DESIGN AND EVALUATION OF INTRAGASTRIC BUOYANT TABLETS OF VENLAFAXINE HYDROCHLORIDE

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Received: 05 January 2017, Revised and Accepted: 13 February 2017

ABSTRACT

Objective: The present study was undertaken to prolong the release of orally administered drug. The aim is to formulate, develop, and evaluate the intragastric buoyant tablets of venlafaxine hydrochloride, which release the drug in a sustained manner over a period of 12 hrs. Different formulations were formulated using the polymers Carbopol 934 P, xanthan gum, hydroxypropyl methylcellulose (HPMC K100M) with varying concentration of drug; Polymer ratio of 1:1, 1:1.5, 1:2, in which sodium bicarbonate acts as gas generating agent, and microcrystalline cellulose as a diluent.

Methods: The tablets were prepared by direct compression and evaluated for tablet thickness, weight variation, tablet hardness, friability, in vitro buoyancy test, in vitro drug release and Fourier transform infrared spectroscopy. Formulations were evaluated by floating time, floating lag time and in vitro drug release. Dissolution profiles were subjected for various kinetic treatments to analyze the release pattern of drug.

Results: It was found that drug release depends on swelling, erosion, and diffusion, thus following the non-Fickian/anomalous type of diffusion. Formulation F8 was considered as an optimized formulation for gastro retentive floating tablet of venlafaxine hydrochloride. The optimized formulation showed sustained drug release and remained buoyant on the surface of the medium for more than 12 hrs. As the concentration of HPMC K100M increases in the formulation the drug release rate was found to be decreased. The optimized formulation was subjected for the stability studies and was found to be stable as no significant change was observed in various evaluated parameters of the formulation.

Conclusion: It can be concluded that floating drug delivery system of venlafaxine hydrochloride can be successfully formulated as an approach to increase gastric residence time, thereby improving its bioavailability.

Keywords: Venlafaxine hydrochloride, Intragastric buoyant, Floating drug delivery systems, Hydroxypropyl methyl cellulose K100M, Carbopol 934 P, Xanthan gum.

INTRODUCTION

Oral controlled drug delivery system is useful to maintain therapeutically effective plasma drug concentration levels for a longer duration thereby reducing the dosing frequency and to minimize fluctuations in the plasma drug concentration at the steady state by delivering the drug in a controlled and reproducible manner [1]. Moreover, it is easy for administration, no patient compliances, and flexibility in the formulation. Many studies have been performed concerning the sustained release dosage form of drug, which have aimed at the prolongation of gastric emptying time, i.e., gastro retentive drug delivery system, which will provide as with new and important therapeutic options, which utilize several approaches such as intragastric floating system [2], high-density system [3], mucoadhesive system [4], and super porous biodegradable hydrogel systems [5]. In gastro retentive system, drugs can remain in the gastric region for several hours and significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility of drugs that are less soluble in a high pH environment. It has applications also for long drug delivery to the stomach and proximal small intestines [6]. Gastro retention helps to provide better availability of new products with new therapeutic possibility and substantial benefits for patients [7]. Drugs that are required to be formulated into gastro-retentive dosage forms include drugs acting locally and primarily absorb in the stomach, drugs that are orally soluble at an alkaline pH, those with a narrow window of absorption, drugs absorbed rapidly from gastrointestinal tract (GIT) and drugs that degrade in colon [8].

Different methods are used depending on the mechanism of buoyancy in the development floating drug delivery system (FDDS). They are effervescent and non-effervescent system [9]. The most commonly used excipients in non-effervescent FDDS are gel forming on highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming polymers such as polycarbonate, polyacrylate, polymethacrylate, and polystyrene. The floating dosage forms involve intimate mixing of drug with a gel forming hydrocolloid, which swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and bulk density of less than unity with in the outer gelatinous barrier [10]. The air trapped by the swollen polymer confers buoyancy to these dosage forms and gel structure act as a reservoir for sustained drug release [11]. The effervescent buoyant delivery system utilizes matrices prepared with swellable polymers such as Methocel polyacrylamides (chitosan) and effervescent components such as sodium bicarbonate and citric or tartaric acid [12] or matrices containing chambers of liquid that gasify at body temperature [13-15]. They are fabricated in such a way that on arrival in the stomach, carbon dioxide is liberated by the acidity of the gastric contents and entrapped in a gelified hydrocolloid which produces an upward movement of the dosage form and maintains its buoyancy.

Venlafaxine hydrochloride is a unique anti-depressant and is referred to as a serotonin-nor epinephrine-dopamine reuptake inhibitors [16]. Venlafaxine hydrochloride helps in releasing a small quantity of drug, advantage fortomating a depressive disorder. It has a short bioavailability of 12.6% and biological half-life of 5 hrs. Therefore, the frequent administration is necessary to maintain the therapeutic concentration of the drug with in the therapeutic index. To overcome the drawbacks,
the present study, gastric retentive controlled release dosage form of
the drug in the form of tablet was formulated [17] with Carbopol 934P
xanthan gum, and hydroxypropyl methylcellulose (HPMC K100M)
with varying concentration of drug: Polymer ratio (1:1, 1:1.5, 1:2).

The aim of the present study was not only preparing intragastric
buoyant tablet but also to release the drug in controlled system.
Polymers were added in different concentrations with varying amount
of retardant material and investigated the release profile of the drug
by in vitro dissolution study to achieve an extended retention in the
upper GIT, to enhance the absorption and improve the bioavailability.

MATERIALS AND METHODS

Materials
Vanlafaxine hydrochloride and HPMC K100 M was procured as a gift
sample from Aurobindo Pharma, Carbopol 934P and xanthan gum
from Himedia Laboratories, microcrystalline cellulose and magnesium
stearate from SD Fine Chemicals.

Methods
Preparation of venlafaxine hydrochloride floating tablets
Floating matrix tablet were prepared using direct compression
technique [18-21] with the use of a different polymer with varying
concentration (1:1, 1:1.5, 1:2) i.e., drug to polymer ratio as shown in
Table 1. All polymer and drug were passed through sieve no.80
separately. Then drug was mixed for 10 minutes with polymers and
other excipients in weight proportion as mentioned in the table. The
powder blend was then lubricated with magnesium stearate and talc.
Finally, this lubricated blend was subjected to compression into tablets
using 10-mm flat-face on a 16 stationary rotary punching tablet
machine. The composition of all the formulations is given in Table 1.

Evaluation of powder blend
The powder blends of all formulation were evaluated for bulk density,
tapped density [22], angle of repose [23], Carr’s compresibility
index [24], and Hausner ratio [25].

Evaluation of tablets
The prepared intragastric buoyant tablets were subjected to weight
variation, hardness by using Monsanto hardness tester, thickness
using Vernier Calliper, friability using Roche friabilator and drug
content [26,27].

Swelling index
The swelling of tablet involves the absorption of a liquid resulting in an
increase in weight and volume. Liquid uptake by the particle may be due
to saturation of capillary spaces within the particles. The liquid enters
the particles through pores and bind to a large molecule, breaking
the hydrogen bond, and resulting in the swelling of particle [28,29].
The extent of swelling can be measured in terms of % weight gain by the
particle. The measurement of swelling rate of the floating matrix tablet
was carried to gain, insight the observed phenomenon of drug release
with the rates of polymer hydration. Swelling index of the dosage form is
conducted using USP dissolution apparatus-II in 900 ml of 0.1 N
hydrochloric acid (HCl) which is maintained at 37±0.5°C, rotated at
50 rpm. At selected regular intervals, the tablet was withdrawn, and the
excess water was blotted with tissue paper, and the swelling index was
calculated using following formula.

\[
\% \text{Swelling index} = \frac{(W_f - W_i) / W_i} \times 100
\]

Where, \(W_f\) = Weight of the swollen tablet,
\(W_i\) = Initial weight of the tablet.

Buoyancy studies
The in vitro buoyancy (floating behavior) [30] of the tablets was
determined by floating lag time (FLT). The tablets were placed in
100 ml beaker containing 0.1 N HCl (pH 1.2). The time taken by
the tablet to reach the surface and float was determined by the FLT [31].
The duration of the time the dosage form constantly remained on the
surface was determined as of total floating time (TFT).

Uniformity of drug content
The drug content was performed to check the dose uniformity in
the formulation. Randomly 10 tablets were weighed and powdered.
A quantity equivalent to 100 mg of venlafaxine hydrochloride was
added into a 100 ml volumetric flask and dissolved in 0.1 N HCl,
shaken for 10 minutes and made up to the volume with 0.1 N HCl.
After suitable dilutions, the drug content was determined by ultraviolet (UV)
spectrophotometer at 224 nm against blank.

In vitro release studies for floating tablets
The release rate of the drug venlafaxine hydrochloride floating
tablets was determined using USP Type II dissolution apparatus. The
dissolution was carried out using 900 ml of simulated gastric fluid
(pH 1.2) as dissolution media, maintained at 37 ± 0.1°C and rotated
at 50 rpm for 12 hrs. 5 ml of the samples were withdrawn at suitable
time intervals, and the samples were replaced with fresh dissolution
medium [16,32]. The samples were filtered through 0.45 µm membrane
filter and diluted if necessary. Absorbances of these solutions were
measured at 224 nm using UV-visible spectrophotometer. Samples
were assayed in triplicate.

Mechanism of drug release
To analyze the mechanism of drug release rate kinetics from the
intragastric buoyant tablets, the obtained data were fitted into
zero order, first order, Higuchi, and Koresmeyer–Peppas release
model [33-35].

Stability studies
Stability studies of pharmaceutical products were done as per
ICH guidelines. These studies are designed to increase the rate of
chemical or physical degradation of the drug substance or product
using exaggerated storage conditions. The optimized formulation
was stored at different storage conditions at elevated temperatures
such as 25°C±2°C/60±5% RH, 30°C±2°C/65±5% RH,
and 40°C±2°C/75±5% RH for 90 days. The samples were withdrawn
at intervals of 30 days and checked for physical changes, hardness,
friability, drug content, FLT, and percentage drug release.

RESULTS AND DISCUSSION
To check the integrity of the drug in the formulation, Fourier transform
infrared (FTIR) spectra of pure drug venlafaxine hydrochloride,

<table>
<thead>
<tr>
<th>Ingredient’s (mg/tablet)</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>Vanlafaxine 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 934</td>
<td>75</td>
<td>112.5</td>
<td>150</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Xanthan gum</td>
<td>75</td>
<td>112.5</td>
<td>150</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>HPMC K100M</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>MCC</td>
<td>95</td>
<td>57.5</td>
<td>20</td>
<td>95</td>
<td>57.5</td>
<td>20</td>
<td>95</td>
<td>57.5</td>
<td>20</td>
</tr>
<tr>
<td>Sodium bicarbonate</td>
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<td>70</td>
<td>70</td>
<td>70</td>
<td>70</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
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</tr>
<tr>
<td>Talc</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

HPMC: Hydroxy propyl methyl cellulose, MCC: Micro crystalline cellulose, HCl: Hydrochloric acid


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Table 2: Evaluation parameters of powder blend

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Angle of repose (°)</th>
<th>Bulk density (gm/cc)</th>
<th>Tapped density (gm/cc)</th>
<th>Compressibility index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>29°±1.00</td>
<td>0.36±0.004</td>
<td>0.41±0.018</td>
<td>11.8±0.08</td>
</tr>
<tr>
<td>F2</td>
<td>30°±1.00</td>
<td>0.37±0.001</td>
<td>0.44±0.017</td>
<td>13.4±0.08</td>
</tr>
<tr>
<td>F3</td>
<td>32°±1.00</td>
<td>0.38±0.005</td>
<td>0.44±0.004</td>
<td>13.3±0.06</td>
</tr>
<tr>
<td>F4</td>
<td>34°±1.00</td>
<td>0.35±0.005</td>
<td>0.41±0.003</td>
<td>14.2±1.4</td>
</tr>
<tr>
<td>F5</td>
<td>32°±1.00</td>
<td>0.34±0.004</td>
<td>0.40±0.018</td>
<td>14.8±1.2</td>
</tr>
<tr>
<td>F6</td>
<td>33°±1.00</td>
<td>0.35±0.002</td>
<td>0.42±0.001</td>
<td>16.2±0.7</td>
</tr>
<tr>
<td>F7</td>
<td>28°±1.00</td>
<td>0.35±0.002</td>
<td>0.40±0.005</td>
<td>12.6±0.9</td>
</tr>
<tr>
<td>F8</td>
<td>28°±1.00</td>
<td>0.36±0.003</td>
<td>0.41±0.002</td>
<td>12.7±1.1</td>
</tr>
<tr>
<td>F9</td>
<td>31°±1.00</td>
<td>0.36±0.005</td>
<td>0.42±0.004</td>
<td>14.2±1.3</td>
</tr>
</tbody>
</table>

Table 3: Evaluation parameters of formulations

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Thickness (mm)</th>
<th>Hardness (kg/cm²)</th>
<th>Friability (%)</th>
<th>Weight variation (mg)</th>
<th>Drug content (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>3.67±0.04</td>
<td>5.3±0.02</td>
<td>0.65±0.07</td>
<td>331.2±1.3</td>
<td>98.06±0.02</td>
</tr>
<tr>
<td>F2</td>
<td>3.68±0.07</td>
<td>5.6±0.05</td>
<td>0.5±0.09</td>
<td>330.7±1.4</td>
<td>98.39±0.01</td>
</tr>
<tr>
<td>F3</td>
<td>3.42±0.02</td>
<td>5.4±0.03</td>
<td>0.5±0.05</td>
<td>331.5±1.7</td>
<td>97.22±0.01</td>
</tr>
<tr>
<td>F4</td>
<td>3.71±0.04</td>
<td>5.4±0.01</td>
<td>0.5±0.11</td>
<td>330.2±2.1</td>
<td>99.02±0.01</td>
</tr>
<tr>
<td>F5</td>
<td>3.67±0.09</td>
<td>5.8±0.04</td>
<td>0.47±0.08</td>
<td>329.8±2.3</td>
<td>97.18±0.00</td>
</tr>
<tr>
<td>F6</td>
<td>3.63±0.11</td>
<td>6.1±0.02</td>
<td>0.47±0.12</td>
<td>329.2±2.1</td>
<td>97.56±0.01</td>
</tr>
<tr>
<td>F7</td>
<td>3.74±0.02</td>
<td>5.4±0.03</td>
<td>0.5±0.04</td>
<td>328.7±1.8</td>
<td>97.19±0.02</td>
</tr>
<tr>
<td>F8</td>
<td>3.76±0.01</td>
<td>5.5±0.01</td>
<td>0.5±0.07</td>
<td>328.7±1.8</td>
<td>98.45±0.01</td>
</tr>
<tr>
<td>F9</td>
<td>3.69±0.05</td>
<td>5.7±0.05</td>
<td>0.5±0.06</td>
<td>331.4±1.2</td>
<td>98.28±0.02</td>
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</tbody>
</table>

Table 4: Buoyancy studies of formulations

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>FLT (seconds)</th>
<th>Floating duration (hrs)</th>
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<tbody>
<tr>
<td>F1</td>
<td>52</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F2</td>
<td>58</td>
<td>10</td>
</tr>
<tr>
<td>F3</td>
<td>76</td>
<td>10</td>
</tr>
<tr>
<td>F4</td>
<td>29</td>
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<tr>
<td>F5</td>
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<td>F7</td>
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<td>&gt;12</td>
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<tr>
<td>F8</td>
<td>32</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F9</td>
<td>39</td>
<td>&gt;12</td>
</tr>
</tbody>
</table>

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Pre compression parameters

Floating tablets of venlafaxine hydrochloride were developed to increase the gastric residence time of the drug so that they can be retained in the stomach for longer time and help in the controlled release of drug up to 12 hrs [36]. Different grades of viscosities of the polymers such as Carbopol 934, xanthan gum, HPMC K100M are known to be beneficial in improving floating property and release characteristics. The pre-compression parameters obtained for all formulations are tabulated in Table 2. The value of the angle of repose indicates good flow property of powder blend. Carr’s index value indicates that the powder blend has the required flow property for direct compression.

Post compression parameters

The floating tablets were prepared by direct compression method using the polymers Carbopol 934, xanthan gum, HPMC K100M to provide sufficient drug release retardation and provide sufficient buoyancy to the tablets. The results are shown in Table 3. The prepared floating tablets were evaluated for thickness, hardness, friability, average weight variation, drug content, all the studies were performed in triplicates, and the results were expressed in ± standard deviation. The hardness for the tablets ensures the good handling characteristics of all the batches. The percentage friability was <1% in all the formulations ensuring that the tablets were mechanically stable. The weight variation for different formulations was found to be in the acceptable limit. The drug content uniformity in all the formulations was calculated and the presence of the active ingredient was found to be 97.19-98.45%, with low standard deviation indicates batch-to-batch consistency.

Swelling index

Swelling index for all the formulations was carried out in the distilled water and simulated gastric fluid (0.1 N HCl). It was found that the formulation showed rapid uptake of distilled water whereas there was gradual constant uptake of simulated gastric fluid (Fig. 1). The tablets containing Carbopol 934 and HPMC K100M showed maximum swelling in 12 hrs with a sharp increase up to 8 hrs which may be due to increased concentration of HPMC K100M which retain water and form a thick swollen mass.

Buoyancy studies

The in vitro floating behavior of the tablets was studied by placing them in beaker containing 0.1 N HCl (pH 1.2). The gas generating agents immediately evolves carbon dioxide in the presence of HCl solution generating sufficient porosity which helped the dosage unit to float. Formulation F1-F3 prepared with Carbopol 934 started floating after 52 seconds and remains buoyant for 10 hrs till they were completely eroded. On the other hand, formulation F4-F6 prepared with xanthan gum which shows a floating time of 8 hrs and formulation of F7-F9 prepared with HPMC K100M show decrease in FLT to 34 seconds and increased floating duration time to >12 hrs. This may be due to the difference in concentration of polymers and gas generating agent [37]. This might be due to high viscosity polymer HPMC K100M maintains the integrity of the tablets for longer duration by reducing the effect of erosion thus resulting in an increase in floating time. The results are shown in Table 4. Thus, it can be concluded that the batch containing HPMC polymers showed good FLT and TFT.
In vitro drug release studies

In vitro drug release studies were carried out using USP dissolution apparatus Type II at 50 rpm. The drug release at different time intervals was measured using a UV-visible spectrophotometer at 224 nm. To check the 100% dissolution release profile, formulations were subjected to dissolution studies for 12 hrs. Among the nine formulations, F8 was best and shows 98.34% drug release in the end of 12 hrs. It is evident from the in vitro dissolution data that increase in HPMC K100M concentration decreases the release rate which might be due to increase in diffusional path length, which the drug molecule may have to travel. It also indicates that higher viscosity of the polymer concentrations greatly retard the release of drug. Hence, formulation F8 was selected as the optimized formulation. The results are shown in Table 5.

Table 5: Percentage drug release of formulations

<table>
<thead>
<tr>
<th>Time (hrs)</th>
<th>Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F1</td>
</tr>
<tr>
<td>1</td>
<td>24.87</td>
</tr>
<tr>
<td>2</td>
<td>36.24</td>
</tr>
<tr>
<td>4</td>
<td>58.16</td>
</tr>
<tr>
<td>6</td>
<td>76.08</td>
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<td>8</td>
<td>87.28</td>
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<tr>
<td>10</td>
<td>94.79</td>
</tr>
<tr>
<td>12</td>
<td>96.53</td>
</tr>
</tbody>
</table>

Table 6: Correlation coefficients of different mathematical models for F-1 to F-9

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Zero order R²</th>
<th>First order R²</th>
<th>Higuchi R²</th>
<th>Peppas R²</th>
<th>N value</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.891</td>
<td>0.938</td>
<td>0.961</td>
<td>0.964</td>
<td>0.612</td>
</tr>
<tr>
<td>F2</td>
<td>0.912</td>
<td>0.947</td>
<td>0.984</td>
<td>0.972</td>
<td>0.579</td>
</tr>
<tr>
<td>F3</td>
<td>0.934</td>
<td>0.979</td>
<td>0.987</td>
<td>0.987</td>
<td>0.586</td>
</tr>
<tr>
<td>F4</td>
<td>0.830</td>
<td>0.872</td>
<td>0.857</td>
<td>0.878</td>
<td>0.457</td>
</tr>
<tr>
<td>F5</td>
<td>0.886</td>
<td>0.907</td>
<td>0.893</td>
<td>0.885</td>
<td>0.466</td>
</tr>
<tr>
<td>F6</td>
<td>0.898</td>
<td>0.926</td>
<td>0.935</td>
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<td>0.569</td>
</tr>
<tr>
<td>F7</td>
<td>0.925</td>
<td>0.947</td>
<td>0.990</td>
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</tr>
<tr>
<td>F8</td>
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<td>0.998</td>
<td>0.987</td>
<td>0.660</td>
</tr>
<tr>
<td>F9</td>
<td>0.974</td>
<td>0.958</td>
<td>0.995</td>
<td>0.982</td>
<td>0.716</td>
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</table>

Table 7: Stability studies of optimized formulation F8

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>25°C±2°C/60% RH±5% RH, 30°C±2°C/65% RH±5% RH, 40°C±2°C/75% RH±5% RH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness</td>
<td>Drug content (%)</td>
</tr>
<tr>
<td>(kg/cm²)</td>
<td>(%)</td>
</tr>
<tr>
<td>30</td>
<td>5.56</td>
</tr>
<tr>
<td>60</td>
<td>5.56</td>
</tr>
<tr>
<td>90</td>
<td>5.48</td>
</tr>
</tbody>
</table>

TFT: Total floating time is 0.998 and were found to be linear, which indicates that the drug release depended on the square root of the time and predominantly controlled by diffusion process. The mechanism of drug release is predicted using Korsmeyer–Peppas equation. The n value of optimized formulation F8 is 0.66. This indicates that the drug release depends on swelling, diffusion, and erosion. All formulations follow then on - Fickian/anomalous type of diffusion.

Stability studies

Stability studies were carried out on selected formulations (F8) as per ICH guidelines. There was not much variation in matrix integrity of the tablets at all the temperature conditions. There were no significant changes in drug content, physical stability, hardness, friability, drug release, FIT (Table 7) for the selected formulation F8 after 90 days.

Comparison with marketed product

The marketed product released 96.16% drug in 10 hrs, whereas the optimized formulation F8 released 98.3% drug in 12 hrs. Thus, comparative study of the marketed product of venlafaxine hydrochloride showed that the optimized formulation F8 has better control over release rate when compared with the commercial product (Fig. 2).

CONCLUSION

FDDS are retained in the stomach for a longer time and assist in improving the oral controlled delivery of drugs that have an absorption window in the particular region of the GIT as well as for controlling
the release of the drug having site-specific absorption limitation. Venlafaxine hydrochloride, an antidepressant drug exhibits pH dependent solubility. Hence, an attempt was made to develop gastro retentive delivery system of venlafaxine hydrochloride which increased the bioavailability of venlafaxine hydrochloride and also to reduce the frequency of administration, thereby improving patient compliance and therapeutic efficacy.

In the present study, formulations F1-F9 were prepared by direct compression. The dissolution studies were carried out for 12 hrs. When compared to other formulations, F8 showed good FLT and TFT. Based on all these results, formulation F8 was selected as the optimized formulation and was compared to the marketed product. It was found that the optimized formulation F8 has better control over release rate in comparison to the commercial product. The drug-polymer ratios, viscosity of polymers, were found to influence the drug release and floating properties of the prepared tablets. From the results, it can be concluded that as the concentration of the polymer increased FLT decreased and the percentage drug release was prolonged. Viscosity of the polymer also showed a directly proportional relationship with swelling characteristics of the tablets. The optimized formulation (F8) was subjected for stability studies as per ICH guidelines with no significant change in the various evaluated parameters of the formulations. Overall, this study concludes that viscosity is a major factor affecting the release and floating properties of the gastric floating drug delivery system [38]. The use of hydrophobic retardant and hydrophilic polymer in combination had its own advantages of maintaining integrity and buoyancy of tablets. And also in initial burst effect was minimized. It could be concluded that for proper floating duration and in vitro release, the hydrophobic retardant and hydrophilic polymer must be used in proper ratio [39].

REFERENCES