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# FORMULATION AND EVALUATION OF SUBLINGUAL TABLET OF PAROXETINE HCL

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**Abstract**: Paroxetine HCl is a potent and selective inhibitor of 5-hydroxytryptamine (5-HT, serotonin) uptake. it is a BCS class – I drug. Half life is 24 hr. Paroxetine HCl undergoes extensive first-pass metabolism leading to poor bioavailability. The aim of the present investigation was to formulate and evaluate sublingual tablet of paroxetine HCl to improve disintegration and dissolution rate, may avoid hepatic first pass metabolism and also for better Patient compliance. Paroxetine HCl sublingual tablets were prepared by direct compression method using Sodium starch glycolate, Cross povidone, Cross carmelose sodium and their mixture as super disintegrant and MCC and Lactose as diluents, The prepared tablets were evaluated for uniformity of weight, thickness, friability, content uniformity, hardness, disintegration time, wetting time, *in-vitro* drug release, and *ex-vivo* permeation study. Stability study of optimized formulation was performed as per ICH guideline Q1C. The optimized batch F4 contains 8% SSG + CCS Mix ratio (1:1) and MCC: Lactose (1:1) showed greater drug dissolution (more than 100 % within 9 min), satisfactory *in vitro* disintegration time. Drug excipients compatibility study checked by FTIR and DSC showed no interaction between drug and excipients Stability study of optimized formulation showed that optimized formulation was stable at accelerated environment condition.

**Keywords:** Sublingual tablet, Paroxetine HCl , sodium starch glycolate, disintegration, dissolution study

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## INTRODUCTION

Depression is a common illness worldwide, with an estimated 350 million people affected. Depression is different from usual mood fluctuations and short-lived emotional responses to challenges in everyday life. Especially when long-lasting and with moderate or severe intensity, depression may become a serious health condition. It can cause the affected person to suffer greatly and function poorly at work, at school and in the family. At its worst, depression can lead to suicide. Approximately 1 million deaths every year occurs due to depression. Depression is the leading cause of disability worldwide, and is a major contributor to the global burden of disease. Women are more affected by depression than men. At its worst, depression can lead to suicide.[2]

Paroxetine HCl is a potent and selective inhibitor of 5-hydroxytryptamine (5-HT, serotonin) uptake. Used in treatment of obsessive compulsive disorder (OCD), panic disorder and social anxiety disorder/social phobia.[1] it is a BCS class – I drug. Half life is 24 hr[5]

Paroxetine HCl is well absorbed after oral dosing and undergoes extensive first pass metabolism, as a consequence, the amount of paroxetine available to the systemic circulation is less than that absorbed from the gastrointestinal tract and results in poor oral bioavailability 31±15% [3].

Partial saturation of the first-pass effect and reduced plasma clearance occur as the body burden increases with higher single dosing or on multiple dosing. This results in disproportionate increases in plasma concentrations of paroxetine and hence pharmacokinetic parameters are not constant, resulting in non linear kinetics.[4] drug associated with greater numbers of adverse gastrointestinal effects. Difficulty in swallowing conventional tablets and capsules is common among all age groups, especially in elder, as paediatric, geriatric & psychiatric patients

To solve the above cited problems, sublingual tablet of paroxetine HCl is better alternative.

- to provide fast disintegration and dissolution in the oral cavity, without the need for water or chewing
- Avoid gastrointestinal side effects .
- To reduce hepatic first pass metabolism.
- To improve Patient compliance

Chewable tablets are also available in the market but patients for whom chewing is difficult or painful cannot use chewable tablets. Therefore, the present work is concerned with the development of Mouth Dissolving Tablets of Paroxetine Hydrochloride to improve the bioavailability and patient's compliance.[5]

Sublingual administration of the drug means placement of the drug 'under the tongue' and drug reaches directly in to the blood stream through the ventral surface of the tongue and floor of the mouth. The drug solutes are rapidly absorbed into the reticulated vein which lies underneath the oral mucosa, and transported through the facial veins, internal jugular vein, and braciocephalic vein and then drained into systemic circulation. [7]

Sublingual route provides systemic delivery of drugs through the mucosal membranes lining the floor of the mouth to the systemic circulation. Systemic drug delivery provide immediate onset of pharmacological effect through the sublingual route. [8]

Drugs having short delivery and infrequent dosing regimen could be delivered successfully through sublingual route because of high permeability and rich blood supply, the sublingual route produces a rapid onset of action. [9]

Advantages of Sublingual Tablet.... [7] [10-11]

- Drug is directly entered into systemic circulation so there is no loss of drug by first pass effect.
- Higher bioavailability and onset of action compare to oral route.
- Rapid absorption due to high vascularization beneath the tongue.
- Reduce the side effect due to low dose and high efficacy.
- Provide fast dissolution or disintegration in oral cavity without water or chewing action.
- Convenience in administration of drug and accurate dosing as compared to liquid formulations.
- Relatively large contact surface area provides rapid and extensive absorption
- Water is not required for swallowing the dosage form, which is convenient feature for patients who are traveling and do not have immediate access to water.
- It provides advantages of liquid formulations in the form of solid dosage form.

- Ease of administration to patients who refuse to swallow a tablet, such as pediatric, geriatric patients and psychiatric patients.
- Due to rapidity in action these sublingual dosage forms are widely used in emergency conditions e.g. asthma, angina.
- pH in the mouth is relatively neutral so drug will be more stable.
- Less variability in therapeutic effect, more predictable pharmacokinetics
- Optimal effect achieved with less drugs, less side effects
- Conventional processing and packaging equipments allow the manufacturing of tablets at low cost.
- Flexible formulation options
- Improved patient compliance.

**MATERIALS AND METHODS:**

Paroxetine HCl was gifted by torrent pharmaceutical Ltd, India. Sodium starch glycolate, Croscarmellose sodium, cross providone, PVP K30, mannitol,was supplied by Finar Chemicals Ltd., Ahmedabad, micro crystalline cellulose, Aspartame was supplied by Yarrow chem., Mumbai, India India. All the materials used were of pharmaceutical or analytical grade.

**Drug-Excipients Compatibility Study**

During the studies, possible interaction of drug with various ingredients proposed for use in final dosage form was checked. The drug-excipient compatibility study was carried out by using Differential Scanning Calorimetry (DSC) and Fourier Transform Infrared (FTIR) spectroscopy. FTIR study was conducted using KBr powder mixing method on FTIR spectrophotometer (FTIR-1700, Shimadzu, Kyoto, Japan) and the spectrums were recorded in the wavelength region of 4000 - 400 $cm^{-1}$. DSC study of pure drug, HPMC E15 and optimized batch was performed using DSC instrument (DSC- 60, Shimadzu, Kyoto, Japan). In this process, samples (3-5mg) were weighed into aluminum cell and scanned at 30 to 300 º C, at 100 ml/min nitrogen flow rate against blank DSC aluminum cell as a reference.

**Analytical method development**

Calibration curve of paroxetine HCL in pH 6.8 phosphate buffer Accurately weighed 10 mg of Paroxetine HCl was transferred to 100 ml volumetric flask and dissolved in pH 6.8 phosphate

buffer respectively and the volume adjusted up to 100 ml with respective solution to get the final concentration of drug 100 µg/ml. The above stock solution (100 µg/ml) was further diluted to get concentration of Paroxetine HCl in the range of 20-70 µg/ml. Absorbance of each solution was measured using Shimadzu 1800 UV-Visible double beam spectrophotometer by putting phosphate buffer pH 6.8 as a reference standard. The above solutions were scanned for the maximum absorbance using Shimadzu 1800 UV/Visible double beam spectrophotometer. The λmax for Paroxetine HCl was found to be 293 nm in pH 6.8 phosphate buffer.

**Preparation of Sublingual Tablets By Direct Compression Method**

Sublingual tablets of Paroxetine HCl were prepared by direct compression. All the ingredients were passed through # 80 sieve separately. Then the ingredients were weighed and mixed in geometrical order and compressed into tablets of 150 mg by direct compression method using 8mm flat punches on a Double Rotary Tablet Compression Machine (Rimek 10 station minipress). Following were the different 16 batches prepared by using three disintegrants for the optimization of disintegrant

**Preliminary Screening**

The batches were prepared for screening and selection of superdisintegrant and diluents. The prepared batches were further evaluated for evaluation tests.

**Table:1 Formula for preliminary screening using MCC**

| Ingredient | Quantity per tablet (150 mg) | | | | | |
|---|---|---|---|---|---|---|
| | B1 | B2 | B3 | B4 | B5 | B6 |
| Paroxetine HCl | 20 | 20 | 20 | 20 | 20 | 20 |
| Cross carmelose sodium | 6 | - | - | - | - | - |
| Cross povidone | - | 6 | - | - | - | - |
| Sodium starch glycolate | - | - | 6 | | - | - |
| SSG+CCS (1:1) | - | - | - | 6 | | - |
| SSG+CP (1:1) | - | - | - | - | 6 | |
| CCS+CP (1:1) | | | | | | 6 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Aspartame | 9 | 9 | 9 | 9 | 9 | 9 |
| Microcrystalline cellulose | 40 | 40 | 40 | 40 | 40 | 40 |
| Mannitol | 69 | 69 | 69 | 69 | 69 | 69 |
| PVP K30 | 2.25 | 2.25 | 2.25 | 2.25 | 2.25 | 2.25 |
| Talc | 2.25 | 2.25 | 2.25 | 2.25 | 2.25 | 2.25 |
| Magnesium stearate | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |

**Table 2: Evaluation Parameter of of trial batches (B1 to B6)**

| Batch | Hardness ($Kg/cm^2$) | Wetting time (Sec) | Disintegration time (Sec) | Drug content | %Friability | % CPR (15 MIN) |
|---|---|---|---|---|---|---|
| B1 | 4.97±0.10 | 77.35±1.44 | 65.33±1.53 | 98.83 | 0.38 | 84.15 |
| B2 | 4.83±0.06 | 82.9±1.58 | 71.00±1.03 | 104.53 | 0.42 | 82.43 |
| B3 | 4.00±0.10 | 70.53±1.65 | 61.260±1.0 | 102.74 | 0.29 | 78.48 |
| B4 | 4.17±0.06 | 63.52±0.53 | 54.38±0.58 | 99.83 | 0.26 | 94.24 |
| B5 | 4.03±0.15 | 74.56±1.23 | 62.33±1.15 | 95.37 | 0.35 | 86.98 |
| B6 | 4.53±0.12 | 71.32±1.15 | 58.51±0.58 | 101.65 | 0.44 | 83.44 |

Batches B1-B6 were prepared to evaluate different super disintegrant. As shown in Table 2 and. Batch B4 contain SSG + CCS Mixture (1:1) showed minimum Disintegration time and wetting time with maximum amount of release. So, Batch B4 was selected for further study. As need of high release in short time we tried partial replacement of microcrystalline cellulose with Lactose in Batches S1-S6.

**Table 3: Formula for preliminary screening using MCC with Lactose**

| Ingredient | Quantity per tablet (150 mg) | | | | | |
|---|---|---|---|---|---|---|
| | S1 | S2 | S3 | S4 | S5 | S6 |
| Paroxetine HCl | 20 | 20 | 20 | 20 | 20 | 20 |
| Cross carmelose sodium | 6 | - | - | - | - | - |
| Cross povidone | - | 6 | - | - | - | - |
| Sodium starch glycolate | - | - | 6 | | - | - |
| SSG+CCS (1:1) | - | - | - | 6 | | - |
| SSG+CP (1:1) | - | - | - | - | 6 | |
| CCS+CP (1:1) | | | | | | 6 |
| Aspartame | 9 | 9 | 9 | 9 | 9 | 9 |
| Microcrystalline cellulose | 20 | 20 | 20 | 20 | 20 | 20 |
| Lactose | 20 | 20 | 20 | 20 | 20 | 20 |
| Mannitol | 69 | 69 | 69 | 69 | 69 | 69 |
| PVP K30 | 2.25 | 2.25 | 2.25 | 2.25 | 2.25 | 2.25 |
| Talc | 2.25 | 2.25 | 2.25 | 2.25 | 2.25 | 2.25 |
| Aerosil | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.6 |

**Table 4:Evaluation Parameter of of trial batches (S1 to S6)**

| Batch | Hardness ($Kg/cm^2$) | Wetting time (sec) | Disintegration time(Sec) | Drug content | %friability | % CPR (15 MIN) |
|---|---|---|---|---|---|---|
| S1 | 4.70±1.48 | 68.27±0.78 | 54.25± 1.52 | 98.72 | 0.32 | 97.76 |
| S2 | 4.96±2.52 | 70.72±2.87 | 61.34±2.64 | 101.23 | 0.29 | 98.55 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **S3** | 4.48±1.65 | 58.19±1.34 | 49.79±1.08 | 99.64 | 0.36 | 90.15 |
| **S4** | 4.78±0.78 | 57.17±0.65 | 38.08±0.58 | 99.97 | 0.22 | 100.95 |
| **S5** | 4.23±0.56 | 69.44±1.75 | 58.46±1.69 | 98.29 | 0.37 | 93.53 |
| **S6** | 4.16±2.78 | 65.78±1.44 | 54.15±1.36 | 99.04 | 0.31 | 89.62 |

Batches S1-S6 was prepared to checked effect of diluents with different super disintegrants as shown in table 5.7 and 5.8. As compared with above batches of microcrystalline cellulose partially replacement of lactose increase wetting time and decrease Disintegration time as well as it shows improvement of dissolution efficacy as a result batch S4 selected for further study

**Optimization of Tablet Using Different Concentration of Super Disintegrant**

**Table 5: Formula For optimization of Super Disintegrant**

| INGRADIENTS | Quantity per tablet (150 mg) | | | |
|---|---|---|---|---|
| | **F1** | **F2** | **F3** | **F4** |
| **Paroxetine HCl** | 20 | 20 | 20 | 20 |
| **SSG+CCS (1:1)** | 3 | 6 | 9 | 12 |
| **Aspartame** | 9 | 9 | 9 | 9 |
| **Microcrystalline cellulose** | 20 | 20 | 20 | 20 |
| **Lactose** | 20 | 20 | 20 | 20 |
| **Mannitol** | 72 | 69 | 66 | 63 |
| **PVP K30** | 2.25 | 2.25 | 2.25 | 2.25 |
| **Talc** | 2.25 | 2.25 | 2.25 | 2.25 |
| **Aerosil** | 1.5 | 1.5 | 1.5 | 1.5 |

### 4.7 Ex-Vivo Permeation of Sublingual Tablets

The *ex-vivo* sublingual permeation was carried out for optimized batch of full factorial design. The permeation study of Paroxetine HCl through the goat sublingual mucosa was performed using Franz diffusion cell at 37 ± 0.5ºC. Fresh goat sublingual mucosa was mounted between the donor and receptor compartments. The sublingual tablet was placed with the core facing the mucosa, and the compartments were clamped together. The donor compartment was filled with 1 ml of phosphate buffer pH 6.8.The receptor compartment (72 ml capacity) was filled with phosphate buffer pH 6.8and the hydrodynamics in the compartment was maintained by stirring with a magnetic bead at uniform slow speed. Five milliliter samples were withdrawn at predetermined time intervals and analyzed for drug content by UV spectrophotometer at 293 nm.

### 4.8 Stability studies of the optimized formulation

Stability testing of drug products begins as a part of drug discovery and ends with the demise of the compound or commercial product. To assess the drug and formulation stability, stability studies were done according to ICH guidelines. The stability studies were carried out on the most satisfactory formulations as per ICH guidelines. The most satisfactory formulation sealed in aluminum packaging and kept in humidity chamber maintained 40 ± 2 °C / 75 ± 5 %RH for 1 month. The optimized formulation sealed in aluminum foil was also kept at room temperature and humidity condition. At the end of studies, samples were analyzed for the wetting time, disintegrating time, *in-vitro* drug release and % drug content.

## RESULTS AND DISCUSSION

### Drug excipients compatibility study

The FTIR spectrum of paroxetine hydrochloride showed one band at about,3338.89 $cm^{-1}$ due to N-H stretching (3500-3200). A band appeared at 1530.12 $cm^{-1}$ due to aromatic C-C stretching of ring carbons. A band at 1222.91 $cm^{-1}$ (1300-1000) represents C-O stretching and a band at 2918.16 $cm^{-1}$ (2950-2850) represents C-H symmetric stretching shown. It was observed that there were no changes in main peaks in the FTIR spectra of a mixture of drug and excipients. The FTIR study demonstrate that no physical or chemical interactions of Paroxetine with excipients. Shown in fig. 1 and 2

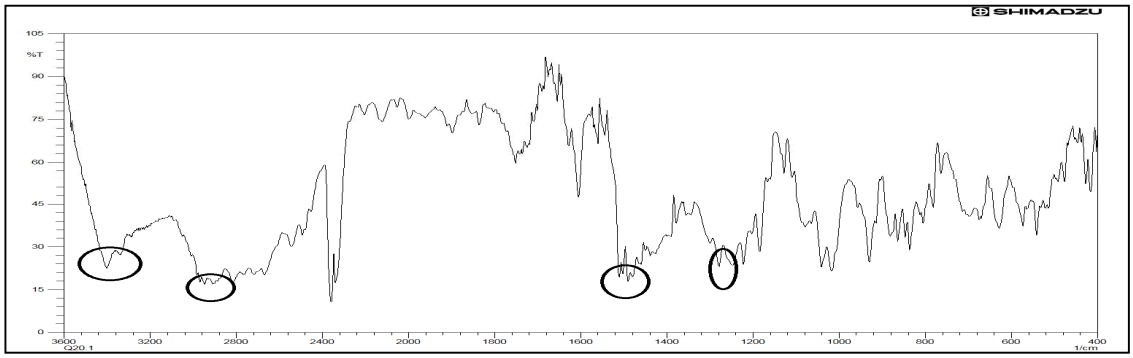


**Figure 1: FT-IR spectrum of Paroxetine HCL**

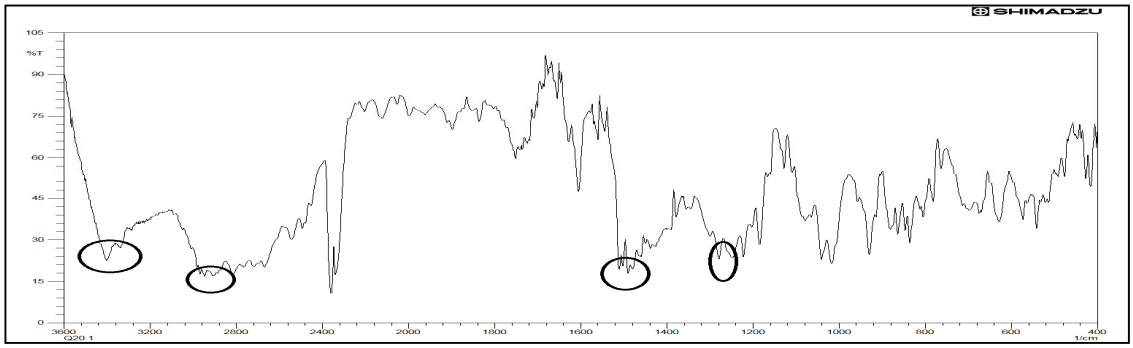


**Figure 2: FT-IR spectra of drug+excipients**

The pure Paroxetine HC drug and drug excipients were subjected to differential scanning

calorimetric study performed on a SHIMADZU DSC-60 instrument for drug excipients compatibility

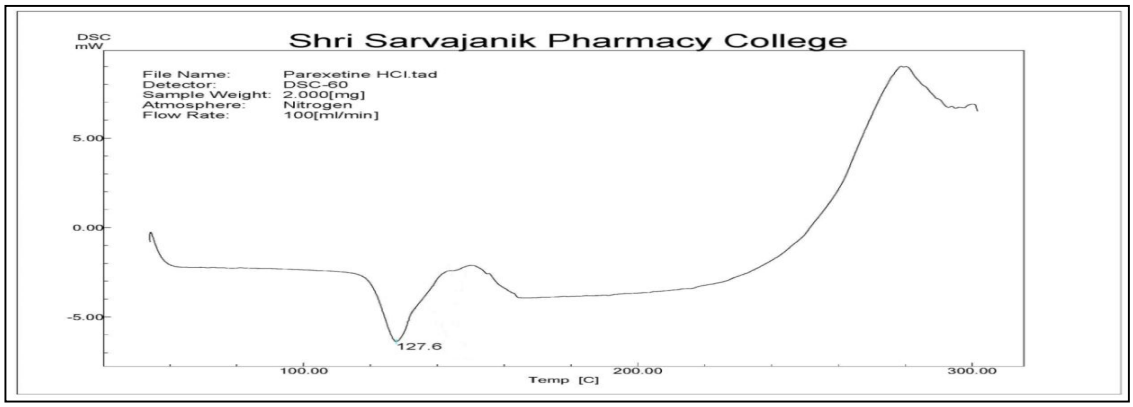


**Figure 3: DSC Spectra of Paroxetine HCl**

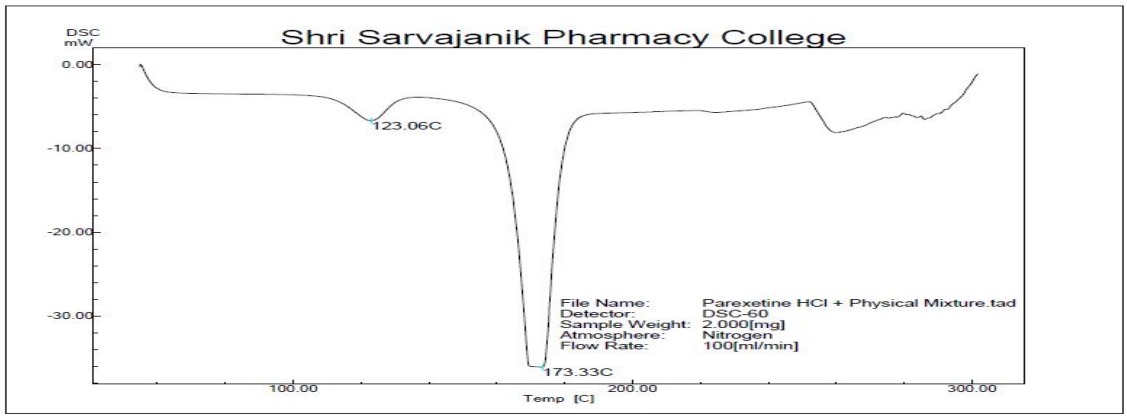


**Figure 4: DSC Spectra of drug + excipients**

it shows peak of pure drug and formulation at 127.6ºC and123.06ºC respectively. Result into; there is no interaction between drug with excipients. Which are shows in Figure 3 and 4.

**Analytical method development**

The drug was analyzed using UV visible spectrophotometer. The UV spectrum of drug solution in phosphate buffer pH 6.8 is shown in Figure 5. The drug exhibited λmax at 293nm. The calibration curve was generated using different concentration (1-10 µg/ml) of drug solutions in the Beer-Lambert law. The data for calibration curve are shown in Table 6 and calibration curve is shown in Figure 6

**Table 6: Calibration data of Paroxetine HCl in Phosphate buffer pH 6.8**

| Sr. No | Concentration (µg/ml) | Absorbance | | | Avg Absorbance | STDV (N=3 ) |
|---|---|---|---|---|---|---|
| 1. | 10 | 0.125 | 0.126 | 0.127 | 0.126 | ±0.001 |
| 2. | 20 | 0.245 | 0.247 | 0.249 | 0.247 | ±0.002 |
| 3. | 30 | 0.355 | 0.356 | 0.356 | 0.356 | ±0.0005 |
| 4. | 40 | 0.464 | 0.464 | 0.465 | 0.464 | ±0.0005 |
| 5. | 50 | 0.583 | 0.588 | 0.586 | 0.586 | ±0.0025 |
| 6. | 60 | 0.688 | 0.691 | 0.690 | 0.690 | ±0.0015 |
| 7. | 70 | 0.811 | 0.810 | 0.810 | 0.810 | ±0.0015 |
| Absorbance (y) = 0.011 * Concentration (x) + 0.015 | | | | | | |
| Correlation coefficients ($R^2$) = 0.999 | | | | | | |

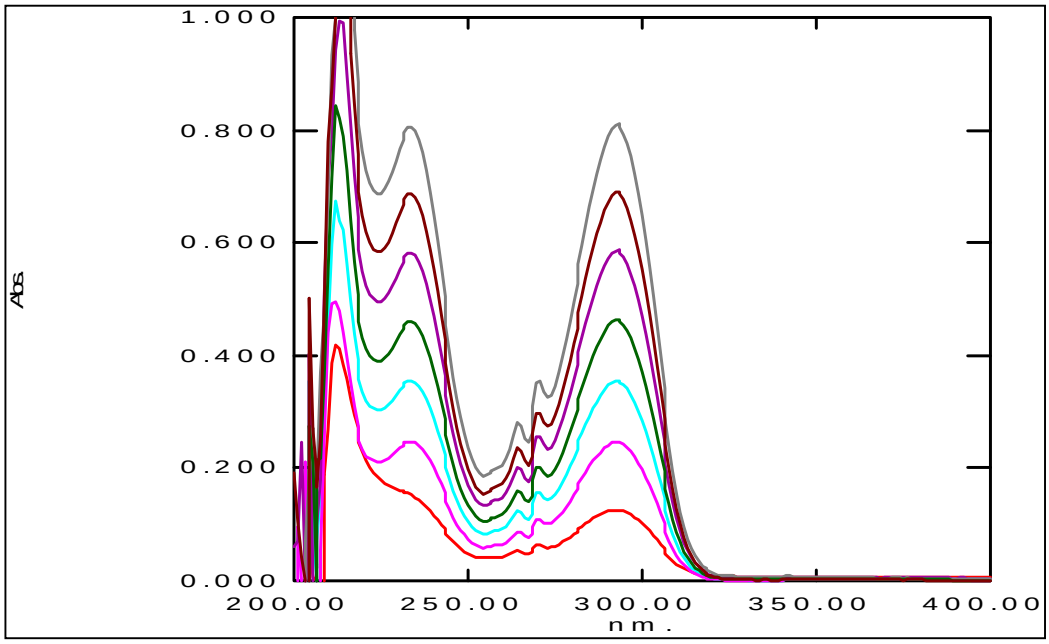


**Figure 5: UV Spectrum Of 10- 70 µg/ml Paroxetine HCl 6.8 pH Phosphate Buffer**

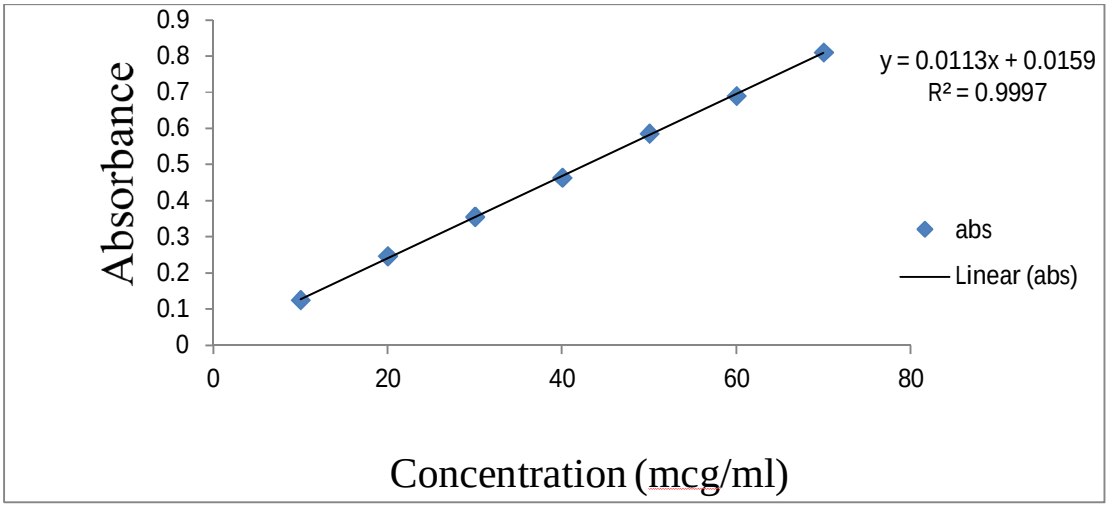


**Figure 6: Calibration Curve of Paroxetine HCl in Phosphate buffer pH 6.8**

**PRELIMINARY TRIALS**

Various preliminary trials were carried out to choose a suitable selection of superdisintegrant and diluents. Batches B1-B6 were prepared to evaluate different super disintegrant. As shown in Table 1 and 2. Batch B4 contain SSG + CCS Mixture (1:1) showed minimum Disintegration time and wetting time with maximum amount of release. So, Batch B4 was selected for further study. As need of high release in short time we tried partial replacement of microcrystalline

cellulose with Lactose in Batches S1-S6. Batches S1-S6 was prepared to checked effect of diluents with different super disintegrants as shown in table 4 . As compared with above batches of microcrystalline cellulose partially replacement of lactose increase wetting time and decrease Disintegration time as well as it shows improvement of dissolution efficacy as a result batch S4 selected for further study

**Preformulation Screening**

The evaluation was carried out using the parameters like bulk density, tapped density, Hausner's ratio, Carr's index, and angle of repose as per the procedure described in Preformulation study. The results are given in table 6

**Table 6: Pre compression Evaluation**

| Batch | Flow property n=3 | Bulk density | Tapped density | Carr's index | Hausner ratio |
|---|---|---|---|---|---|
| F1 | 24.12±0.86 | 0.527 | 0.622 | 15.24 | 1.179 |
| F2 | 28.06±0.56 | 0.539 | 0.632 | 14.68 | 1.172 |
| F3 | 25.67±0.40 | 0.537 | 0.632 | 15.02 | 1.177 |
| F4 | 24.38±0.67 | 0.551 | 0.642 | 14.10 | 1.162 |

The results of the Hausner's ratio (less than 1.25) and the angle of repose (between25˚-30˚) reflected that the powder blend had good flow property. So the flow of the prepared mass from the hopper was able to fill the die completely for compression. The Carr's index obtained was less than 15% so that showed good compressibility of mass. After the lubrication the blend ready for compression had good flow property and excellent compressibility.

**Table 7: Evaluation parameters of physicochemical characterization**

| Batch | Hardness ($Kg/cm^2$) | %Friability | Weight Variation | Drug content | Disintegration time(sec) | Wetting time(se) |
|---|---|---|---|---|---|---|
| F1 | 4.12±0.21 | 0.26 | 150.7±1.87 | 99.67 | 47.67±0.84 | 60.56±1.38 |
| F2 | 4.98±0.40 | 0.18 | 150.4±1.88 | 98.20 | 38.33±0.98 | 50.23±0.79 |
| F3 | 4.87±0.18 | 0.17 | 149.8±1.59 | 99.98 | 29.58±0.56 | 49.00±0.47 |
| F4 | 4.69±0.38 | 0.16 | 151.1±1.79 | 100.12 | 19.57±0.78 | 47.15±0.83 |

**Table 8 : In-vitro drug release studies of batches (F1 to F4)**

| Time (min) | Cumulative percentage release | | | |
|---|---|---|---|---|
| | F1 | F2 | F3 | F4 |
| 0 | 0 | 0 | 0 | 0 |
| 1 | 38.97 ±0.85 | 46.80 ±0.75 | 51.10 ± 1.50 | 55.40 ± 0.82 |
| 2 | 46.73±1.02 | 51.75 ±0.85 | 57.65 ± 1.15 | 60.41±1.26 |
| 3 | 53.71±0.95 | 58.43 ±1.1 | 62.77 ± 2.19 | 69.43± 1.28 |
| 4 | 56.09±2.85 | 61.60 ±1.25 | 68.67 ±1.57 | 76.14± 1.58 |
| 5 | 58.85±0.93 | 75.31 ±1.54 | 78.87 ± 0.54 | 82.43± 0.79 |
| 6 | 61.99±0.86 | 78.13 ±1.27 | 84.02± 1.40 | 89.90 ± 2.96 |
| 7 | 64.36 ±0.74 | 82.06 ±3.01 | 88.74± 2.03 | 95.81 ± 0.61 |
| 8 | 69.46 ±2.45 | 85.60 ±1.54 | 91.89± 0.82 | 98.98 ±1.29 |
| 9 | 73.01 ±0.98 | 87.58 ±2.5 | 94.65 ± 0.49 | 100.17 ± 0.85 |
| 10 | 75.38 ±0.76 | 90.83±0.41 | 98.97 ± 0.77 | |
| 12 | 82.17 ±2.04 | 94.24±1.02 | 98.99 ± 1.53 | |
| 15 | 90.26 ±0.75 | 98.19 ±0.86 | | |

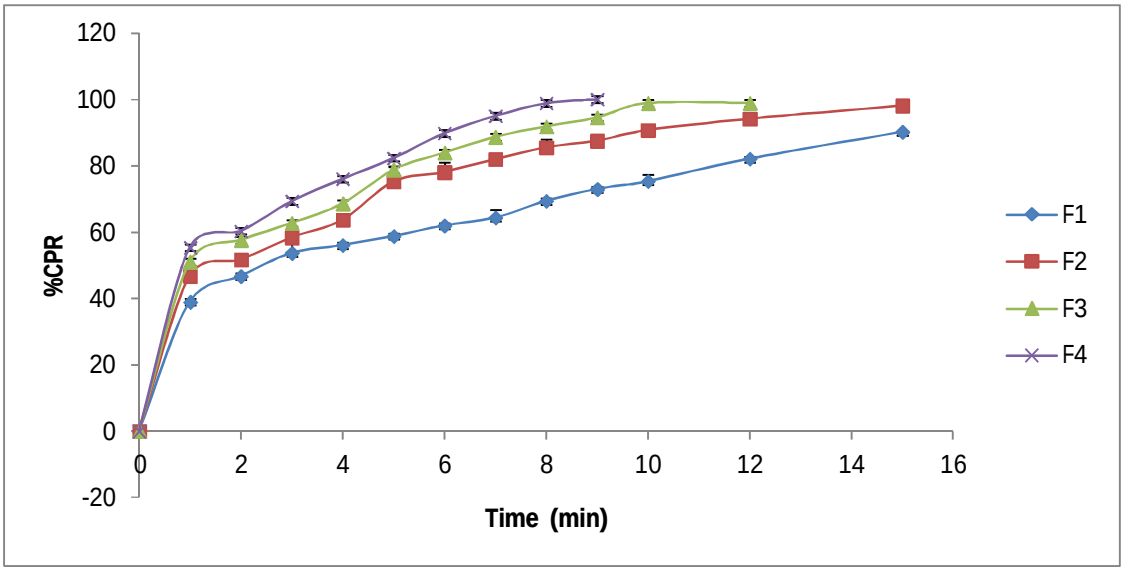


**Figure 7: Dissolution plot of cumulative percentage release v/s time**

All the prepared tablets showed acceptable pharmaceutical properties. The hardness values of formulations were within the range of 4-5 kg/cm2. Friability values of all formulations were less than 1% was an indication of good mechanical resistance of the tablets. In determinations of

tablet weights, according to the IP less than 7.5 % or more than 7.5% weight variation is acceptable in the tablet formulation having average weight more than 150 mg. All formulations were found to be within IP limits as per weight variation test. The uniformity of content was found with in Pharmacopeia limits of 98-102%. Wetting time and Disintegration time result that as the amount of Microcrystalline increase it leads to increase in wetting time and decrease the Disintegration time (table 7).The In-vitro drug release study result shows in table 8 and figure 7 Amongst all batches F4 batch have 8% of SSG + CCS mix and diluent ratio (Lactose: MCC) 1:1give best release. So F4 batch took for further study like ex-vivo permeation study And Stability study

**Ex Vivo Permeation Study of Optimized Batch**

**Table 9: *Ex-vivo* study permeation of the optimized batch (B4)**

| Time (min) | Drug permeation (%) |
|---|---|
| 0 | 0 |
| 2.5 | 56.15 |
| 5 | 66.92 |
| 10 | 79.23 |
| 15 | 82.31 |
| 20 | 83.15 |
| 25 | 88.20 |
| 30 | 93.85 |

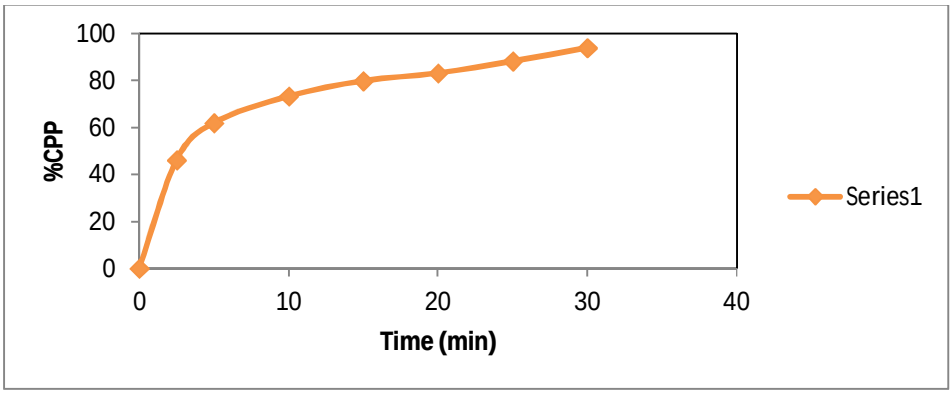


**Fig 8: Ex-vivo permeation study of optimized batch**

Formulation B4 was subjected to an *ex-vivo* sublingual permeation study using a Franz diffusion cell. The results showed drug permeation of 93.85% in 30 min as shown in table 9 and figure 8.

**Stability Studies of Optimized Formulation**

The stability studies were carried out on the most satisfactory formulations (Batch F4) as per ICH guidelines Q1C. The stability studies were performed at 40 ± 2 °C / 75 ± 5% RH conditions for 1 month. At the end of studies, samples were analyzed for the weight variation, thickness, friability, hardness, wetting time, Disintegration time,drug content and *in vitro* dissolution. The optimized formulations stored at 40 ± 2 °C /75 ± 5 % were found stable. After storage at 40 ± 2 °C / 75 ± 5 %, no shaped formation in the tablets was found. Assay of drug as well as cumulative percentage drug release was nearly similar before and after storage. (Figure 5.17) So, it was clear that drug was thermally stable as well as not affected by high humidity at 40 ± 2 °C /75 ± 5 %, but *in vitro* drug release was slightly changed.

**Table 10: Evaluation data after stability study of optimized batch**

| Parameter | F4 (Initial) | F4 (After storage at 40 ± 2 °C / 75 ± 5 %) |
|---|---|---|
| **Hardness ($kg/cm^2$)** | 4.69±0.38 | 4.67 ± 0.12 |
| **Weight variation** | 151.1±1.79 | 150.8±0.53 |
| **% friability** | 0.24 | 0.26 |
| **Drug content** | 100.12 | 100.54 |
| **Disintegration time(sec)** | 19.57±0.78 | 19.68 ± 1.53 |
| **Wetting time(sec)** | 47.15±0.83 | 46.38 ± 2.52 |

**Table 11: In vitro drug release after stability study of optimize batch**

| Time (min) | % CPR ( initial ) | % CPR(After storage at40 ± 2 °C / 75 ± 5 %) |
|---|---|---|
| **0** | 0 | 0 |
| **1** | 55.40 | 56.15 |
| **2** | 60.41 | 62.44 |

| | | |
|---|---|---|
| 3 | 69.43 | 70.32 |
| 4 | 76.14 | 76.78 |
| 5 | 82.43 | 82.59 |
| 6 | 89.90 | 90.28 |
| 7 | 95.81 | 96.08 |
| 8 | 98.98 | 99.18 |
| 9 | 100.17 | 100.15 |

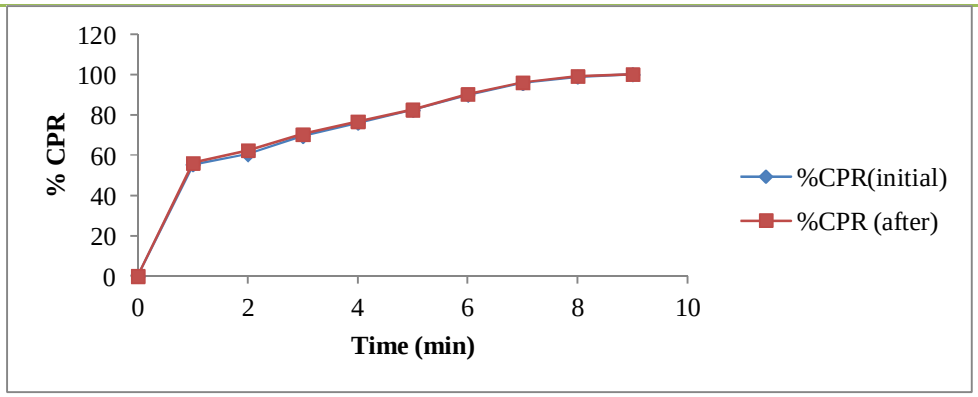


**Fig 9: In vitro drug release after stability study of optimize batch**

## CONCLUSION

From this research study, it is concluded that development of Sublingual tablet of Paroxetine HCl is one of the alternative route of administration to avoid gastrointestinal side effects and also first pass metabolism and provide immediate release. In addition, this formulation gives immediate action after administration and enhance patient compliance. A combination of Lactose with Microcrystalline cellulose and SSG + CCS results in immediate release of drug from tablet. Similarly, Ex- vivo permeation study shows 93.85% drug release of the immediate release tablet, this can be used in once a day tablet. The prepared formulation is stable at 40 ± 2 °C / 75 ± 5 % for 1 month.

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