DEVELOPMENT AND EVALUATION OF SUSTAINED RELEASE FORMULATIONS OF VENLAFAXINE HYDROCHLORIDE

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ABSTRACT

In the present study, Venlafaxine was chosen as a model drug which is an Anti-Depressant. Because of its short life (5-11 hr) and its high water solubility it was chosen as a suitable candidate for sustain matrix tablet formulation. It was formulated into matrix tablet using hydrophilic polymer such as HPMC, Eudragit RS100, and Ethyl cellulose as release retards. All the precompression parameters were found to be within the standard limits. Tablets were evaluated for hardness, friability, thickness, drug content, in-Vitro release, swelling and stability studies. The effect of polymer concentration binary polymer mixture and wet granulation method on drug release profile was studied. It was observed that the type of polymer and its concentration has influence the drug release from matrix tablet. Matrix tablet content a blend of HPMC and ethyl cellulose successfully sustained the release of Venlafaxine for a period of 17 hr. Precompression parameter indicated that granules used for preparing tablets with free flowing. Post-compresional parameters were within the acceptable limit. The concentration of Venlafaxine was kept constant, lactose used as filler.

The sustained release from ethyl cellulose and HPMC was due to interaction between ethylcellulose chain ionic polymer and HPMC chain, non-ionic polymer, which resulted in favorable increase in the water uptake capacity and gel viscosity, leading to better control over the release of Venlafaxine. F4 showed the sustained release of Venlafaxine as desired. The study revealed that the ethyl cellulose and HPMC can be used for the formulation of sustained release matrix tablet of Venlafaxine.

KEY WORDS: Venlafaxine, Matrix tablet, HPMC, Ethyl cellulose, Eudragit RS100, Wet granulation.

INTRODUCTION

Sustained Release Dosage Forms

To the date, for every disease or disorder state of the patient, proper medication is of prime importance to maintain the patient in good health. To achieve this, the medicine or drug is administered conventionally by one or more of several well defined and popular routes of drug administration including oral, parenteral, rectal, alveolar, ocular and topical. Among these above mentioned popular routes, oral conventional route of drug administration lies at the top of the hierarchy of the conventional routes. It is a reasonable assumption that drug concentration at the site of action is related to drug plasma level and that, in the great majority of cases, the intensity of effect is some function of drug concentration at the target site. The objective of the most therapeutic regimens is to rapidly raise the plasma concentration to the required level and then to hold it constant for the desired duration of treatment. The extent to which this situation can be achieved depends on many factors, including the minimum effective concentration of the drug, the level at which side effects occur, the dose administered, the rate of drug release from the dosage form, the rate of elimination and the frequency of dosing. Provided that the dose size and frequency of administration are correct, therapeutic ‘steady state’ levels of the drug can be achieved rapidly and maintained by the repetitive administration of conventional oral dosage forms.

Traditionally patient only takes medication during the day time hours. Plasma levels can therefore fall to sub-therapeutic levels overnight. However, there are a number of major deficiencies of conventional dosage forms, few of which are listed here.
Inconvenience and/or difficult use of drugs with very short duration of action or biological half-life.

- Need for frequent dosing
- Potential for “peak-valley” plasma levels, leading to toxicity and side effects and incomplete therapy.
- Poor patient compliance, due to adverse effects, forgetfulness, and inconvenience of dosage forms.
- Frequently needed for large systemic concentrations in order to achieve adequate concentration at target site or action.
- Potential variations in oral absorption due to variations in; GIT pH profile, presence and type of food and transit time in gut.

Like every failure that sets ahead the path of successes, these above mentioned major deficiencies of drug therapy based on repetitive administration of conventional single oral dosage form, have lead to the development of a more specialized group of oral dosage forms (modified release drug products). Thus, various modified drug products have been developed to release the active drug from the product at a controlled rate. The term controlled release drug products was previously used to describe various types of oral extended-release dosage forms, including sustained release, sustained action, slow release, long action, and retarded release. Many of these terms for controlled-release dosage forms were introduced by drug companies to reflect a special design for a controlled release drug product or for use as a marketing term. The United States Pharmacopoeia (USP) has adopted the term “extended release” whereas the British Pharmacopoeia (BP) has adopted the term “slow release”. The Food and Drug Administration (FDA) of the United States has adopted the term “prolonged release”. Both USP and FDA employ the term “delayed release” for enteric coated products.

**MATERIALS AND METHODS**

All other chemicals and reagents used were of “analytical reagents” (AR) grade.

**Instruments and Equipments:**

- UV visible double beam spectrophotometer (Model-UV1601, Shimadzu, Japan)
- FT-IR spectrophotometer (Model-8400S, Shimadzu, Japan)
- Single pan electronic balance (Model AW-220, Shimadzu, Japan)
- Sieves
- Bulk Density Apparatus digital model (Veego)
- KBR IR Press
- Monsanto hardness tester
- Vernier Caliper
- Roche Friability Tester (Lab Hosp)
- USP Tablet Dissolution Apparatus Type II (Model-DT 60, Veego)

**Profile of drug Venlafaxine HCl**

Venlafaxine Hydrochloride (VFX) is an orally active serotonin noradrenaline reuptake inhibitor used for the treatment of major depressive disorders.®

**Structure:**

![Venlafaxine Hydrochloride](image)

**Molecular formula:** C₁₇H₂₇NO₂ HCl
**Molecular weight:** 313.87
**CAS:** [99300-78-4]
**Chemical name:** (R/S)-1-[2-(dimethylamino)-1(4 methoxyphenyl) ethyl] cyclohexanol hydrochloride or (±)-1-[α-[(dimethylamino)methyl]-p-methoxybenzyl] cyclohexanol hydrochloride.

**Solubility:** 572 mg/ml
**Melting point:** 215-217°C
**Partition coefficient:** (octanol/water) 0.43
**Proprietary names:** Dobupal; Efexor; Effexor; Trevil or; Trewilor, Vandral

**Pharmacokinetics**

Venlafaxine is well absorbed and extensively metabolized in the liver. O-desmethylvenlafaxine (ODV) is the only major active metabolite. On the basis of mass balance studies, at least 92% of a single dose of venlafaxine is absorbed. Approximately 87% of a venlafaxine dose is recovered in the urine within 48 hours as either unchanged venlafaxine (5%), unconjugated ODV (29%), conjugated ODV (26%), or other minor inactive metabolites (27%). Renal elimination of venlafaxine and its metabolites is the primary route of excretion. The relative bioavailability of venlafaxine from a tablet was 100% when compared to an oral solution. Food has no significant effect on the absorption of venlafaxine or on the formation of ODV.
Pharmacodynamics
The mechanism of the antidepressant action of Venlafaxine HCl in humans is believed to be associated with its potentiation of neurotransmitter activity in the CNS.
Preclinical studies have shown that Venlafaxine HCl and its active metabolite, o-desmethylenlafaxine (ODV), are potent inhibitors of neuronal serotonin and norepinephrine uptake and weak inhibitors of dopamine reuptake. Venlafaxine HCl and ODV have no significant affinity for muscarinic, histaminergic, or α-1 adrenergic receptors in vitro. Pharmacologic activity at these receptors is hypothesized to be associated with the various anticholinergic, sedative, and cardiovascular effects seen with other psychotropic drugs. Venlafaxine HCl and ODV do not possess monoamine oxidase (MAO) inhibitory activity.

Hydroxy propyl methyl cellulose (HPMC)

**Chemical name:** Cellulose 2- hydroxyl propyl methyl ether
**Synonym:** Cellulose, Hypromellose, 2-Hydroxypropylmethyl ether, Methyl hydroxy propyl cellulose, Methocel, Pharmacoat, Metolose.
**Description:** Hypromellose is an odourless and tasteless white or creamy white fibrous or granular powder.
**Physical properties:**
- **Solubility:** soluble in cold water, forming a colloidal solution; practically insoluble in hot water, dehydrated alcohol, chloroform and ether.
- **pH:** A 1%w/w solution has a pH of 5.5-8.0.
- **Melting point:** Browns at 190-200°C; chars at 225-230°C;
- **Tg is at 170-180°C.**
- **Autoignition temperature:** 360°C
- **Bulk density:** 0.341 gm/cm³
- **Tapped density:** 0.557 gm/cm³
- **Enzyme resistance:** Comparatively enzyme resistant
- **Gel formation:** undergoes a reversible transformation from solution to gel upon heating and cooling respectively.
- **Gel point:** 50-900C
- **Ash value:** 1.5-3 % depending upon the grade.
- **Specific gravity:** 1.3

**Surface activity:** provides some surfactancy in solutions, surface tension for such solutions range from 42-56 dynes/cm.
**Storage:** stored in well closed containers

**Applications in pharmaceutical formulation or technology:**
- Widely used in oral and topical pharmaceutical formulations.
- Concentrations between 2% and 5% w/w may be used as a binder in either wet or dry granulation processes.
- High viscosity grades may be used to retard the release of drugs from the matrix at levels of 10-80% w/w in tablets and capsules.
- Low viscosity grades are used in aqueous film coating solutions.

**Ethylcellulose**
**Chemical name:** Cellulose Ethyl Ether
**Synonym:** Aquacoat ECD, Aqualon, Ethocel, Surelease
**Description:** Ethyl cellulose is a tasteless, free flowing, white to light tan coloured powder.
**Physical properties:**
- **Solubility:** soluble in cold water, forming a viscous colloidal solution, practically insoluble in cold water, ethanol (95%), and ether10.
- **pH:** 6.0-7.8
- **Density(bulk):** 0.4g/cm³
- **Specific gravity:** 1.12-1.15g/cm³
- **Moisture content:** EC absorbs very little water from humid air.

**Applications In pharmaceutical formulation or technology:**
- The main use of ethyl cellulose in oral formulations is as a hydrophobic coating agent for tablets and granules.
- Modified release tablet formulations may also be produced using ethyl cellulose as a matrix former.
- High viscosity grades are used in drug micro encapsulation.
- In tablet formulations, ethyl cellulose may additionally be employed as a binder, ethyl cellulose being blended dry, as wet granulated with a solvent such as ethanol (95%).

**Eudragit RS100**
**Chemical name:** Poly [ethyl acrylate, methyl methacrylate, trimethyl ammonioethyl methacrylate chloride]1:2:0.1
**Synonym:** Kollicoat MAE 30D, Kollicoat MAE 30DP
**Description:** Solutions are colourless or slightly yellow in color, they have an odour characteristic of solvents\(^{11}\).

**Physical properties**
- **Acid value:** 300-330
- **Alkali value:** 12.1-18.3
- **Density (bulk):** 0.390g/cm\(^3\)
- **Density (tapped):** 0.424g/cm\(^3\)
- **Viscosity:** ≤ 15mPas
- **Refractive index:** 1.38-1.385

**Stability and storage conditions:**
Dry powder polymeric forms are stable at temp less than 30\(^{0}\)C. Dry powders are stable for atleast three years if stored in tightly closed containers at less than 30\(^{0}\)C.

**Applications:**
Eudragit RS are used to form water insoluble film coating for sustained release products. Also used in oral capsule and tablet formulations as film coating agents.

**Preparation of Matrices by wet Granulation**
Different tablet formulations were prepared by wet granulation technique. All the powders were passed through ASTM (American Society of Testing and Materials) 80 mesh. Required quantities of drug, polymer, diluent and dry binders such as ethylcellulose and eudragit were mixed thoroughly.
Sufficient quantity of ethanol(95%) was sprinkled over the powder mixture to obtain enough cohesiveness. The cohesive mass was then sieved through 16/22 mesh. The granules were dried at 40\(^{0}\)C for 12 hours and thereafter kept in desicator for 12 hours. Once dry, the granules retained on 22 mesh were mixed with granules that passed through 22 mesh. Talc and magnesium stearate were finally added as glidant and lubricant and mixed well with granules for 5 minutes.

**Formulation code:**
Tablets containing HPMC in wet granulation and dicalcium phosphate - F

**RESULTS**

**Characterization of Venlafaxine Hydrochloride**
The characterization of drug was carried out by conducting various physicochemical tests including melting point determination, spectral analysis such as UV spectrum and IR Spectrum for pure Venlafaxine HCl.
The melting point was found to be in the range of 215\(^{0}\)C – 217\(^{0}\)C which is in good agreement with the reported values.

**UV Spectroscopy:**
UV absorption spectrum showed \(\lambda_{\text{max}}\) to be 226.5 nm. The graph of absorbance vs. concentration for pure Venlafaxine HCl was found to be linear in the concentration range of 5 – 50 \(\mu\)g/ml at 226.5 nm. Hence the drug obeys Lambert – beer’s law in this range.

**DISCUSSION**
The current investigation deals with the optimization of Sustained release matrix tablets of Venlafaxine Hcl using hydrophilic Polymers. Polymers used were HPMC K100M, Ethyl cellulose and Eudragit RS100. The hydrophilic matrices for Venlafaxine Hcl (water soluble drug) containing a blend of one or more gel forming polymers. The compositions of the formulations. The concentration of Venlafaxine Hclwas kept constant at 75mg. Lactose was used as filler.

**Characterization of Venlafaxine HCL**

**Melting point**
The melting point was found to be in the range of 215\(^{0}\)C – 217\(^{0}\)C which was in good agreement with the reported values.

**Spectroscopic Studies**

**UV Spectroscopy (Determination of \(\lambda_{\text{max}}\))**
The \(\lambda_{\text{max}}\) of Venlafaxine Hcl was found to be at 226.5 nm in distilled water and phosphate buffer of pH 6.8. Standard graph of Venlafaxine Hcl in distilled water and phosphate buffer of pH 6.8 irrespectively. Good linearity was observed with the plot. Its ‘r’ value in distilled water was 0.99983 and in phosphate buffer of pH 6.8 the value was 0.9993 which were very nearer to ‘1’ and hence obeyed “Beer –Lambert” law.

**Determination of infrared absorption spectrum**
The FT-IR spectra of Venlafaxine Hcl is shown in figure no 5 and spectral assignments for Venlafaxine Hcl the IR spectrum indicated characteristic peaks belonging to functional group such as principle peaks at wave no 3320, 1622 and 1250.

**Determination of Inraction between Drug and used polymers**
The FT-IR spectra of all combinations containing drug and one or more polymers also shows the characteristic peaks same as that of the pure drug at wave no is shown The FT-IR spectrum of all the combinations containing drug and one or more polymer shows same or slightly shift in peak values when compared with the characteristic peak values of the pure drug. Thus, from the above it is concluded that there is no interaction between the Venlafaxine Hcl and used polymers.

**Evaluation of Granules**
The granules were prepared by wet granulation method using 10 % (w/w) starch paste as binder. Pre-
compressional parameters i.e. angle of repose (21.60 to 24.30), percent compressibility (15), and Hausner’s ratios (1.08 to 1.20) These results indicate that granules are good flowing in character. The results of angle of repose (<30) indicate good flow properties of the granules. This was further supported by lower Hausner’s ratios, lower compressibility index values. Compressibility index values up to 15% result in good to excellent flow properties. And thus the granules were suitable for compression.

**Evaluation of Tablets**

The results of Postcompressional parameters All the formulations showed uniform thickness. In a weight variation test, the pharmacopoeial limit for percentage deviation for the tablets of more than 300mg is ± 5%. The average percentage deviation of all the tablet formulations was found to be within the above limit, and hence all the formulations passed the test for uniformity of weight as per the official requirements. Good uniformity in drug content was found among different batches of tablets, and percentage of drug content was more than 95%. The all formulations shows required hardness this could be due to presence of starch paste which is generally responsible for more hardness of the tablet. In the present study the percentage friability for all the formulations was below 1% indicating that the friability is within the prescribed limits. All the tablet formulations showed acceptable properties and complied with the in-house specifications for weight variation Postcompressational parameters i.e. hardness, friability, thickness, weight variation, and drug content were with in acceptable official IP limits.

**Dissolution Study**

In-vitro drug release study for the prepared matrix tablets were conducted for period of 15-17 hours using a USP XXVI type II (paddle) apparatus at 37°C ± 0.5°C and 50 rpm speed. The dissolution studies were carried out in triplicate in phosphate buffer of pH 6.8 under sink condition. At first half an hour and then every 1-hour interval samples of 5 ml were withdrawn from dissolution medium and replaced with fresh medium to maintain the volume constant. After filtration and appropriate dilution, the sample solution was analyzed at 226.5 nm for Venlafaxine Hclby a UV- spectrophotometer.

HPMC K100M is semi-synthetic, non-ionic cellulose ether which is widely used in sustained release dosage forms because of its non-toxic nature, its capacity to accommodate high levels of drug loading and its non pH – dependence. The drug release from hydrophilic matrix tablets is controlled by a hydrated viscous layer formed at the tablet periphery, this gel layer act as a barrier to drug release.

The drug release data for HPMC K100M formulation and drug release profiles The formulation with HPMC K100M 20 %, releases drug 98.85 % in 8 hrs, the formulation with HPMC k100M30 %, releases drug 98.12 % in 10 hrs. And the formulation with HPMC K100m40 %, releases drug 97.86 % in 11 hrs.

The HPMC contains hydropropyl (hydrophilic) and methoxy groups and hence retard drug release, main aspects of HPMC govern its performance in SR matrix system is rapid formation viscous gel layer upon hydration. And once gel layer is formed, the viscosity of the gel layer regulates the overall rate of drug release. In the present study we have increased polymer level from 20 to 40 % due to that dramatically retard of Venlafaxine Hclis observed means study indicate that increasing the concentration of the gelling polymer HPMC in the matrix led to slower drug release but because of low viscosity grade of HPMC the polymer is not able to retard the release the drug upto 17hrs.

So, the formulations containing only HPMC K100M could not retard the drug release of Venlafaxine Hclupto 17hrs due to faster release from this polymer may lead to toxic effect.

From the above single polymer dissolution study it is clear that single polymer were not able to control the drug release for 17 hrs so there is need to use combination of two or more polymer.

**Stability Study**

Stability studies were conducted on the selected formulations of Venlafaxine Hcl (F4) to assess their stability with respect to their physical appearance, drug content and drug release characteristics after storage at 40°C / 75±5% RH for 3 months to assess their long term stability. When the matrix tablets of Venlafaxine Hcl (F4) were stored at 40°C / ambient RH for 3 months there was no change either in physical appearance or in drug content shown in Table No 30.

When the dissolution study was conducted in phosphate buffer (pH 6.8) as described above, no significant difference was observed in the percentage of Venlafaxine Hclrelease from the selected formulations (F4) stored at 40°C / ambient RH for 3 months when compared to that released from the same formulations before storage. The insignificant change either in the physical appearance, drug content or dissolution profile of the selected
formulations (F4) after storage at 40°C / 75±5% RH for 3 months indicate that the formulations could provide a minimum shelf life of 2 years.

**CONCLUSION**

The ultimate aim of the present study was to prepare sustained release matrix tablet of Venlafaxine HCL using hydrophilic polymers like EC and Eudragit by wet granulation technique. The hydrophilic matrix tablet prepared were containing a blend of one more gel forming polymer. The conc. Of Venlafaxine HCL was kept constant. Lactose was used as filler. Following conclusions were made.

- The FT-IR study indicates that there is no interaction of the drug with polymer used for the study.
- Precompression parameter indicated that granules prepared with 10% w/w starch paste were free flowing.
- Postcompression parameter (hardness, friability, thickness and drug content) was within the acceptable limit.
- Formulation containing only a single polymer could not control the release of Venlafaxine HCL as desired.
- Matrix tablet of Venlafaxine HCL that contained a blend of HPMC successfully sustained the release of Venlafaxine HCL for a period of 17 hrs.
- The swelling behavior of F4 showed that matrices containing a minimum HPMC achieve higher swelling index, HEC/HPMC combination of ionic and non-ionic polymer, swelling was higher and more control over the release of Venlafaxine HCL was observed.
- The control release from HPMC combination was due to interaction between chain, ionic polymer and HPMC chain, non-ionic polymer, which resulted in favourable increase in the water uptake capacity and gel.

- The drug release mechanisms for formulations were best described by Higuchi’s equation. The formulations followed anomalous behavior.

**REFERENCES**


**Table 1** Formulation design of Venlafaxine hydrochloride tablets by wet granulation method using HPMC

<table>
<thead>
<tr>
<th>Ingredients(per tablet)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine HCl</td>
<td>84.87</td>
<td>84.87</td>
<td>84.87</td>
<td>84.87</td>
<td>84.87</td>
<td>84.87</td>
</tr>
<tr>
<td>Hydroxypropylmethyl celluloseK100M</td>
<td>84.87</td>
<td>169.74</td>
<td>169.74</td>
<td>169.74</td>
<td>169.74</td>
<td>169.74</td>
</tr>
<tr>
<td>Ethylcellullose(2%/w/w)</td>
<td>-</td>
<td>-</td>
<td>8</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ethylcellulose(4%/w/w)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>16</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>EudragitRS100(4%/w/w)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>16</td>
<td>-</td>
</tr>
<tr>
<td>EudragitRS100(8%/w/w)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>32</td>
</tr>
<tr>
<td>Ethanol (95%)</td>
<td>qs</td>
<td>qs</td>
<td>qs</td>
<td>qs</td>
<td>qs</td>
<td>qs</td>
</tr>
<tr>
<td>Dicalcium phosphate</td>
<td>222.6</td>
<td>137.39</td>
<td>129.39</td>
<td>121.39</td>
<td>121.39</td>
<td>105.39</td>
</tr>
<tr>
<td>Magnesium stearate(%/w/w)</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Talc (%/w/w)</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>
Table 2: Pharmacokinetic parameters of Venlafaxine HCl

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral absorption</td>
<td>&gt; 92%</td>
</tr>
<tr>
<td>Plasma half-life (ODV)</td>
<td>5h (11 h)</td>
</tr>
<tr>
<td>Volume of distribution (ODV)</td>
<td>7.51 kg⁻¹ (5.71 kg⁻¹)</td>
</tr>
<tr>
<td>Plasma protein binding (ODV)</td>
<td>27% (30%)</td>
</tr>
<tr>
<td>Plasma clearance (ODV)</td>
<td>1.2-1.7 l/h/kg (0.4 l/h/kg)</td>
</tr>
</tbody>
</table>

(ODV) – O-desmethylvenlafaxine

Table 3: Hypromellose is available in various grades that vary in viscosity and extent of substitution

<table>
<thead>
<tr>
<th>Methocel grade</th>
<th>Nominal Viscosity (mPas)</th>
</tr>
</thead>
<tbody>
<tr>
<td>K100LVP</td>
<td>100</td>
</tr>
<tr>
<td>K4M</td>
<td>4000</td>
</tr>
<tr>
<td>K15M</td>
<td>15000</td>
</tr>
<tr>
<td>K100MP</td>
<td>100000</td>
</tr>
<tr>
<td>E4MP</td>
<td>4000</td>
</tr>
<tr>
<td>E10MP CR</td>
<td>10000</td>
</tr>
<tr>
<td>E3 PREM. LV</td>
<td>-</td>
</tr>
<tr>
<td>E3P PREM. LV</td>
<td>-</td>
</tr>
<tr>
<td>E6P PREM. LV</td>
<td>-</td>
</tr>
<tr>
<td>E15P PREM. LV</td>
<td>-</td>
</tr>
<tr>
<td>K3 PREM. LV</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 4: Wavelength of maximum absorption (λ_{max}) in different solvents

<table>
<thead>
<tr>
<th>Sr.No</th>
<th>Solvent</th>
<th>λ_{max}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Water</td>
<td>226.5 nm</td>
</tr>
<tr>
<td>2</td>
<td>0.1 N HCL</td>
<td>226.5 nm</td>
</tr>
<tr>
<td>3</td>
<td>pH 6.8 Phosphate Buffer</td>
<td>226.5 nm</td>
</tr>
</tbody>
</table>

Table 5: Data for Standard Curve Parameters

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Coefficient of correlation (R²)</th>
<th>Equation of line (Y=mx+C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>0.9993</td>
<td>y = 0.0046x + 0.0018</td>
</tr>
<tr>
<td>0.1 N HCL</td>
<td>0.9992</td>
<td>y = 0.0399x + 0.0075</td>
</tr>
<tr>
<td>pH 6.8 Phosphate Buffer</td>
<td>0.9991</td>
<td>y = 0.0372x + 0.0212</td>
</tr>
</tbody>
</table>

Table 6: IR interpretation of Venlafaxine, HPMC K100M, and granules containing EC 1% w/v and EC 2% w/v as a granulatin agent

<table>
<thead>
<tr>
<th>Peaks cm⁻¹</th>
<th>Groups</th>
<th>Stretching/Deformation</th>
</tr>
</thead>
<tbody>
<tr>
<td>3320</td>
<td>O-H</td>
<td>Stretching</td>
</tr>
<tr>
<td>1208</td>
<td>C-O</td>
<td>Stretching</td>
</tr>
<tr>
<td>2875</td>
<td>Aliphatic C-H</td>
<td>Stretching</td>
</tr>
<tr>
<td>1245</td>
<td>Asymmetric C-O-C</td>
<td>Stretching</td>
</tr>
<tr>
<td>1039</td>
<td>Symmetric C-O-C</td>
<td>Stretching</td>
</tr>
</tbody>
</table>
Table 7: Dissolution profile of formulation containing HPMC K100M as a diluent and ethanol alone as a granulating agent

<table>
<thead>
<tr>
<th>Time (hr)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>Marketed</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>32.45</td>
<td>17.54</td>
<td>13.50</td>
<td>10.11</td>
<td>15.66</td>
<td>12.57</td>
<td>3.42</td>
</tr>
<tr>
<td>1</td>
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Fig 1. UV Spectrum of Venlafaxine HCl
B. IR spectrum interpretation:

Fig 2: Standard Curve of Venlafaxine HCL

\[
y = 0.0372x + 0.0212 \\
R^2 = 0.9991
\]

Fig 3: IR spectrum indicated characteristics peaks belonging to measure functional groups such as principal peaks at wave number 3320, 1622, 1250 cm\(^{-1}\)

Fig 4: IR spectrum of Venlafaxine, HPMC K100M, and granules containing EC 1% w/v and EC 2% w/v as a granulating agent
Fig: 5 IR spectrum of Venlafaxine, HPMC K100M, and granules containing ERS 2% w/v and ERS 4% w/v as a granulating agent

Fig: 6 Dissolution data of formulation containing HPMC K100M

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