FORMULATION DEVELOPMENT AND EVALUATION OF VENLAFAXINE HCL SUSTAINED RELEASE MATRIX TABLET

RAHUL THORAT1, PURUSHOTTAM PATIL2, RASHMI AAGE2, PRASHANT PURANIK3, VIRAJ SALVE1
1Govt.College of Pharmacy, Aurangabad. 431005, 2Y. B. Chavan College of Pharmacy, Aurangabad. 431001 (M.S) India.
Email: prpratigcoop@gmail.com
Received: 27 Jun 2013, Revised and Accepted: 30 July 2013

ABSTRACT
Objectives: The purpose of research work is to prepare Sustained Release Dosage Form (SRDF) of Venlafaxine HCl. As its half life is 5-6 Hrs and having good solubility (BCS Class I) it is suitable candidate for sustained release tablet dosage form.

Method: It was formulated to matrix tablet by direct compression method using Carbopol 971P and Ethyl cellulose as sustaining polymers. Differential Scanning Calorimetry (DSC) study shows that drug and other excipients are compatible with each other. The effects of polymers concentration on drug release profile were investigated. A 3^2 full factorial design was applied to systemically optimize the drug formulation. Concentration of Carbopol 971P and Ethyl cellulose are selected as independent variables and % Cumulative release of drug for 3 and 24 hrs (Q3, Q24) were selected as dependent variables.

Results: All precompressional and post compressional parameters were within official limit. Batch FS containing Carbopol 20% and Ethyl cellulose (20cps) 10% shows drug release upto 95.47% in 24 Hrs selected as optimized batch. ANOVA data shows models were significant. Drug release kinetics study shown that it follows Korsmeyer Peppas model (r2=0.9922) and release exponent (n=0.4365) shows mechanism is Fickian type.

Conclusion: Hence by formulating its sustained release matrix tablets of 24 Hrs creates new hope for patient as improving patient compliance and decreasing frequency of administration.

Keywords: Sustained release matrix tablet, Venlafaxine HCl, Carbopol 971P, Ethyl cellulose etc.

INTRODUCTION[1-7]
SRDF provides the initial release of the drug sufficient to provide a therapeutic dose soon after administration and then a gradual release over an extended period. Recently, SRDF became a very useful tool in medical practice offering a wide range of actual and perceived advantages to the patients. The basic rationale for sustained drug delivery is to alter the drug release and also to formulate such dosage form that improves patient compliance. To target chronic diseases it is the best suitable dosage form. An appropriate formulation can make the absorption, distribution, metabolism and elimination (ADME) profile of a drug much more favourable. Venlafaxine HCl is an orally active serotonin noradrenalin reuptake inhibitor used in the treatment of major depressive disorders. The successful treatment of depression depends on the maintenance of effective drug concentration level in the body for which a constant and uniform supply of drug is desired. It is a highly water soluble drug (Class I) with the biological half life of 5 Hrs thus requires two to three time daily dosing to maintain plasma drug concentration. So providing its slow release to maintain therapeutic level is the major need of this formulation.

MATERIALS AND METHODS

Materials
Venlafaxine HCl was received as a gift sample from Lupin Research Park, Aurangabad. Ethyl cellulose was gifted from Colorcon Asia Pvt Ltd, Goa. MCC PH102 was obtained from Signet Chemicals, Mumbai. Carbopol 971P, PVP K30, Magnesium stearate, Talc were purchase from Dipa Chemicals, Aurangabad. All other chemical and reagent were of analytical grade.

Methods

A) Drug identification and drug-excipients compatibility study[8-23]

1) Melting Point
Melting point of Venlafaxine HCl was determined by taking a small amount of sample in a capillary tube closed at one end and placed in a Digital melting point apparatus. (Veego Digital Melting point apparatus) The melting point was recorded.

2) UV Spectrum and Calibration curve of Venlafaxine HCl
The UV spectrum of Venlafaxine HCl was obtained using Shimadzu UV1700. Accurately weighed 25 mg of the drug was dissolved in sufficient quantity of buffer pH 6.8 and volume made up to 25 ml known as stock solution (1000 µg/ml). 1ml of aliquot was withdrawn and volume was made up to 100 ml using buffer pH 6.8 to obtain the concentration of 10µg/ml. Subsequently aliquots were removed to give 2-10µg/ml. The resultant solution was scanned from 400 to 200 nm.

3) Fourier Transform Infra-Red Spectra (FTIR)
The drug sample was placed in FTIR cuvette. The drug sample was scanned over the range of 4000-400 cm⁻¹ on an FTIR (Prestige 21 SHIMADZU). The FTIR spectra of drug sample were recorded. Similarly, the procedure repeated by dispersing a sample (drug, drug and polymer 1:1) as well as mixture of drug and polymers (1:1:1:1) in FTIR cuvette.

4) Differential Scanning Calorimetry (DSC)
The thermal behaviour of Venlafaxine HCl was studied using Shimadzu DSC TA60 W5 Thermal Analyzer. Accurately weighed samples of (For drug 6.06 mg) were hermetically sealed in aluminium pan and heated at a constant rate of 20°C/min over temperature range of 100 to 300°C. The DSC thermogram was recorded. The physical mixtures of drug with polymers for compatibility studies were prepared by triturating drug and drug and polymers (1:1) in a dried mortar for 5 min and kept as it is for 24 hrs.

B) Preparation of Tablet[24-25]
Matrix tablets of Venlafaxine HCl were prepared by direct compression method using 10 mm flat-faced punch 10mm of 12 stations (Lab Press Machinery Pvt. Ltd, Ahmadabad, India.) The active ingredient and the excipients were passed through 60 mesh sieve and thoroughly mixed using a polybag for 10 minutes. PVP K30 was used as binding agent and magnesium stearate, talc were added
to the above blend as flow promoters and further mixed for another 10 minutes. In all the formulations the amount of Venlafaxine HCl was kept constant (75mg). Table 1 shows different matrix tablets of Venlafaxine HCl using Carbopol 971P and Ethyl cellulose.

### Table 1: Formulation of 3² Factorial Design Batches

<table>
<thead>
<tr>
<th>Ingredients (mg) / batch</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine HCl</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Carbopol 971P</td>
<td>45</td>
<td>45</td>
<td>45</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Ethyl cellulose</td>
<td>15</td>
<td>30</td>
<td>45</td>
<td>15</td>
<td>30</td>
<td>45</td>
<td>15</td>
<td>30</td>
<td>45</td>
</tr>
<tr>
<td>PVP K30</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>MCC 102</td>
<td>146</td>
<td>131</td>
<td>116</td>
<td>131</td>
<td>116</td>
<td>101</td>
<td>116</td>
<td>101</td>
<td>86</td>
</tr>
<tr>
<td>Mg. Stearate</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Talc</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
</tr>
</tbody>
</table>

### C) Evaluation of flow properties for Factorial blend

The quality of tablets depends upon the quality of powder from which it is prepared. The powder of factorial batches were evaluated for Bulk density, Tapped density, Carr’s index (compressibility), Angle of repose and Hausner’s ratio. The evaluated parameters of powder are reported in the Table 4.

1) Bulk density

Apparent bulk density (ρb) was determined by pouring the blend into a graduated cylinder. The bulk volume (Vb) and weight of the powder (M) was determined. The bulk density (ρb) was calculated using following formula:

\[
\text{Bulk Density} = \frac{M}{V_b}
\]

2) Tapped density

The measuring cylinder containing a known mass of blend (M) was tapped for a fixed time (100 tapping). The minimum volume (Vt) occupied in the cylinder and weight of the blend was measured. The tapped density (ρt) was calculated using following formula.

\[
\text{Tapped Density} = \frac{M}{V_t}
\]

3) Carr’s index

The Carr’s index is expression that shows the compressibility of the powder. It is calculated by using the formula,

\[
\text{Carr’s Index} = \left(\frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}}\right) \times 100
\]

4) Hausner’s ratio

The Hausner’s ratio (H) is an indicator of flowability of the powder. It is calculated by the formula,

\[
H = \frac{\rho_t}{\rho_b}
\]

5) Angle of repose

It is a maximum angle possible between the surface of pile and the horizontal plane. The lesser the angle of repose, more is the free flowing powder and vice-versa. The angle of repose for the powder of each formulation was determined by the method.

D) Evaluation of Tablets

Tablets are evaluated for following official and non official tests.

1) Appearance

The appearance, colour and any other flaws like chips, cracks, surface texture etc. are other important morphological characteristics were observed.

2) Weight variation test

Five tablets were taken and average weight of the tablet was determined. The tablets were weighed individually and the weight variation was determined.

3) Hardness

Tablet hardness is defined as force required to crushing the tablet in diametric compression test. The hardness was measured with Monsanto hardness tester.

4) Friability

Twenty tablets were weighed and subjected to friability test in Roche friabilator. The pre-weighed sample was placed in friabilator which rotates at 25 rpm for 4 min. dropping the tablets through a distance of 6 inch with each revolution. This process was repeated for all formulations and the percentage friability was calculated.

5) Drug content

Randomly selected 1 tablet from each batch was crushed in a mortar and pestle. The crushed powder equivalent to 100 mg of Venlafaxine HCl was taken and dissolved in 100 ml of buffer pH 6.8 (1000µg). Then filtered through Whatman filter paper No 42. The concentration of Venlafaxine HCl was determined by measuring the absorbance at 225nm. Aliquots were taken from stock solution and diluted with buffer pH 6.8 and analyzed by UV-Visible Spectrophotometer (UV-1700 SHIMADZU).

6) In vitro drug release study

The drug release rate from Venlafaxine HCl SR matrix tablets (n=3) was determined using USP apparatus type II (Labindia, India). The dissolution test was performed using 900 ml of 0.1N HCl for first 2 Hrs and then buffer pH 6.8 for remaining 22 hrs at 37 ± 0.5°C and 50 rpm. The drug release and drug release kinetics was calculated by PCP disso ver. 3.0. The cumulative drug release of all 9 batches is reported in the Tables 6 and Fig. 6 resp.

E) Statistical analysis by Design Expert Software

A 3² full factorial design was selected and the 2 factors were evaluated at 3 levels, respectively. The percentages of Carbopol 971P (X1), Ethyl cellulose (X2) were selected as independent variables and the dependent variables were Q3, Q24. The data obtained were treated using Stat Ease Design Expert 7.1.6 software and analyzed statistically using analysis of variance (ANOVA) (Table 7, 8). The data were also subjected to 3-D response surface methodology to study the interaction of Carbopol 971P (X1), Ethyl cellulose (X2) on dependent variables. [Fig 7, 8]

F) Kinetics analysis of drug release

To analyze the mechanism of drug release from the tablet the In vitro dissolution data were fitted to zero order, first order, Higuchi release model, Hixon and Crowell powder dissolution method and Korsmeyer Peppas model by using PCP Disso Version 3 software, and the model with the higher correlation coefficient was considered to be the best model. The observations summarized in the Table 9.

758
RESULTS AND DISCUSSION[38-50]

A) Drug Identification and drug-excipients compatibility study

1) Melting Point

The melting point of Venlafaxine HCl was determined on Digital melting point apparatus was found to be 213º-216ºC which is in good agreement with reported melting point.

2) UV Spectrum and Calibration curve of Venlafaxine HCl

The UV spectrum of Venlafaxine HCl solution (10µg/ml) exhibited wavelength of absorbance maximum at 225 nm which complies with the reported and calibration curve shows r²=0.999

3) Fourier Transform Infra Red Spectrophotometer (FTIR)

In all physical mixtures of drug and polymer, there was neither masking of single characteristic peak nor existence of additional peak in the spectra. (Fig. 2, 3 and Table 2) so we can conclude that drug and polymers are compatible with each other.

4) Differential scanning calorimeter (DSC)

The endothermic peak at 210.94ºC of blend can be attributed as that of Venlafaxine HCl. (214.67 ºC) Thus the thermogram showed that the Venlafaxine HCl, Carbopol 971P, Ethyl cellulose are compatible with each other since there is no significant difference in endothermic peak of pure drug (Table 3) and physical mixture of drug with other excipients.

C) Evaluation of flow properties for Factorial blends

1) Bulk density

The bulk density of powder is important parameter in the compressibility of the powder. The bulk density was between 0.410 to 0.437gm/cm³.

2) Tapped density

The tapped density of powder is important parameters in the compressibility of the powder. The tapped density was found to be 0.497 to 0.567 gm/cm³.

3) Carr’s index

The Carr’s index is indicator of compressibility. The value below 21 % shows fair to passable compressibility. It was found to be 16.32 to 23.50 % indicating passable compressibility.

---

Fig. 1: UV Spectrum and Calibration curve of Venlafaxine HCl
Table 2: Fourier Transform Infrared spectral assignments with excipients

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Functional Group</th>
<th>Reported Values</th>
<th>Venlafaxine HCl</th>
<th>Factorial Tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OH</td>
<td>3300-3400</td>
<td>3321.42</td>
<td>3321.42</td>
</tr>
<tr>
<td>2</td>
<td>C6H5</td>
<td>1500-1600</td>
<td>1514.12</td>
<td>1514.12</td>
</tr>
<tr>
<td>3</td>
<td>Aliphatic CH</td>
<td>2800-3000</td>
<td>2943.37</td>
<td>2936.21</td>
</tr>
<tr>
<td>4</td>
<td>C-O-C</td>
<td>1000-1200</td>
<td>1039.63</td>
<td>1039.63</td>
</tr>
</tbody>
</table>
Fig. 4: DSC Thermogram of Venlafaxine HCl

Fig. 5: DSC Thermogram of physical mixture

Table 3: DSC compatibility of drug and mixture

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Parameters</th>
<th>Venlafaxine HCl</th>
<th>Physical Mixture</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Peak obtained °C</td>
<td>214.67</td>
<td>210.94</td>
</tr>
</tbody>
</table>

Table 4: Powder Flow properties of factorial batches

<table>
<thead>
<tr>
<th>Batch</th>
<th>Bulk Density (gm/cm³)</th>
<th>Tapped Density (gm/cm³)</th>
<th>Carr's Index (%)</th>
<th>Hausner's Ratio</th>
<th>Angle of Repose (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.423±0.26</td>
<td>0.512±0.19</td>
<td>17.38±1.09</td>
<td>1.21±0.09</td>
<td>27.12±1.21</td>
</tr>
<tr>
<td>F2</td>
<td>0.419±0.07</td>
<td>0.499±0.07</td>
<td>16.32±1.78</td>
<td>1.19±0.04</td>
<td>29.24±1.05</td>
</tr>
<tr>
<td>F3</td>
<td>0.437±0.19</td>
<td>0.567±0.01</td>
<td>22.92±1.02</td>
<td>1.24±0.08</td>
<td>25.36±1.29</td>
</tr>
<tr>
<td>F4</td>
<td>0.417±0.01</td>
<td>0.494±0.05</td>
<td>16.59±1.35</td>
<td>1.18±0.048</td>
<td>25.12±1.01</td>
</tr>
<tr>
<td>F5</td>
<td>0.413±0.06</td>
<td>0.497±0.36</td>
<td>16.90±1.81</td>
<td>1.20±0.126</td>
<td>26.42±1.23</td>
</tr>
<tr>
<td>F6</td>
<td>0.420±0.21</td>
<td>0.527±0.005</td>
<td>20.30±2.13</td>
<td>1.25±0.043</td>
<td>28.54±1.12</td>
</tr>
<tr>
<td>F7</td>
<td>0.431±0.01</td>
<td>0.521±0.013</td>
<td>17.27±1.23</td>
<td>1.20±0.094</td>
<td>27.18±1.32</td>
</tr>
<tr>
<td>F8</td>
<td>0.428±0.17</td>
<td>0.535±0.028</td>
<td>20.00±1.62</td>
<td>1.25±0.060</td>
<td>29.36±1.14</td>
</tr>
<tr>
<td>F9</td>
<td>0.41±0.01</td>
<td>0.536±0.031</td>
<td>23.50±1.26</td>
<td>1.30±0.041</td>
<td>27.48±1.26</td>
</tr>
</tbody>
</table>

All values are mean±SD, n=3
4) Hauser’s ratio

The Hauser ratio is another parameter indicating the flow properties. It was found to be 1.18 to 1.30 indicating good to passable flowability.

5) Angle of repose

The angle of repose can be correlated with type of flow of powder. The angle of repose 20 to 30° indicates the good flow while the angle of repose more 30° indicates poor flow properties and angle of repose below 20° indicates excellent flow properties. The angle of repose was found to be within the range of 25.12° to 29.36° indicating good flowability.

D) Evaluation of Tablets

The tablets from the factorial batches were evaluated for different evaluation parameters of tablets.

1) Appearance

The tablets from all factorial batches were white, circular. The surface texture was smooth. The thickness of tablets of factorial batches was 3.12 to 3.24 mm and it was found to be within limit of deviation from average value (not more than 5%).

2) Weight variation

For tablet weighing 300 mg or more, not more than two tablets differ from the average weight by 5% deviation. The weight variation within limits indicates uniformity in tablet compression and consequently content of drug in a unit.

3) Hardness

The hardness is important characteristics to be evaluated for handling and transportation properties of the tablets. The hardness of tablets was found to be 6.3 to 8.0 Kg/cm² which indicate good handling and transportation characteristics.

4) Friability

The friability is important characteristics to be evaluated for handling and transportation properties of the tablets. The friability of tablets was less than 0.5% which indicates good handling and transportation characteristics.

5) Drug content

The drug content of the nine formulations was found to be between 97.22 to 101.89% (i.e. variation of ±4%). The value ensures good uniformity of the drug content in the tablet.

6) In vitro drug release studies

In vitro drug release study was carried out using USP dissolution apparatus II in 0.1N HCl for first 2 Hrs and then buffer pH 6.8 for a period of remaining 22 Hrs.

The formulations F5, F6 and F8 comprising of Carbopol 971P 60mg, 60mg, 75mg resp. and Ethyl cellulose 30 mg, 45 mg, 30 mg resp. showed improved drug release upto 24 hrs and minimum burst release with more than 80% release in 24 hrs. Hence formulation with comparatively lower polymer concentration (F5) was selected as optimized formulation. Formulation containing combination of Carbopol 971P and Ethyl cellulose retarded the drug release upto 24 Hrs, but showed 41 to 50% drug release in first 3 Hrs in initial batches which were not appropriate. This burst release may be due to high water solubility of drug and more time required for wetting of tablet. This problem was overcome by increasing the Conc. of Polymers.

E) Statistical analysis by Design Expert Software

i) ANOVA study

The Q1, Q3, for the 9 batches (F1-F9) showed a wide variation (i.e., 35.32-50.28% and 84.69-102.37% resp). Data clearly indicates that the Q1, Q3 values are strongly dependent on the selected independent variables. The coefficients of X1, X2 were found to be significant at p <0.05, hence confirmed the significant effect of all the variables on the selected responses.
Fig. 6: Percent cumulative drug release of formulation F1 to F9

Table 7: Analysis of variance for Q$_3$

<table>
<thead>
<tr>
<th>Source</th>
<th>Sum of Squares</th>
<th>Degrees of Freedom</th>
<th>Mean Square</th>
<th>F Value</th>
<th>P Value</th>
<th>Model Significant/Non Significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>237.81</td>
<td>2</td>
<td>118.91</td>
<td>21.45</td>
<td>0.0018</td>
<td></td>
</tr>
<tr>
<td>A-C</td>
<td>92.28</td>
<td>1</td>
<td>92.28</td>
<td>16.65</td>
<td>0.0065</td>
<td>Significant</td>
</tr>
<tr>
<td>B-EC</td>
<td>145.53</td>
<td>1</td>
<td>145.53</td>
<td>26.26</td>
<td>0.0022</td>
<td></td>
</tr>
<tr>
<td>Residual</td>
<td>33.25</td>
<td>6</td>
<td>5.54</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Cor total</td>
<td>271.06</td>
<td>8</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>R Squared</td>
<td>0.8773</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

Table 8: Analysis of variance for Q$_{24}$

<table>
<thead>
<tr>
<th>Source</th>
<th>Sum of Squares</th>
<th>Degrees of Freedom</th>
<th>Mean Square</th>
<th>F Value</th>
<th>P Value</th>
<th>Model Significant/Non Significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>260.05</td>
<td>5</td>
<td>52.01</td>
<td>21.58</td>
<td>0.0147</td>
<td></td>
</tr>
<tr>
<td>A-C</td>
<td>106.60</td>
<td>1</td>
<td>106.60</td>
<td>44.23</td>
<td>0.0069</td>
<td>Significant</td>
</tr>
<tr>
<td>B-EC</td>
<td>151.30</td>
<td>1</td>
<td>151.30</td>
<td>62.78</td>
<td>0.0042</td>
<td></td>
</tr>
<tr>
<td>R- Squared</td>
<td>0.9729</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Adj R- Squared</td>
<td>0.7082</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Pred R- Squared</td>
<td>0.7082</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Adeq Precision</td>
<td>14.574</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 7: Response surface plot for Q$_3$. 

Design-Expert® Software 
Factor Coding: Actual 

diso 3 hr 

Design points above predicted value 
Design points below predicted value 

X1 = A: c 
X2 = B: ec

i) 3-D Response surface plot

The response surface plots showed that various combinations of independent variables $X_1$, $X_2$ may satisfy any specific requirement (i.e. maximum drug release up to 24 hrs and minimum burst release in 3 hrs) while taking into consideration of various factors involved in dosage form.

F) Kinetics analysis of drug release

The results shown that the factorial design batches follows Korsmeyer Peppas model. The $R$ value of Korsmeyer Peppas was found close to one ($0.9922$) the slow release of the drug from the matrix may be due to the formation of viscous gel of Carbopol 971P. The $n$ values were found to be less than 0.5 ($0.4365$) indicating that the mechanism is diffusion controlled or Fickian type as shown in Table 9.

CONCLUSION

The drug has elimination half life of 5(±2) hours shows that it is a suitable candidate for sustained release formulation. Advantage of this formulation over others is that it is easy to prepare and cost effective. Optimum concentration of Carbopol 971P and Ethyl cellulose based formulations was found to provide the desired release (95.47%) with a reduced frequency of administration. Release Kinetics shows it follows Korsmeyer Peppas model and mechanism is diffusion controlled or Fickian type. Thus, the Objective of the project was to formulate a sustained release matrix type tablet of Venlafaxine Hydrochloride meant for once-a-day administration.

ACKNOWLEDGEMENT

The authors are grateful to Lupin Research Park, Aurangabad for providing Venlafaxine HCl as gift sample and Dr. S.S. Khadabadi Principal Government College of Pharmacy, Aurangabad for necessary support and valuable guidance.

Table 9: Model fitting data of Venlafaxine HCl SR matrix tablet (Optimized batch F5)

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Formulation</th>
<th>Models</th>
<th>$R$</th>
<th>$N$</th>
<th>$K$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F5</td>
<td>Zero Order</td>
<td>0.5964</td>
<td>0.4365</td>
<td>24.597</td>
</tr>
<tr>
<td></td>
<td></td>
<td>First Order</td>
<td>0.9566</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Matrix</td>
<td>0.9754</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Korsmeyer Peppas</td>
<td>0.9922</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hixon Crowell</td>
<td>0.8866</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

REFERENCES