (%) |
|---|---|---|---|---|
| F1 | 5.7±0.015 | 75.82±2.2 | 0.28 | 98.46±0.29 |
| F2 | 6.5±0.053 | 77.27±1.3 | 0.47 | 99.11±0.54 |
| F3 | 6.0±0.018 | 74.79±2.0 | 0.24 | 98.85±0.64 |
| F4 | 5.6±0.011 | 76.85±1.1 | 0.41 | 99.33±0.47 |

**Table 6: Post compression parameters for pregabalin tablet layer**

| Formulation | Hardness ($kg/cm^2$) | Weight variation (mg) | Friability (%) | Drug content (%) |
|---|---|---|---|---|
| F1 | 5.7±0.015 | 450.82±2.2 | 0.28 | 98.46±0.29 |
| F2 | 6.5±0.053 | 451.27±1.3 | 0.47 | 99.11±0.54 |
| F3 | 6.0±0.018 | 450.79±2.0 | 0.24 | 98.85±0.64 |
| F4 | 5.6±0.011 | 452.85±1.1 | 0.41 | 99.33±0.47 |
| F5 | 5.6±0.042 | 448.98±3.1 | 0.50 | 97.43±0.58 |
| F6 | 6.3±0.034 | 453.64±2.4 | 0.43 | 97.51±0.54 |
| F7 | 5.9±0.025 | 450.18±2.6 | 0.49 | 100.86±0.44 |
| F8 | 5.8±0.024 | 454.22±1.4 | 0.37 | 97.47±0.47 |
| F9 | 6.1±0.008 | 447.36±1.7 | 0.48 | 97.47±0.50 |

***In vitro* drug dissolution:**

The dissolution profile of methylcobalamin IR tablets are shown in Figure 5. Results of dissolution profiles of various IR formulations indicated that formulation F2 showed 97.9% drug release at the end of 45 minutes which is more than all the other immediate release methylcobalamin IR formulations and is due to increase in the amount of SSG. Thus due to fast release of drug within 45 min F2 was chosen as the best formulation. This was used to prepare the bilayer optimised tablet.

The *in vitro* dissolution profile of pregabalin SR tablets at different time intervals are shown in Figure 6 and 7. An ideal extended release tablet should release required quantity of drug in order to maintain effective constant plasma drug concentration. PB is freely soluble in water and both basic and acidic aqueous solutions, posses dissociation constant values (pka1 = 4.2 and pka2 =10.6); therefore, the release of drug from the tablets is dependent on the nature of matrix structure formed by the polymer. Formulation batches F1 to F9 were formulated using various types and proportion of HPMC. It was observed that the release rate was slower with higher quantities and higher viscosities of HPMC i.e. (K4M < K100M). The formulation F1 was found to be the most desired release profile for the formulation. The release of formulation F1 was most consistent, accurate and complete as 97.8% of drug was released at 12 h. Now the objective of this study was to formulate a single tablet of PB and MC which will manage neuropathic pain due to damaged or overactive nerves by acting on the brain and help in the regeneration of damaged nerves. The recommended dose of pregabalin is 75 mg twice a day. Based on the efficacy and safety, pregabalin is considered a first line drug in the treatment of central pain. Hence the complete release of PB at 12 h will make the bilayer tablet ideal as twice a day formulation.

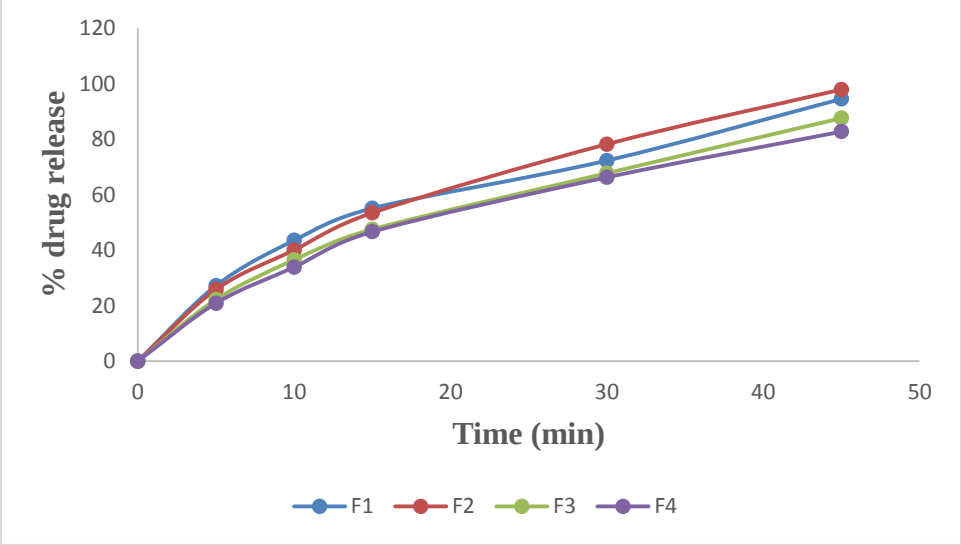


**Figure 5: *In vitro* dissolution profile of methylcobalamin IR tablets**

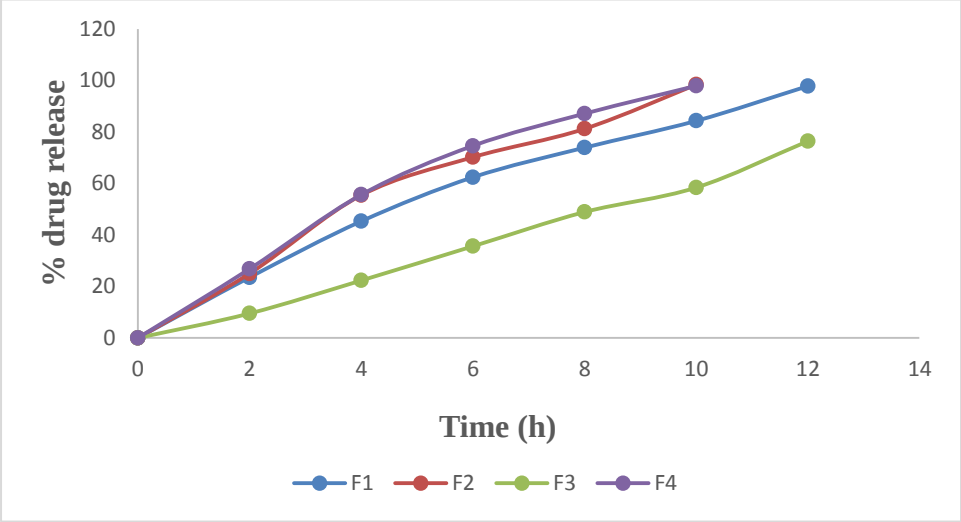


**Figure 6: *In vitro* dissolution profile of pegabalin SR tablets**

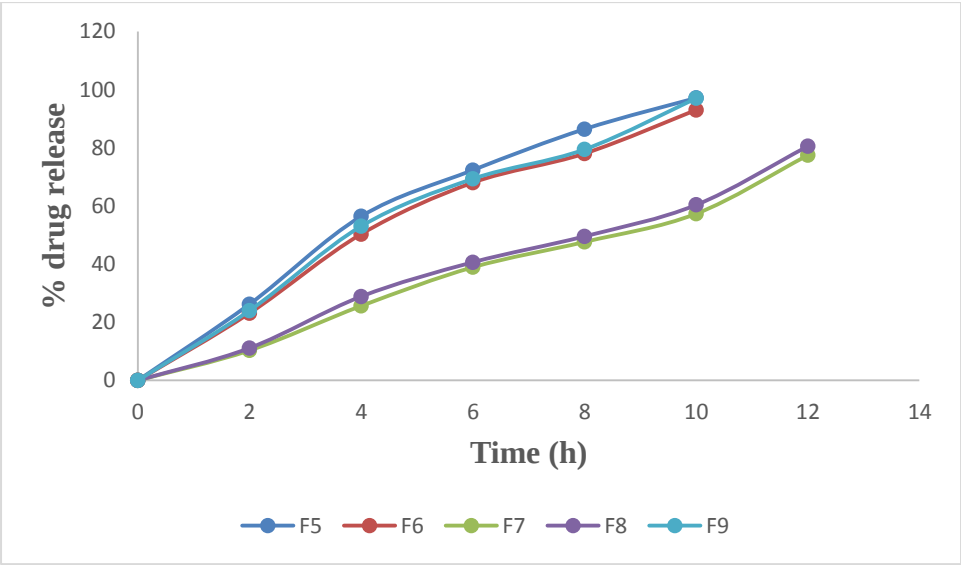


**Figure 7: *In vitro* dissolution profile of pegabalin SR tablets**

**Evaluation of bilayer tablets:**

The bilayer tablets pass the weight variation test and found to be within range at 530±3.04. Friability found to be <1% at 0.21% and hardness at 6.2±0.24 kg/cm$^2$. Drug content was found to be 99.4%.

***In vitro* drug dissolution:**

The dissolution profile of bilayer tablet is shown in Figure 8. *In vitro* drug release study for bilayer tablet, MC IR layer indicated 99.6 % drug release within 45 min. The PB SR layer exhibited slow sustained drug release with 98.8% drug released at end of 12 h.

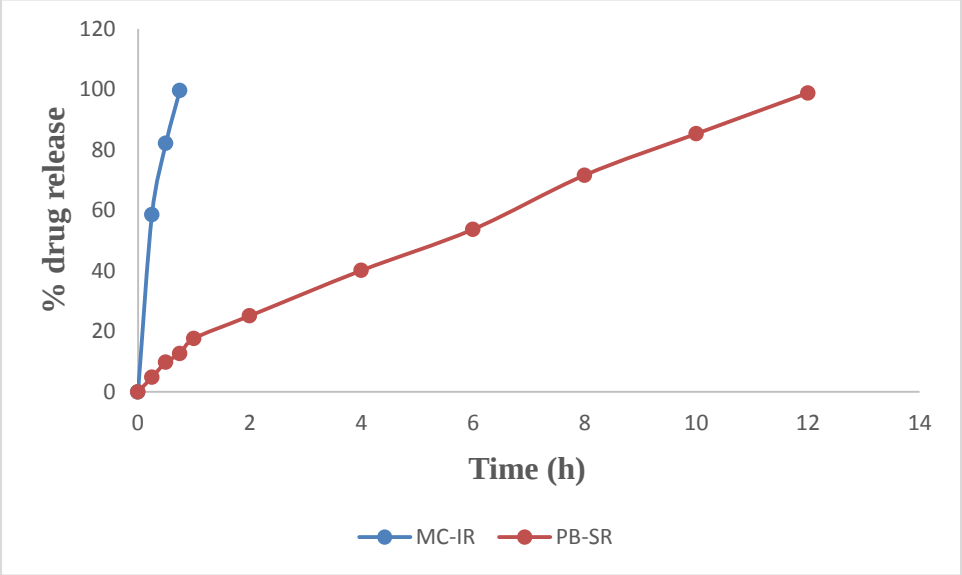


**Figure 8: *In vitro* dissolution profile of bilayer tablet of MC-IR and PB-SR**

**Kinetic analysis:**

In order to obtain the mechanism of drug release from SR layer, the data was fitted according to different release models and the correlation coefficients ($R^2$) were calculated and shown in Table 7. The regression coefficient ($R^2$ ) value for Zero order, First order, Higuchi's, and Peppas plots was found to be 0.9071, 0.8957, 0.9943, 0.9809 respectively.

The drug release data was best explained by zero order equation where they showed the highest linearity ($R^2$ = 0.9871). The Korsmeyer- Peppas equation indicated a good linearity ($R^2$ = 0.9969). The diffusion exponent "n" was between 0.45-0.89, which indicated that the diffusion mechanism follows non-Fickian and further indicates that the drug release was controlled by more than one process that is a coupling of diffusion and erosion mechanisms which is called as anomalous diffusion. We can conclude that diffusion coupled with erosion might be the mechanism of drug release from PB SR layer.

**Table 7: Kinetic analysis of the *in vitro* release data of Dorzolamide hydrochloride**

| Kinetic analysis of the in vitro release data of bilayer tablets | | | | |
|---|---|---|---|---|
| **Zero-order ($R^2$)** | **First-order ($R^2$)** | **Higuchi diffusion model ($R^2$)** | **Korsmeyar-Peppas ($R^2$)** | **Korsmeyar-Peppas diffusion exponent (n)** |
| 0.9071 | 0.8957 | 0.9943 | 0.9809 | 0.61 |

**Stability study:**

Stability study was performed for optimized bilayer tablet formulation at 40$^{o}$C/75% RH for 3 months. Stability testing parameters are shown in Table 8. The physical properties of tablets also did not show any change in appearance, no capping, lamination, and separation of layers. No substantial variance was perceived for 3 months.

**Table 8: Stability testing parameters for bilayer tablets**

| **Parameter** | **Storage Condition 40$^{0}$C±20$^{0}$C & 75%±5% RH** | | | |
|---|---|---|---|---|
| | **Initial** | **1$^{st}$ month** | **2$^{nd}$ month** | **3$^{rd}$ month** |
| Appearance | No change | No change | No change | No change |
| Average weight (mg) | 525 mg | 525 mg | 525 mg | 525 mg |
| Drug content (%) | 99.4 | 99.4 | 99.1 | 99.04 |

## CONCLUSION

Neuropathic pain is intense in nature and difficult to manage. Thus, the primary goal is maximum relief from pain. Non-steroidal analgesics are often insufficient for treatment, whereas PG and MC bilayer tablet seems to be safe by significantly reducing NP at the recommended dose. Hence the bilayer tablet may prove to be effective as a combination therapy for the treatment of neuropathic pain by sequential release of the drug.

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