



## Formulation and Evaluation of Divalproex Sodium Bi-Layered Tablet for the Treatment of Epilepsy

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### KEYWORDS

Bi-layered tablet,  
wet granulation,  
immediate release,  
sustained release.

### ABSTRACT:

**Introduction:** Divalproex sodium is considered as the most important antiepileptic drug and widely used for treatment of epilepsy and bi-polar disorders and prophylaxis of migraine. The present work has been done to formulate bi-layered tablet of Divalproex sodium containing immediate release layer and sustained release layer. Both layers were prepared by wet granulation technique as poor flow property exhibited by pure drug. **Method:** The immediate release layer was formulated by using sodium starch glycolate, crosscarmellose sodium as super disintegrant and evaluated for physical parameters, disintegration time and *in vitro* drug release. **Result:** The optimized immediate release layer (IF6) with highest *in vitro* release of 98.11 was selected for bi-layered tablet formulation. HPMCK4M and HPMC K100M polymer used to retard the drug release from sustained release layer in different proportion and combination and evaluated for physical parameter along with *in vitro* drug release studies. The optimized sustained release layer (SF8) which extends the Divalproex sodium release more than 18 hrs was selected. Finally Bi-layered tablets were prepared by double compression of selected sustained release layer and immediate release layer of Divalproex sodium. **Conclusion:** The tablets were evaluated for hardness, thickness, weight variation, friability, drug content uniformity and *in vitro* drug release. All the physical parameters were in acceptable limit of pharmacopeial specification. The stability studies, shown the bi-layer tablet was stable at 40°C/ 75% RH for a period of 3 months.

### Introduction:

Oral route is most commonly employed route of drug administration. Although different route of administration are used for the delivery of drugs, due to flexibility in dosage form design and patient compliance oral route is preferred [1]. The popularity of the oral route is attributed ease of administration, patient acceptance, accurate dosing, cost effective manufacturing method and generally improved shelf-life of the product [2]. There are several techniques of conventional drug delivery system where tablets, capsules, pills, liquids, are used as drug carrier. Among them, solid formulation do not require sterile conditions and are therefore, less expensive to manufacture [3].

There are several techniques of conventional drug delivery system where tablets, capsules, pills, liquids, are used as drug carrier. Among them, solid formulation do not require sterile conditions and are therefore, less expensive to manufacture<sup>3</sup>. The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness and ease in manufacturing [4]. Tablets are solid dosage forms containing medicinal substances with or without suitable diluents. According to Indian Pharmacopoeia Pharmaceutical tablets are solid, flat or biconvex dishes, unit dosage form, prepared by compressing a drug or a mixture of drugs, with or without diluents [5]. They are varying in size and weight, depending on amount of



medicinal substances and the intended mode of administration. It is most popular dosage form and 70% of the total medicines are dispensed in the form of tablet [6].

#### Advantages of Immediate Release Drug Delivery System:

1. Improved compliance
2. Improved stability, bioavailability
3. Suitable for controlled/sustained release actives
4. Allow high drug loading
5. Ability to provide advantages of liquid medication in the form of solid preparation
6. Adaptable and amenable to existing processing and packaging machinery
7. Cost-effective
8. Improved solubility of the pharmaceutical composition [7].

#### Disadvantages of sustained release formulation:

1. Administration of sustained release medication does not permit the prompt termination of therapy.
2. Flexibility in adjustment of dose regimen is limited.
3. Controlled release forms are designed for normal population; i.e., on the basis of average
4. Drug biological half-lives.
5. Economic factors must also be assessed, since more costly process and equipment are involved in manufacturing of many controlled release dosage forms [8].

#### Materials and methods:

Divalproex sodium was gifted by ROAQ Chemicals Pvt. Ltd. Vadodara. Sodium Starch Glycolate, Crosscarmellose, HPMC K4M, HPMC K100M, Lactose, Micro Crystalline Cellulose, PVP K 30, Ponceau 4R, Magnesium Stearate, Talc by S.D.FineChem.Ltd, Mumbai.

#### Formulation of Immediate release tablet layer:

Table 01: Composition of IR Layer

| Sr. No | Ingredients        | SF1    | SF2    | SF3    | SF4    | SF5    | SF6    | SF7    | SF8    | SF9    |
|--------|--------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| 1      | Divalproex sodium  | 173.25 | 173.25 | 173.25 | 173.25 | 173.25 | 173.25 | 173.25 | 173.25 | 173.25 |
|        |                    |        | 5      | 5      |        |        | 5      | 5      | 5      | 5      |
| 2      | Lactose            | 52.75  | 45.25  | 37.75  | 52.75  | 45.25  | 37.75  | 52.75  | 45.25  | 37.75  |
| 3      | HPMC K4M           | 45     | 52.5   | 60     | -      | -      | -      | 22.5   | 26.25  | 30     |
| 4      | HPMC K100M         | -      | -      | -      | 45     | 52.5   | 60     | 22.5   | 26.25  | 30     |
| 5      | MCC                | 20     | 20     | 20     | 20     | 20     | 20     | 20     | 20     | 20     |
| 6      | Magnesium stearate | 3      | 3      | 3      | 3      | 3      | 3      | 3      | 3      | 3      |
| 7      | Talc               | 6      | 6      | 6      | 6      | 6      | 6      | 6      | 6      | 6      |



| Sr. No. | Ingredients                | IF1  | IF2  | IF3  | IF4  | IF5  | IF6  |
|---------|----------------------------|------|------|------|------|------|------|
| 1       | Divalproex sodium          | 125  | 125  | 125  | 125  | 125  | 125  |
| 2       | Lactose                    | 82   | 79.5 | 82   | 79.5 | 82   | 79.5 |
| 3       | Crosscarmellose sodium     | 10   | 12.5 | -    | -    | 5    | 6.25 |
| 4       | Sodium starch glycolate    | -    | -    | 10   | 12.5 | 5    | 6.25 |
| 5       | Microcrystalline cellulose | 25   | 25   | 25   | 25   | 25   | 25   |
| 6       | Ponceau4R                  | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 |
| 7       | Magnesium stearate         | 3    | 3    | 3    | 3    | 3    | 3    |
| 8       | Talc                       | 5    | 5    | 5    | 5    | 5    | 5    |

**Table 02:** Composition of SR Layer

IRL of Divalproex sodium (DS) was prepared by wet granulation by using different super disintegrant such as SSG and Crosscarmellose sodium. PVP K30 solution with containing coloring agent was used as binding solution. As DS was oily in characteristics, MCC was used as adsorbent. Manufacturing steps-

1. Pass all the ingredients through sieve #80.
2. Mix Divalproex sodium with MCC geometrically and then mix with lactose. Add Super disintegrants and mix for 10 to 15 min in mortar and pestle.
3. Make wet mass using binding agent PVP K30 solution containing color. Pass the cohesive mass through sieve # 16 to get uniform granules.
4. Dry the granules at 50°C for 15 min in hot air oven.
5. Lubricate the granules with lubricating agent and compressed into 250 mg each tablet weight by adjusting hardness. The formulations are shown on table no 13.

#### Preparation of SRL:

Accurately weighed Divalproex sodium and polymer and others ingredients were taken in mortar and pestle and mixed well. The powder was mixed with sufficient quantity for PVP K30 solution until wet mass formed [9]. The cohesive mass obtained was passed through sieve # 16 and the granules were dried in a hot air oven at 50°C for 20 min. The dried granules again passed through sieve # 22 to break the large lumps. Then granules were mixed with talc and magnesium stearate and compressed into 300 mg each tablet by adjusting hardness [10].

#### Preparation of bi-layered tablet

By the study of disintegration and drug release profile of IRL and SRL, best formulations of each layer were chosen and bi-layered tablet were prepared by double compression in single rotatory tableting machine [11].

#### Drug Content for IRF, SRF and Bi-layered tablet:

Ten tablets were weighed and average weight is calculated. All tablets were crushed and powder equivalent to 100 mg drug was dissolved in pH 6.8 phosphate buffer and the volume was made up to 100 ml with pH

6.8 phosphate buffer. The solution was kept in sonicator for 1 hr. From the stock solution, 1 ml solution was taken in 10 ml volumetric flask and the volume was made with pH 6.8 phosphate buffer. Solution was filtered and absorbance was measured [12].

#### In vitro dissolution studies of sustained release layer:

The in vitro release of sustained release layer was carried out for 18 hours using USP type-II apparatus (DT-1200) at 100 rpm for the first 45 minutes in 900 ml 0.1N HCL maintaining at 37 ± 0.5°C and then at phosphate buffer pH 6.8 in 900 ml for another 18 hours [13]. A 5 ml was withdrawn at different time intervals and replaced with an equal volume of fresh medium. The samples were suitably diluted with blank dissolution medium, filtered and analyzed on UV spectrophotometer at 210 nm.

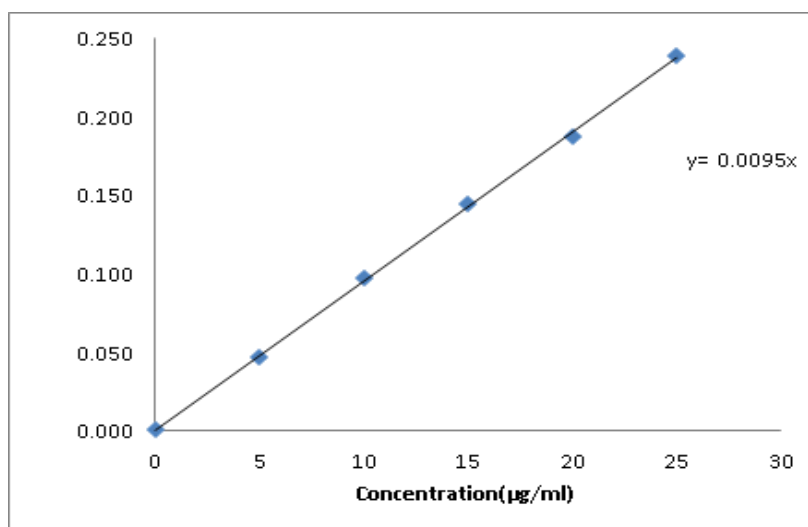


## Results and Discussion

**Calibration curve of Divalproex sodium.** The absorbance was measured in a UV spectrophotometer at 210nm against methano [14].

**Table 03:** Calibration curve of Divalproexsodium.

| Sr.no. | Conc. (µg/ml) | Absorbance |        |        | Mean±SD     |
|--------|---------------|------------|--------|--------|-------------|
|        |               | Trial1     | Trial2 | Trial3 |             |
| 1      | 0             | 0.000      | 0.000  | 0.000  | 0.000±0.000 |
| 2      | 5             | 0.050      | 0.043  | 0.046  | 0.046±0.004 |
| 3      | 10            | 0.097      | 0.095  | 0.098  | 0.097±0.002 |
| 4      | 15            | 0.143      | 0.144  | 0.146  | 0.144±0.002 |
| 5      | 20            | 0.185      | 0.188  | 0.187  | 0.187±0.002 |
| 6      | 25            | 0.240      | 0.237  | 0.237  | 0.238±0.002 |



**Fig01:** Calibration curve of Divalproex sodium

### a. Drug solubility studies:

**Table 04:** Solubility of Drug

| Solvents             | Solubility (mg/ml) |
|----------------------|--------------------|
| Distilled water      | 7.35               |
| Methanol             | 48.45              |
| Chloroform           | 55.24              |
| PhosphatebufferpH6.8 | 29.73              |



b. **Melting Point:** Melting point determined by capillary method and the result as 219°C - 223°C[15].

c. **FT-IRspectrum:**

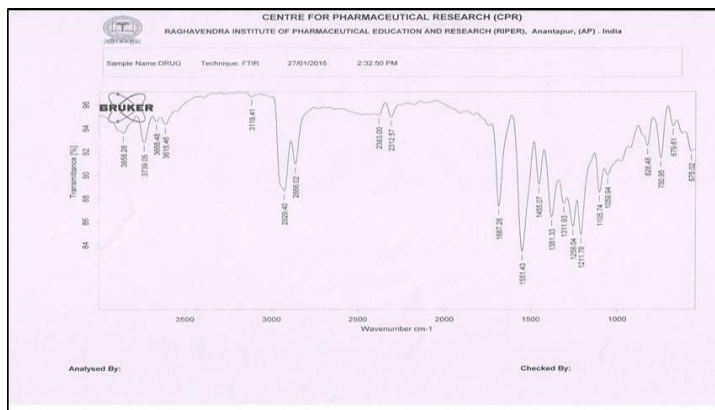


Fig 02: FTIR of Drug Divalproex sodium

Table 05: Compatibility study of drug and excipients using FTIR

| Functional group     | Wavenumber(cm <sup>-1</sup> ) |          |         |                 |             |            |         |         |
|----------------------|-------------------------------|----------|---------|-----------------|-------------|------------|---------|---------|
|                      | Standard peaks                | Puredrug | SSG     | Crosscarmellose | HPMC K4M    | HPMC K100M | Lactose | MCC     |
| AliphaticC-H stretch | 3300-2500                     | 2919.4   | 2950.74 | 2950.80         | 2944.8<br>1 | 2947.67    | 2951.02 | 2954.13 |
| C-H bend             | 1470-1450                     | 1455     | 1386.88 | 1372.74         | 1453.6<br>3 | 1454.07    | 1380.43 | 1450.20 |
| C-Hstretch           | 1300-1000                     | 1211     | 1213.15 | 1210.95         | 1210.2<br>8 | 1211.01    | 1210.39 | 1212.95 |
| Carboxylic acid      | 3100-3300                     | 3119.41  | 3121.29 | 3277.37         | 3121.3<br>2 | 3122.44    | 3123.36 | 3123.77 |
| O-Hbend              | -                             | 1059.94  | 994.78  | 1040.53         | 1047.0<br>9 | 1045.80    | 1025.20 | 1024.50 |

Evaluation Of Pre-Compression Parameters

Table 06: Pre-compression parameters for IRL and SRL

| Formulation | BulkDensityMean ± SD | Tapped Density Mean±SD | Car'sIndexMean ± SD | Haunsers Index Mean±SD | Angle of Repose Mean±SD |
|-------------|----------------------|------------------------|---------------------|------------------------|-------------------------|
| IF1         | 0.557±0.002          | 0.637±0.005            | 12.610±0.217        | 1.145±0.030            | 16.596±0.356            |



|     |             |             |              |             |              |
|-----|-------------|-------------|--------------|-------------|--------------|
| IF2 | 0.556±0.005 | 0.655±0.004 | 15.084±0.226 | 1.174±0.020 | 18.360±0.275 |
| IF3 | 0.523±0.004 | 0.626±0.003 | 15.773±0.109 | 1.164±0.022 | 19.421±0.173 |
| IF4 | 0.585±0.003 | 0.684±0.003 | 13.899±0.177 | 1.163±0.013 | 20.147±0.156 |
| IF5 | 0.612±0.010 | 0.682±0.007 | 11.767±0.206 | 1.133±0.009 | 17.913±0.039 |
| IF6 | 0.666±0.004 | 0.755±0.006 | 11.148±0.157 | 1.142±0.025 | 17.101±0.077 |
| SF1 | 0.592±0.005 | 0.694±0.003 | 13.779±0.206 | 1.154±0.009 | 19.604±0.279 |
| SF2 | 0.591±0.008 | 0.699±0.002 | 14.494±0.328 | 1.169±0.017 | 18.480±0.063 |
| SF3 | 0.605±0.004 | 0.681±0.003 | 11.223±0.186 | 1.133±0.009 | 18.201±0.088 |
| SF4 | 0.623±0.005 | 0.703±0.002 | 11.531±0.127 | 1.132±0.010 | 22.548±0.280 |
| SF5 | 0.596±0.004 | 0.710±0.004 | 16.144±0.249 | 1.200±0.028 | 18.331±0.077 |
| SF6 | 0.591±0.004 | 0.727±0.002 | 18.716±0.397 | 1.256±0.029 | 18.168±0.104 |
| SF7 | 0.615±0.003 | 0.728±0.004 | 14.825±0.673 | 1.174±0.028 | 18.467±0.091 |
| SF8 | 0.512±0.001 | 0.623±0.002 | 17.564±0.436 | 1.243±0.024 | 19.347±0.072 |
| SF9 | 0.620±0.002 | 0.693±0.001 | 10.754±0.181 | 1.124±0.017 | 17.396±0.021 |

#### Post-Compression Evaluation Parameters:

**Table 06:** Post-compression parameters for IRL and SRL

| Batch code | Weight variation<br>Mean±SD | Hardness<br>(kg/cm <sup>2</sup> )<br>Mean±SD | Friability(%)<br>Mean±SD | Thickness<br>Mean±SD | Drug content(%)<br>Mean ± SD | In vitro<br>disintegration time<br>(sec)<br>Mean±SD |
|------------|-----------------------------|----------------------------------------------|--------------------------|----------------------|------------------------------|-----------------------------------------------------|
| IF1        | 249.9±1.57                  | 5.95±0.05                                    | 0.74±0.09                | 2.87±0.04            | 98.12±1.19                   | 120.33±1.52                                         |
| IF2        | 250.3±1.60                  | 4.18±0.10                                    | 0.58±0.04                | 2.91±0.10            | 97.65±1.82                   | 91.66±2.08                                          |
| IF3        | 250.9±1.60                  | 6.35±0.03                                    | 0.56±0.06                | 2.90±0.07            | 98.65±1.28                   | 73.33±2.51                                          |
| IF4        | 251.55±1.99                 | 6.17±0.07                                    | 0.65±0.05                | 2.87±0.03            | 99.61±0.94                   | 48.33±3.05                                          |
| IF5        | 251.45±2.52                 | 4.14±0.04                                    | 0.63±0.03                | 2.92±0.06            | 99.43±1.32                   | 59.33±2.08                                          |
| IF6        | 250.05±1.81                 | 4.53±0.11                                    | 0.69±0.04                | 2.89±0.09            | 99.51±1.81                   | 37.33±1.52                                          |
| SF1        | 302.6±1.41                  | 5.38±0.10                                    | 0.32±0.06                | 3.34±0.09            | 99.38±1.19                   | -                                                   |
| SF2        | 302.9±2.29                  | 4.33±0.02                                    | 0.35±0.02                | 3.30±0.14            | 98.61±1.03                   | -                                                   |
| SF3        | 302.5±1.59                  | 6.14±0.04                                    | 0.43±0.03                | 3.31±0.03            | 97.43±1.28                   | -                                                   |
| SF4        | 301.75±1.14                 | 6.23±0.06                                    | 0.36±0.02                | 3.28±0.05            | 98.57±0.85                   | -                                                   |
| SF5        | 300.65±1.37                 | 5.14±0.03                                    | 0.41±0.06                | 3.30±0.06            | 98.43±1.27                   | -                                                   |



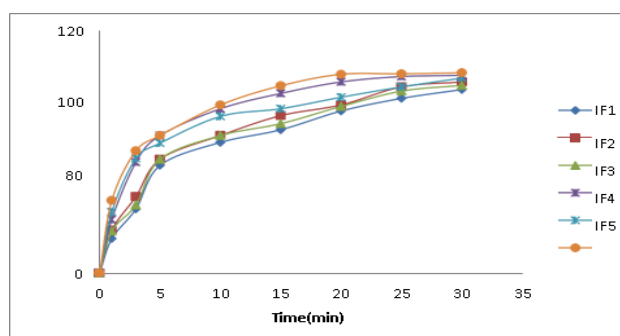
|            |             |           |           |           |            |   |
|------------|-------------|-----------|-----------|-----------|------------|---|
| <b>SF6</b> | 302.30±1.31 | 4.52±0.02 | 0.48±0.03 | 3.33±0.03 | 97.63±0.61 | - |
| <b>SF7</b> | 303.20±1.46 | 6.74±0.04 | 0.42±0.06 | 3.28±0.08 | 99.47±1.04 | - |
| <b>SF8</b> | 301.25±1.55 | 6.16±0.02 | 0.37±0.04 | 3.30±0.04 | 99.51±1.20 | - |
| <b>SF9</b> | 302.42±1.04 | 6.56±0.03 | 0.31±0.03 | 3.32±0.07 | 98.49±0.93 | - |

**Table07:** Post-compression parameters for bi-layered tablet

| Formulation | Weight variation<br>Mean±SD | Hardness<br>Mean±SD | Friability<br>Mean±SD | Thickness<br>Mean±SD | Drugcontent(%)<br>Mean±SD |
|-------------|-----------------------------|---------------------|-----------------------|----------------------|---------------------------|
| <b>BTF</b>  | 550.75±0.46                 | 7.05±0.15           | 0.38±0.01             | 6.28±0.14            | 99.23±0.53                |

**In-vitro dissolution study:****Table 08:** In vitro dissolution study of IRL

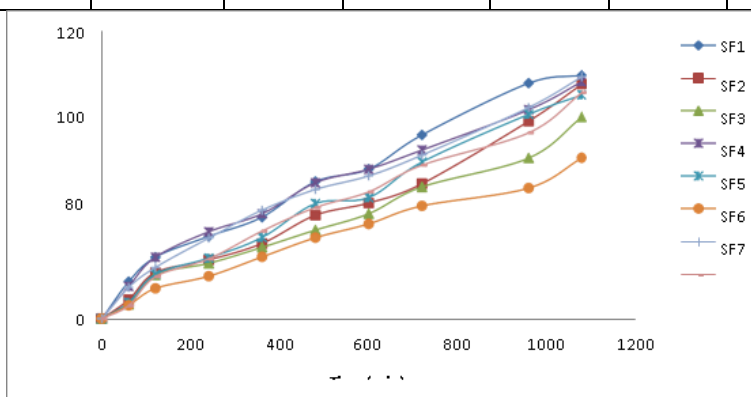
| Time<br>in min | % CUMULATIVE DRUG RELEASE |              |              |              |              |              |
|----------------|---------------------------|--------------|--------------|--------------|--------------|--------------|
|                | IF1                       | IF2          | IF3          | IF4          | IF5          | IF6          |
| 0              | 0.000±0.000               | 0.000±0.000  | 0.000±0.000  | 0.000±0.000  | 0.000±0.000  | 0.000±0.000  |
| 1              | 17.056±0.612              | 21.226±0.872 | 20.847±0.450 | 26.532±1.306 | 30.323±1.125 | 36.008±1.174 |
| 3              | 31.805±1.075              | 31.908±1.280 | 33.738±2.620 | 54.965±2.391 | 56.561±0.778 | 60.653±2.255 |
| 5              | 53.454±2.280              | 56.489±2.100 | 56.488±1.288 | 68.244±0.593 | 64.455±2.346 | 68.247±1.723 |
| 10             | 64.837±2.481              | 68.251±3.001 | 68.250±1.176 | 81.525±0.896 | 77.735±1.791 | 83.424±2.060 |
| 15             | 71.106±1.634              | 78.121±1.913 | 74.141±1.523 | 89.829±1.107 | 81.543±0.873 | 92.918±1.314 |
| 20             | 80.408±1.038              | 83.445±1.088 | 82.685±0.582 | 94.829±0.788 | 87.246±1.865 | 98.624±0.722 |
| 25             | 86.676±1.427              | 92.366±1.472 | 90.280±1.281 | 97.497±0.931 | 92.376±1.325 | 98.827±1.427 |
| 30             | 91.047±2.031              | 94.842±1.632 | 93.135±0.852 | 98.075±1.265 | 96.743±1.731 | 99.404±1.162 |

**Fig 03:** Release profile of immediate release layer



**Table 09:** CDR profile of sustained release layer

| Time in min | % CUMULATIVE DRUG RELEASE |              |              |              |              |              |               |              |
|-------------|---------------------------|--------------|--------------|--------------|--------------|--------------|---------------|--------------|
|             | SF1                       | SF2          | SF3          | SF4          | SF5          | SF6          | SF7           | SF8          |
| 0           | 0.000±0.000               | 0.000±0.000  | 0.000±0.000  | 0.000±0.000  | 0.000±0.000  | 0.000±0.000  | 0.000±0.000   | 0.000±0.000  |
| 60          | 15.408±1.222              | 7.905±1.234  | 6.017±1.508  | 13.469±1.222 | 6.741±1.281  | 5.558±1.591  | 13.006±1.994  | 5.391±0.882  |
| 120         | 25.634±1.764              | 19.263±1.532 | 18.231±1.281 | 25.637±0.732 | 18.521±1.421 | 12.635±0.751 | 21.351±1.317  | 17.527±1.114 |
| 240         | 34.323±2.715              | 24.502±1.083 | 23.091±1.547 | 33.235±1.164 | 25.279±1.003 | 17.697±1.151 | 33.589±1.503  | 24.917±1.426 |
| 360         | 42.342±0.632              | 31.362±1.321 | 29.735±0.941 | 38.852±1.521 | 33.852±1.835 | 25.742±1.427 | 45.247±0.941  | 36.518±0.831 |
| 480         | 57.151±1.196              | 43.141±1.974 | 36.936±1.251 | 56.674±2.061 | 47.993±0.539 | 33.733±2.378 | 53.869±1.510  | 46.331±0.891 |
| 600         | 62.342±0.412              | 48.234±0.826 | 43.752±1.423 | 62.316±1.839 | 50.491±0.694 | 39.513±1.114 | 59.523±1.163  | 52.852±0.792 |
| 720         | 76.620±1.642              | 56.263±2.227 | 54.964±2.137 | 70.315±2.001 | 65.327±1.779 | 47.031±1.480 | 68.215±0.906  | 64.017±0.710 |
| 960         | 98.183±0.352              | 82.430±1.267 | 66.957±1.402 | 87.123±0.645 | 86.182±0.467 | 54.439±2.565 | 88.053±0.676  | 77.498±0.918 |
| 1080        | 101.512±1.093             | 97.816±0.630 | 84.113±1.317 | 98.822±1.325 | 97.692±0.844 | 67.057±1.191 | 100.859±2.165 | 94.298±0.560 |

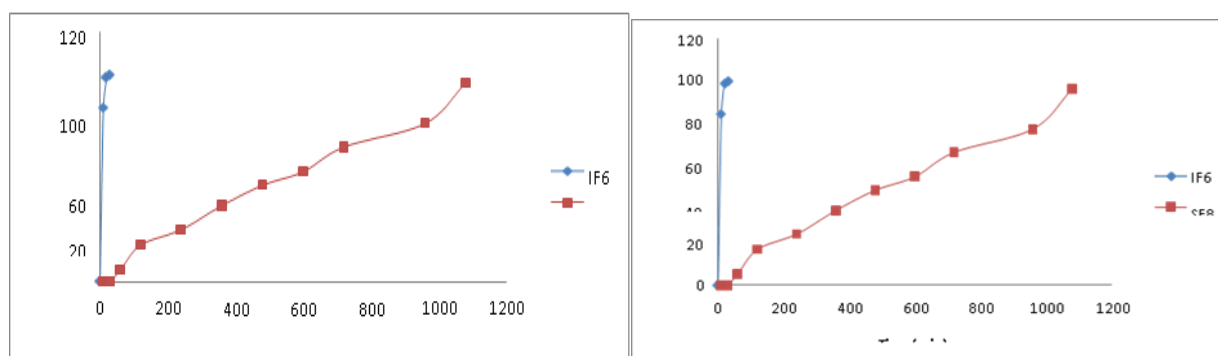


**Fig04:** Release profile of sustained release layer



**Table 10:** Dissolution study of Bi-layered Tablet

| Time in min | %CDR         |              |
|-------------|--------------|--------------|
|             | BTF          |              |
|             | IRL          | SRL          |
| 0           | 0.000±0.000  | 0.000±0.000  |
| 10          | 83.424±1.063 | -            |
| 20          | 98.351±1.147 | -            |
| 30          | 99.413±0.731 | -            |
| 60          | -            | 5.384±1.032  |
| 120         | -            | 17.512±0.853 |
| 240         | -            | 23.483±1.520 |
| 360         | -            | 36.164±0.638 |
| 480         | -            | 46.054±0.825 |
| 600         | -            | 52.854±0.841 |
| 720         | -            | 64.781±0.527 |
| 960         | -            | 76.149±0.952 |
| 1080        | -            | 95.823±0.614 |



**Fig:** Release profile of Bi-layered tablet

**Table 11:** Stability data

| Stability period | 40°C/ 75%RH      |                       |                        |              |               |
|------------------|------------------|-----------------------|------------------------|--------------|---------------|
|                  | Hardness Mean±SD | %Friability Mean ± SD | % Drug content Mean±SD | Drug release |               |
|                  |                  |                       |                        | IRL (30min)  | SRL (1080min) |
| Initial          | 7.05±0.67        | 0.36±0.01             | 99.23±0.5              | 99.413       | 95.823        |



|                |           |           |                 |        |        |
|----------------|-----------|-----------|-----------------|--------|--------|
|                |           |           | 32              |        |        |
| <b>1 month</b> | 7.08±0.49 | 0.43±0.03 | 99.35±0.7<br>51 | 99.581 | 95.421 |
| <b>2 month</b> | 6.41±0.49 | 0.56±0.06 | 98.96±0.7<br>92 | 99.142 | 94.736 |
| <b>3 month</b> | 5.33±0.60 | 0.73±0.03 | 96.94±0.9<br>21 | 98.728 | 94.381 |

The bi-layered tablets were subjected to short term stability study, storing the formulation at 40°C / 75% RH for 3 months. The data for stability studies revealed that no considerable differences in physical parameters, drug content and *in vitro* drug release rate were observed [16].

#### Summery and conclusion:

In the present work bi-layered tablet of Divalproex sodium were prepared by wet granulation method, using super disintegrants such as sodium starch glycolate and croscarmellose for immediate release layer and polymer like HPMC K4M and HPMC K100M for sustained release layer [17]. The prepared tablets of both layers were evaluated for post compression parameters. According to the *in vitro* dissolution profile date one formulation of each layer were selected for bi-layered tablet. IF6 from immediate release formulations as they showed 98.62 % drug release within 20 minute. SF8 from sustained release formulation as they showed 94.29 % drug release within 18 hours [18].

The bilayer tablets were prepared using the selected immediate and sustained release layer.. The hardness of the prepared tablets was found to be in therangeof5.85 to 7.05 kg/cm<sup>2</sup>. The low values of the standard deviation of average weight of the prepared tablets indicate weight uniformity within the batches prepared [19]. The friability of the prepared tablet was found to be less than 1%. The percentage drug content was uniform in all the formulations of prepared bi-layered tablets [19]. *In vitro* drug release pattern of the bi-layered tablets were same as individual layer tablets [20]. The stability study showed that no significant changes in tablet safer 3 months study. Based on the observations, it can be concluded that the formulated bi-layered tablets of Divalproex sodium using super disintegrants, release retardant polymers and different excipients was capable of exhibiting all the properties of bi-layered tablet [21]. They are thus reducing the dose intake, minimize dose related adverse effect, cost

and ultimately improve the patient compliance and drug efficiency.

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