FORMULATION AND EVALUATION OF SUBLINGUAL TABLET OF PAROXETINE HYDROCHLORIDE

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ABSTRACT

The sublingual tablet of Paroxetine hydrochloride was prepared by the direct compression method. The 50 mg tablets were devised using several concentrations of excipients like Pregelatinized starch as a binder, F-Melt M as a diluent, Sodium saccharine as a sweetening agent, Talc and Aerosil as a lubricant and a glidant respectively. Various pre and post evaluation parameters like hardness (kg), thickness (mm), diameter (mm), disintegration time (sec), %drug release at 9 mins, weight variation, friability, etc. were tested. Batch F6 was found to be the best batch with 2mg of Kyron T-314 and 1.25mg of Pregelatinized starch. The optimized batch was selected depending upon the minimum disintegration time and % cumulative release resulting into improvement in the bioavailability, drug efficiency and faster onset of action.

KEYWORDS: Paroxetine hydrochloride, sublingual dosage form, bioavailability, first pass metabolism, disintegration time, Post-menopausal syndrome

INTRODUCTION

A sublingual dosage form is placed beneath the tongue where it is submerged with saliva and due to presence of a highly vascularized region, the drug quickly reaches into systemic
circulation.[1] The medication is rapidly absorbed and avoids extensive first pass metabolism which holds advantageous over the oral ingestion route. Therefore, the peak plasma levels are achieved quickly pertaining to rapid onset of action. This is helpful specially in the case of emergency conditions where immediate action is needed, the action needs to be terminated (by spitting out the tablet) or the patient is unable to swallow.[2] This objective can be achieved by using novel excipients which will work as disintegrator, binder and glidant together to formulate a sublingual tablet. Menopause is ‘cessation of menses permanently which results in the loss of development of ovarian follicles. Post-menopause is the stage after menopause. Various symptoms like depression, headaches, hot-flashes, insomnia, irritability, mood swings, etc. are observed due to hormonal changes and declining levels of estrogen. This decrease in estrogen levels brings change in regulation of serotonin and nor-epinephrine, thus contributing to depression.[3,4] Paroxetine HCl (K+ form) is an anti-depressant used to treat post-menopausal syndrome (PMS) at a lower dose (7.5 mg), depression, panic attacks, obsessive-compulsive disorder (OCD), generalized anxiety disorders (GAD), and post-traumatic stress disorder (PTSD). It is a phenylpiperidine derivative, most potent inhibitor of 5-HT reuptake and belongs to the SSRI class (selective serotonin reuptake inhibitor) which helps to maintain adequate serotonin concentration in the brain. It acts by inhibiting the presynaptic uptake of serotonin by the SERT receptors which create an increased level of serotonin in the synaptic cleft exhibiting various symptoms. It is well absorbed by oral route; drug is mostly absorbed from the gastrointestinal tract and 95% plasma protein bound.[4] The bioavailability varies between 30-60% with a time of 2-8 (mean: 4.3) hours to reach the peak plasma concentration It is available as Paroxetine HCl salt with a pKa value of 9.9 and having low solubility in water. It is highly lipophilic. The elimination half-life of paroxetine is about 21 hours and highly metabolized by liver that is partially saturable. It is majorly excreted in urine, minorly in feces, mostly as metabolites and to a lesser extent as unchanged drug.[5] It is also used to treat disorders like Irritable Bowel Syndrome (IBS), Major Depressive Disorder (MDD), Premature Ejaculation, Premenstrual Dysphoric Disorder, Social Anxiety Disorder (SAD).[6,7] It reduces the vasomotor symptoms associated with menopause.[7] A sublingual tablet of paroxetine prepared will show lesser disintegration time within 30 secs, better drug release profile and greater bioavailability by avoiding first-pass metabolism, thus, improving the efficacy of drug. The present work was conducted using a systematic approach of experimental design models and statistical analysis for the development of a Sublingual tablet of Paroxetine HCl.
MATERIALS
The sublingual tablets of Paroxetine HCl were formulated by Direct Compression method with a total weight of 100mg for each tablet in all the formulation batches. The drug API is mixed with various excipients. Kyron t-314 was used as super disintegrating agent in the concentration 2-10%. It is a cation exchanger which facilitates tablet compression prompting greater hardness and improving the permeability of anionic drugs. It increases drug potential for rapid absorption and improved bioavailability.\(^8\) It also exhibits taste masking property and is derived from cross linked polymer of poly-carboxylic acid as per USP/NF and has a \(K^+\) ionic form.\(^9\) F-Melt Type-M was provided by ‘Gangwal Chemicals’ and selected as a diluent; it is a co-processed excipient composed of Magnesium alumino-metasilicate (Neusilin- 2-9%), D-mannitol (55-70%), Microcrystalline cellulose (10-25%), Xylitol (2-9%), Crospovidone (5-13%). It improves the quality of granules imparting better flow properties and enhances overall quality of tablet.\(^10\) Pregelatinized starch was incorporated as a binder in the formulation. It is composed of- 15% free amylo-pectin, 5% free amylase and 80% unmodified starch. When used in the concentration of 5-10%, it enhances flow and compression properties. It is self-lubricating, bland, odorless, capable of digestion and can also be used as a diluent (5-75%) as well as a disintegrant (5-10%).\(^11\) Sweetening agent, sodium saccharin was added to mask the bitter taste of drug(1-2%).\(^12\) Talc and Aerosil act as a lubricant and a glidant respectively. Aerosil is a moisture absorbent and a thickening agent when used in concentration of 0.125-0.5%.\(^13\) Less than 2% of talc (also known as a clay mineral), composed of hydrated magnesium silica, prevents the cake formation, thereby, further improving the property of the formulation.\(^14\)

METHODS
Drug-excipient compatibility studies by Fourier transform infrared & Differential scanning calorimetry (FTIR &DSC)
By using FTIR and DSC, compatibility studies were carried out to find out any interactions between drug and excipients. The FTIR spectroscopy study of pure Paroxetine HCl was performed using Shimadzu 8400S and characterization of the drug and excipients was accomplished using DSC study.

Direct Compression method
For commercial preparation of sublingual tablets, direct compression method is generally used. This process doesn’t require any granulating steps other than lubrication and
compression and hence, is a cost effective and effortless process in which the ingredients are jumbled well. These tablets possess better strength and undergo rapid disintegration.\textsuperscript{[15]}

This formulation contains the excipients of directly compressible grade such as super disintegrant and lubricant. All the powders were weighed for required quantities and passed through a 60 mesh-size sieve. The diluent, drug and disintegrating agent were mixed and binder with sweetening agent was added to it. The blend was then dried at 50\(^{\circ}\) in a hot air oven for 15 min to remove any moisture. Aerosil and talc were added lastly and blended thoroughly for about 5-6 minutes. Using a rotary tablet compression machine (BB tooling), the powder blend was directly compressed to form the sublingual tablets of 50mg weight and a diameter of about 3mm.

**Optimization of Sublingual tablet by using 3\(^{2}\) Full Factorial design**

An experimental design must be used to optimize different factors influencing the formulation and produce a pharmaceutical product of desired quality. The 3\(^{2}\) full factorial design was systemized to fulfil the objective of optimization of the sublingual tablets of Paroxetine HCl. The two selected factors were concentration of the Super disintegrating agent (X\(_{1}\)) and concentration of the binder (X\(_{2}\)). Each factor was checked at three levels (-1, 0, +1). The dependent variables were swelling index (Y\(_{1}\)) and % drug release (Y\(_{2}\)) at 9 min. Design Expert 11 software was used to obtain correlation between the independent variables and dependent variables. The composition of batches formulated are shown in Table 1.

**Formulation of batches according to Full factorial design:**

**Table 1: Layout of 3\(^{2}\) factorial design.**

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>X(_{1})</th>
<th>X(_{2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration of super disintegrating agent (Kyron T-314) (mg)</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Concentration of dry powder binder (PVP K-30) (mg)</td>
<td>4</td>
<td>1.5</td>
</tr>
<tr>
<td>Dependent variables</td>
<td>Y(_{1})</td>
<td>Y(_{2})</td>
</tr>
<tr>
<td>Disintegration time (in secs)</td>
<td>6.1</td>
<td>1.5</td>
</tr>
<tr>
<td>% Drug release at 9 min</td>
<td>2.5</td>
<td>3.5</td>
</tr>
</tbody>
</table>
Formulation of batches according to $3^2$ full factorial design

Table 2: Formulation of batches from B1 to B9.

<table>
<thead>
<tr>
<th>API &amp; Excipients</th>
<th>B1</th>
<th>B2</th>
<th>B3</th>
<th>B4</th>
<th>B5</th>
<th>B6</th>
<th>B7</th>
<th>B8</th>
<th>B9</th>
</tr>
</thead>
<tbody>
<tr>
<td>API</td>
<td>7.5mg</td>
<td>7.5mg</td>
<td>7.5mg</td>
<td>7.5mg</td>
<td>7.5mg</td>
<td>7.5mg</td>
<td>7.5mg</td>
<td>7.5mg</td>
<td>7.5mg</td>
</tr>
<tr>
<td>Kyron T-314</td>
<td>1mg</td>
<td>1mg</td>
<td>1mg</td>
<td>2mg</td>
<td>2mg</td>
<td>2mg</td>
<td>3mg</td>
<td>3mg</td>
<td>3mg</td>
</tr>
<tr>
<td>Pre-gelatinized starch</td>
<td>1.75 mg</td>
<td>0.75 mg</td>
<td>1.25 mg</td>
<td>1.75 mg</td>
<td>0.75 mg</td>
<td>1.25 mg</td>
<td>1.75 mg</td>
<td>0.75 mg</td>
<td>1.25 mg</td>
</tr>
<tr>
<td>F-Melt M</td>
<td>37.75 mg</td>
<td>38.75 mg</td>
<td>38.25 mg</td>
<td>37.25 mg</td>
<td>38.25 mg</td>
<td>37.75 mg</td>
<td>36.75 mg</td>
<td>37.75 mg</td>
<td>37.25 mg</td>
</tr>
<tr>
<td>Na Saccharin</td>
<td>1mg</td>
<td>1mg</td>
<td>1mg</td>
<td>1mg</td>
<td>1mg</td>
<td>1mg</td>
<td>1mg</td>
<td>1mg</td>
<td>1mg</td>
</tr>
<tr>
<td>Aerosil</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
</tr>
<tr>
<td>Talc</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
<td>0.5mg</td>
</tr>
<tr>
<td>Total</td>
<td>50 mg</td>
<td>50 mg</td>
<td>50 mg</td>
<td>50 mg</td>
<td>50 mg</td>
<td>50 mg</td>
<td>50 mg</td>
<td>50 mg</td>
<td>50 mg</td>
</tr>
</tbody>
</table>

Evaluation Parameters

Pre-compression parameters

1) Angle of repose

The powder is poured through the funnel to form a heap. The tip of the funnel should be adjusted in such a way that it remains close to the tip of the pile. Stop pouring the powder when the pile reaches a predetermined height. To get the angle of repose, divide the height of the pile by the radius of the base of the cone and the inverse tangent of this in the angle of repose.

$$\tan \theta = \frac{h}{r}$$

$h = \text{height of pile, } r = \text{radius of pile}$

2) Bulk density

Take defined amount powder in a 50ml graduated cylinder which is joined to a bulk density tester. The equipment will give the bulk density of powder.

Bulk density is calculated using the following formula:

$$\text{bulk density} = \frac{\text{weight of powder (g)}}{\text{bulk volume of powder}}$$

3) Tapped density

A defined quantity of powder is placed in a graduated cylinder which is joined to the tap density tester. The equipment gives the tapped density of the mass of powder. The tapped density can be calculated manually by placing the powder in the cylinder and dropping the cylinder 3 times from height of 1 inch at every interval of 2 second. Tapped density is...
calculated by following formula:

\[
tapped \ density = \frac{weight \ of \ powder (g)}{volume \ of \ powder}
\]

4) **Carr’s compressibility index**
To maintain the weight uniformity Carr’s index is an important parameter. It is calculated by using a given formula.

\[
% \ compressibility = \left( \frac{\text{bulk density} - \text{tap density}}{\text{bulk density}} \right) \times 100
\]

5) **Hausner’s ratio**
The flow properties can be defined by Hausner’s ratio. Hausner’s ratio can be calculated by following formula:

\[
Hausner's \ ratio = \frac{tapped \ density}{bulk \ density}
\]

**Post-compression parameters**
1. **Disintegration time (DT)**
Disintegration test was carried out as per United State Pharmacopeia. Disintegration test for sublingual tablets was carried out in disintegration apparatus for the oral tablets but in absence covering the plastic disc. 3 tablets from each batch were tested for its disintegration time. 22mins and 2 mins are specified as allowable limits for disintegration.

2. **Dissolution**
USP type II (paddle apparatus) was used for dissolution. A 500ml of 6.8 phosphate buffer is used as a medium and the paddle was allowed to rotate 75 rpm. Temperature is maintained 37±0.5°c. 3 tablets were tested and placed in the apparatus. 5 ml of aliquot was collected after specific interval by replacing the medium with same volume of buffer. The samples were then analyzed using UV spectroscopy for drug release and drug content at 9 min.\(^{[15]}\)

3. **Weight variation**
20 tablets are selected at random, individual weight and the average weight of the tablet is noted. None of the tablets must deviate from the average weight by more than ±7.5%.
4. **Friability**
10 tablets were initially weighed ($W_i$) and placed in a Roche Friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, deducted, and reweighed ($W_f$).\[^{[15]}\]

The percentage friability of the tablets was calculated by:

\[
\text{Friability} = \frac{W_i - W_f}{W_i} \times 100
\]

**Hardness test**
This test was carried out for three tablets from each batch using Monsanto hardness tester and average value of them was taken.

**RESULT AND DISCUSSION**

**Pre-formulation studies**

1. **Organoleptic characteristics of paroxetine HCl**:

   **Table 3: Characteristics of paroxetine HCL.**
   
<table>
<thead>
<tr>
<th>Color</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odor</td>
<td>Odorless</td>
</tr>
<tr>
<td>Taste</td>
<td>Slightly bitter</td>
</tr>
</tbody>
</table>

2. **Melting point characterization**
Melting point of the drug was measured using Veego melting point apparatus. A small amount of drug was taken in capillary which was closed from one end and placed in the apparatus and the temperature at which the drug starts melting was noted.

3. **UV spectroscopic analysis of Paroxetine HCl**
Preparation of calibration curve of Paroxetine HCl using suitable solvent:

**Preparation of phosphate buffer 6.8**
Phosphate buffer 6.8 was made according to IP. 35.084 g of disodium hydrogen phosphate and 13.872 g of potassium dihydrogen phosphate was accurately weighed and dissolved in sufficient amounts of distilled water to make 1000mL. The pH of the buffer was measured using a pH meter.

**Preparation of stock solution**
Accurately weighed 25mg of drug was taken and transferred 25mL volumetric flask. Then
phosphate buffer 6.8pH was added to flask to make volume up to 25mL. This solution had the concentration of 1000mcg/mL.

**Preparation of aliquot**
From the stock solution 1mL of sample was taken into 10mL of volumetric flask and volume was made up by adding 9mL of phosphate buffer and this gave 100mcg/mL of solution. Serial dilution was carried out for 1mL, 2mL, 3mL, 4mL, 5mL, 6mL, 7mL, 8mL samples and diluted up to 10mL to get concentration of 10mcg/mL, 20mcg/mL, 30mcg/mL, 40mcg/mL, 50mcg/mL, 60mcg/mL, 70mcg/mL and 80mcg/mL respectively.

**Determination of UV absorption maxima**
From the above prepared aliquot, the middle concentration (50mcg/mL) was taken and scanned for absorbance between 200-400nm using UV-visible spectroscopy. Paroxetine exhibits UV absorption maxima at 293nm.

**Drug excipient study using FTIR**
A. Paroxetine HCl
FTIR spectroscopy of pure Paroxetine was determined and the functional groups were identified.

![Figure 1: FTIR of Paroxetine HCl](image_url)
Table 4: Interpretation of FTIR spectra.

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Observed Frequency (cm(^{-1}))</th>
<th>Reported frequency (cm(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-H</td>
<td>3400.27</td>
<td>3500-3100</td>
</tr>
<tr>
<td>C=O(aldehyde)</td>
<td>2815</td>
<td>2800-2900</td>
</tr>
<tr>
<td>C=O(aromatic)</td>
<td>1500</td>
<td>1600-1475</td>
</tr>
<tr>
<td>C-F</td>
<td>1276</td>
<td>1400-1000</td>
</tr>
</tbody>
</table>

The major group of Paroxetine HCl were found to be stretching of amine group, carbonyl group (aldehyde), aromatic group and C-F group.

B. Paroxetine HCl + Pregelatinized starch

![Figure 2: FTIR of Paroxetine HCl + Pregelatinized starch.](image)

C. Paroxetine HCl + Excipients

![Figure 3: FTIR of Paroxetine HCl + Excipients.](image)
FTIR spectra study of Paroxetine HCl and its excipients is measured to check the compatibility. Any change or shift in the peak of the drug indicates that there is interaction between drug and its excipients. The figure-3 shows that the major peaks of functional groups of the drug were evitable in the mixture and no change in shift was observed. All in all, the drug is compatible with other excipients used in the formulation since there is no interaction.

**Drug Excipient compatibility studies using DSC**

![Figure 4: DSC of Paroxetine HCl.](image1)

![Figure 5: DSC of Paroxetine + Excipients.](image2)

Differential Scanning Calorimetry is used for characterization of the compound. Purity of the drug is confirmed by obtaining the melting point range in DSC curve. In order to check the
interactions between the drug and its excipients, DSC curve is used. Overlay of DSC depicts the occurrence of interaction on the basis of change in shift of the peak of drug. The range of melting point of paroxetine HCl was 118.15°C-130.44°C which resembles with the range of drug (120°-138°). Absence of interaction is seen as the drug peak remains constant and no shifting is observed in the overlay of DSC, when drug and excipients are physically mixed.

Optimization of sublingual tablets of Paroxetine HCl using 3² full factorial design

Pre-compression parameters

Table 5: Pre-compression parameters.

<table>
<thead>
<tr>
<th>Parameter</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>Angle of repose</td>
<td>22.32</td>
<td>23.1</td>
<td>22.45</td>
<td>23.56</td>
<td>22.23</td>
<td>23.21</td>
<td>22.20</td>
<td>22.27</td>
<td>22.65</td>
</tr>
<tr>
<td>Hauser’s ratio</td>
<td>1.24</td>
<td>1.31</td>
<td>1.11</td>
<td>1.09</td>
<td>1.15</td>
<td>1.27</td>
<td>1.35</td>
<td>1.13</td>
<td>1.26</td>
</tr>
</tbody>
</table>

Post compression parameters

Table 5: Post compression parameters.

<table>
<thead>
<tr>
<th>Parameters</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>Hardness(kg)</td>
<td>6.4±</td>
<td>0.2</td>
<td>3.8±</td>
<td>0.3</td>
<td>5.1±</td>
<td>0.5</td>
<td>6.2±</td>
<td>0.4</td>
<td>4.2±</td>
</tr>
<tr>
<td>Thickness(mm)</td>
<td>2.9±</td>
<td>0.02</td>
<td>3.2±</td>
<td>0.02</td>
<td>2.81±</td>
<td>0.03</td>
<td>3.01±</td>
<td>0.03</td>
<td>3.28±</td>
</tr>
<tr>
<td>Diameter(mm)</td>
<td>6.2±</td>
<td>0.02</td>
<td>6.11±</td>
<td>0.02</td>
<td>5.70±</td>
<td>0.01</td>
<td>5.50±</td>
<td>0.02</td>
<td>5.90±</td>
</tr>
<tr>
<td>Disintegration time(sec)</td>
<td>51±</td>
<td>1</td>
<td>57±</td>
<td>1</td>
<td>56±2</td>
<td>26±2</td>
<td>21±1</td>
<td>15±3</td>
<td>19±2</td>
</tr>
<tr>
<td>Drug release at 9 mins</td>
<td>78.41</td>
<td>±0.31</td>
<td>80.71</td>
<td>±0.32</td>
<td>83.05</td>
<td>±0.22</td>
<td>92.21</td>
<td>±0.20</td>
<td>91.41</td>
</tr>
<tr>
<td>Drug content</td>
<td>98.8±</td>
<td>±2.36</td>
<td>101.4±</td>
<td>±6.06</td>
<td>95.61</td>
<td>±0.35</td>
<td>99.24</td>
<td>±2.88</td>
<td>98.02</td>
</tr>
<tr>
<td>Weight variation</td>
<td>100.2±</td>
<td>±0.88</td>
<td>100.5±</td>
<td>±1.68</td>
<td>100.4±</td>
<td>±0.74</td>
<td>100.2±</td>
<td>±1.54</td>
<td>100.8±</td>
</tr>
<tr>
<td>Friability</td>
<td>0.57</td>
<td>0.67</td>
<td>0.61</td>
<td>0.42</td>
<td>0.55</td>
<td>0.29</td>
<td>0.72</td>
<td>0.31</td>
<td>0.40</td>
</tr>
</tbody>
</table>

The statistical analysis of the design batches was performed by multiple linear regression analysis using Design Expert 13®. The coefficients showing p value >0.05 were removed from the regression to generate reduced model. The refined model may be used for calculations of residuals or for drawing contour plots using design expert. The summary of results of regression analysis of full and refined models (p<0.05) for Disintegration time in seconds (Y1) and % Drug release at 9 minutes (Y2). The polynomial equations can be used to draw conclusions after considering the magnitude of coefficient and the mathematical sign it carries, i.e., positive or negative. Those coefficients were found to be insignificant at p >
0.05, their values were omitted from the full model to generate the reduced model. The high values of correlation coefficient for Y1 and Y2 indicate a good fit.

**Factorial Equation for Disintegration time (Y1)**

\[ Y1 = 18.22 - 17.83X1 - 0.6667X2 + 0.7500(X1)(X2) + 16.17(X1)^2 + 3.67(X2)^2 \]

**Factorial Equation for % Drug release at 9 minutes (Y2)**

\[ Y2 = 96.75 + 6.18(X1) - 0.5833(X2) + 0.0750(X1)(X2) - 7.21(X1)^2 - 3.96(X2)^2 \]

**Effect of X1 and X2 on % Drug release**

The polynomial equations can be used to draw conclusions after considering the magnitude of coefficient and the mathematical sign it carries, i.e., positive or negative. The coefficient obtained shows that coefficient b1, b2 were negative and b12, b22 and b12 were positive. The negative sign for b1, b2 indicated that Kyron T-314 and Pregelatinized starch were significantly affecting % drug release in opposite manner. After the optimized concentration excipients were started to show negative effects. The magnitude of coefficient showed that X1 has more effective than X2 on % drug release. The response surface plot and contour plot of effect of Kyron T-314 and Pregelatinized starch on % drug release are shown in below Figures.

**Figure 6: Counter plot of response Y1.**

**Figure 7: 3D plot of Response Y1.**
CONCLUSION
A sublingual tablet of Paroxetine HCl was formulated using the direct compression method. The drug Paroxetine HCl belongs to the class of selective serotonin reuptake inhibitors, mostly used for treating depression. Its lower dose (7.5mg) is used to treat post-menopausal syndrome. The marketed preparation of Paroxetine HCl shows slow onset of action and 50% of the drug undergoes first pass metabolism. Thus, to attain a fast onset of action and avoid the first pass metabolism, a sublingual tablet of Paroxetine HCl was devised. During the study, Kyron T-314 and Pregelatinized starch were used as a disintegrating agent and binder respectively as they provide better properties among their classes. Initially, the data from the study indicated that the disintegration time and binding property is directly proportional to the concentration of disintegrating agent and binder. Physical parameters of the tablets like hardness, friability, weight variation, etc. were tested for each formulation which resulted in sustainable limits. The batch F6 can be considered as the optimized batch with minimum disintegration time (15 secs). The optimized formulation batch F6 showed better drug releasing profile compared to other formulations. The following conclusions can be drawn from this study: - For the optimum batch F6- -The total weight of F6 batch was 50mg consisting of Paroxetine HCl-7.5mg, Kyron T-314-2mg, Pregelatinized starch-1.75mg, sodium saccharine-1mg, Aerosil and talc 0.5 mg each.

- The optimum batch(F6) values for the Precompression parameters like Angle of repose, Carr's index, Hausner's ratio and the Post compression parameters such as Hardness, thickness, friability, weight variation, disintegration time, wetting time etc. fall in the required standard range.
- The batch, thus, fulfils our objective of formulating cost effective sublingual tablets that
quickly disintegrate when placed beneath the tongue and provide fast release action to provide its post-menopausal activity effectively.

- Hence, it can be concluded that the formulation in batch F6 is stable and effective for its quick action and is a better alternative to the conventional tablet.

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