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Formulation & Evaluation of Fast Disintegrating Tablet of Solid Dispersion of Sertraline HCl

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ABSTRACT

Sertraline HCl belongs to a class of drugs known as selective serotonin reuptake inhibitors (SSRIs). It acts by increasing the levels of serotonin, a neurotransmitter in the brain that helps regulate mood, emotions, and behavior. The present study was aimed to enhance the solubility of poorly water-soluble drug (BCS Class II) Sertraline HCl using water-soluble polymer. Due to its low solubility and its short absolute bioavailability of 44%, SD formulation of drug Sertraline HCl was prepared by using carrier Poloxamer 188 in 1:1, 1:3 & 1:5 drug to polymer ratio by Solvent evaporation method. The solid dispersions were evaluated for solubility, drug content, and % practical yield. The XRD study indicated that the crystalline nature of Sertraline HCl was reduced to an amorphous form. From the in vitro drug release profile, it can be seen that formulation S3 shows higher dissolution rate i.e. 95.48±0.31% compared with other formulations. It is predicted that, increasing concentration of carrier, increases the drug dissolution rate. The fast disintegrating tablets of Sertraline HCl were formulated by direct compression method using Sodium starch glycolate, Crospovidone, Croscarmellose sodium in different ratio as superdisintegrants. All the formulations were evaluated for various evaluation parameters i.e. thickness, hardness, weight variation, friability, disintegration time, wetting time, water absorption ratio & drug content. The formulation containing Crospovidone (F6) batch showed highest drug release i.e. 98.18±1.95% at the end of 30min.

Keywords: Bioavailability, Solubility, Solid Dispersion, Solvent evaporation method,

INTRODUCTION

Sertraline HCl is a BCS class II medication with limited solubility and high permeability. The current work aims to improve the solubility of Sertraline HCl utilizing a solid dispersion technique with a carrier, which may result in increased absorption and hence higher bioavailability. Oral bioavailability of medications is determined by their solubility and/or dissolution rate; hence, one of the significant issues with these orally delivered

pharmaceuticals is their limited solubility in biological fluids, resulting in poor bioavailability following oral administration. A solid dispersion is one or more active substances dispersed in an inert carrier or matrix in the solid form. Is a well-known method for increasing the dissolution rate and bioavailability of medicines that are poorly water soluble. The carriers utilized must be physiologically inert chemicals that are readily water-soluble or water insoluble for rapid or controlled dissolution, respectively. To accelerate the dissolution rate of a slightly water-soluble medication, it is dispersed at the molecular level in a rapidly water-soluble inert carrier to produce a solid dispersion. Successful dispersion of the medication in the carrier at the molecular level results in the creation of a homogenous phase of the solid dispersion. When such a product comes into contact with stomach fluid, the water-soluble carrier rapidly dissolves, resulting in the fast release of the medicine at the optimal molecular level, causing disintegrating and therefore improving bioavailability. [1, 2]

FAST DISINTEGRATING TABLET

Fast-disintegrating tablets dissolve or disintegrate in a matter of seconds when put in the mouth without water. Tablets that dissolve quickly are solid doses forms that don't require chewing. Tablets that dissolve quickly are placed in the mouth and allowed to dissolve into saliva. [3]

Due to the oral mucosa's high vascularization, medications taken through it can bypass the GIT and instead reach the systemic circulation, where they first undergo liver processing. This causes the medicine to have a quicker onset of action and a higher bioavailability than that of traditional tablets. Patients who are immobile, elderly, or mentally ill, or who are pediatric patients, can easily get these medications. One very common characteristic for patients when traveling is that these tablets don't require water to be swallowed. [3]

Other names for the FDT include rapid dissolving, rapid melting, rapid dispersion, rapid melt, and quick disintegrating tablets. Orally disintegrating tablets are the category for all FDTs that have received FDA approval. For tablets that scatter or dissolve in the mouth in less than three minutes before swallowing, the European Pharmacopoeia has adopted the name "Orodispersible." These tablets are easier for patients to swallow since they break down into tiny grains or melt in the mouth from a solid to a gel-like consistency. A decent FDT takes anywhere from a few seconds to almost a minute to disintegrate. [4]

MATERIALS & METHODS

Sertraline HCl was gift sample by Harika Drugs private limited Hyderabad, Telangana; Poloxamer 188 was purchased from Yarrow Chem products Mumbai. Sodium starch glycolate, Crospovidone, Croscarmellose sodium, Microcrystalline cellulose, Mannitol, Magnesium Stearate, Talc were provided by Research lab fine chem. Industries, Mumbai.

PREFORMULATION STUDIES OF SERTRALINE HCl

The different physicochemical characteristics of the drugs and excipients were tested.

Identification and Characterization of Sertraline HCl [5, 6, 7]

1. Organoleptic Evaluation

The drug sample was evaluated for its color, taste odour and appearance.

2. Melting Point:

Melting point of drug sample was determined by capillary method by using melting point apparatus.

3. Solubility Profile

The solubility of sertraline HCl was determined by adding excess amount of drug in the solvent and equilibrium solubility was determined by taking supernatant and analyzed by using spectrophotometer at 273 λmax.

UV SPECTROSCOPIC ANALYSIS OF SERTRALINE HCl [8, 9]

UV-Spectroscopic Analysis of Drug

A. Determination of Absorption Maxima (λmax)

The solution containing 10 µg/ml of Sertraline HCl in phosphate buffer, pH 6.8 was prepared and scanned over the range of 200-400 nm against phosphate buffer pH 6.8 as a blank using UV Spectrophotometer. The wavelength (λmax) was found to be 273 nm.

B. Preparation of Standard Calibration Curve of Sertraline HCl

The stock solution of Sertraline HCl was prepared by adding accurately weighed 10 mg of Sertraline HCl in 100 ml volumetric flasks containing phosphate buffer solution pH 6.8 to obtain the stock solution of 100µg/ml. From stock solution different aliquots were taken in series of 1, 2, 3, 4, 5, 6 ml in 10 ml volumetric flask and diluted with phosphate buffer solution pH 6.8 to obtain a series of concentration 10ug/ml – 60ug/ml. The absorption of the solutions was measured in UV spectrometer at 273 nm. The calibration curve was plotted for absorbance Vs concentration and values of slope, intercept and coefficient of correlation were calculated.

Drug- Excipient Compatibility Studies

1. FT-IR Spectroscopy of sertraline HCl [10]

Infrared spectra matching approach was used for the detection of any possible chemical reaction between the drug and the excipients. A drug and polymer were prepared and mixed & it was scanned from 200 to 400 cm-1 on JASCO (Model FTIR-4600) Spectrophotometer. The interaction between drug-excipients was observed from IR spectral studies by observing any shift in peaks of drug in the spectrum of physical mixture of drug.

PREPARATION OF SOLID DISPERSION

1. Preparation of Solid Dispersions by Solvent Evaporation Method [11]

Sertraline HCl + Poloxamer 188 in (1:1,1:3,1:5) ratio were prepared by solvent evaporation method. Weight accurately of Poloxamer 188 (polymer) and sertraline HCl (drug) placed into china dish. Add a sufficient volume of ethanol to dissolve completely with continuous stirring. Allow mixture to evaporate completely on

a water bath at 45^0C with continuous stirring to obtain dry mass. The dried mass was pulverized and passed through 60 mesh sizes. Different optimized combinations of solid dispersion with different polymers were prepared and evaluated for different evaluation parameters.

Table 1: Formulation of Drug and Polymer using by Solvent evaporation method

Formulations	Compositions	Ratio
S1	Sertraline HCl + Poloxamer 188	1:1
S2	Sertraline HCl + Poloxamer 188	1:3
S3	Sertraline HCl + Poloxamer 188	1:5

EVALUATION OF SOLID DISPERSION [5, 12]

The solid dispersion of sertraline HCl was prepared and then subjected to evaluation parameter such as solubility study, percentage yield, drug content, dissolution study.

1. Physical Appearance

It includes the visual inspection of solid dispersion. All the batches of drug and polymer solid dispersions were evaluated for color and appearance.

2. Solubility Study

The saturation solubility was performed by adding an excess amount of pure drug & solid dispersion in 10 ml phosphate buffer pH 6.8 in a glass vials. Mixed vigorously for 30 mins and shaken mechanically for 24 hr. at 37°C ± 0.5°C. then vials are centrifuged for 10 mins at 2500 RPM. The saturated solutions were filtered through Whatmann filter paper. And filtrates were suitably diluted, analyzed using UV spectrophotometer at 273 nm.

3. Percentage Yield

Yield was calculated with respect to dry product. Based on the practical yield (P.Y) obtained and the calculated theoretical yield (T.Y), % yield was calculated by using the following formula:

$$\textbf{PY (\%) = [Practical weight / Theoretical weight (Drug +Carrier)] x 100} \quad \text{…. Eqn 1}$$

Where,

a = Practical weight of solid dispersion preparation. b = Theoretical weight of solid dispersion obtained.

It was calculated to know about % practical yield or efficiency of any method which will help in selection of appropriate method.

4. Drug Content

Accurately weighed solid dispersion equivalent to 25 mg of Sertraline HCl was transferred to volumetric flask containing 100 ml with ethanol and sonicated for 30 min for complete solubilization of the drug. The solution was filtered and measured at 273nm in a double beam UV spectrophotometer (Jasso UV-730 Double beam spectrophotometer,).

5. *In-Vitro* Drug Release Study Pure Drug and Solid Dispersion Prepared by Solvent Evaporation Method

All the formulations of solid dispersions of Sertraline HCl prepared by Solvent Evaporation Method were subjected to in vitro release study. In vitro drug release studies were carried out using the USP Type II Dissolution test apparatus (Electrolab Model TDT-08L) set with a paddle speed of 50 rpm. Dissolution was performed in 900 ml Phosphate buffer pH 6.8 maintained at 37 °C ± 0.50C. The drug 25mg of Sertraline HCl was taken in a muslin cloth and tied to the rotating paddle kept in vessel of dissolution apparatus, the paddle was rotated at 50 rpm. The 5 ml sample was withdrawn at predetermined time interval and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced. The solution was filtered through Whatmann filter paper. The filtrate was analyzed by UV-Visible spectrophotometer. Three trials for each batch were performed and average percentage drug release was determined.

6. **FT-IR Study of Solid Dispersion**

Procedure of FTIR study mentioned in above experimental work

FORMULATION OF FAST DISINTEGRATING TABLET OF SOLID DISPERSION OF SERTRALINE HCl

After evaluation of solid dispersion of Sertraline HCl prepared by Solvent Evaporation Method. The fast-disintegrating tablets were prepared by using solid dispersion of S3 formulation.

Table 2: Formulation of Fast Disintegrating Tablet of Solid Dispersion of Sertraline HCl

Formulations	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ingredients	Unit Formula (mg per tablet)								
Solid dispersion (equivalent 25 mg drug)	152	152	152	152	152	152	152	152	152

Sodium starch glycolate	6	11	16	-	-	-	-	-	-
Crospovidone	-	-	-	6	11	16	-	-	-
Croscarmellose sodium	-	-	-	-	-	-	6	11	16
Microcrystalline Cellulose	5	5	5	5	5	5	5	5	5
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Mannitol	83	78	73	83	78	73	83	78	73
Total	**250**	**250**	**250**	**250**	**250**	**250**	**250**	**250**	**250**

EVALUATION OF POWDER BLEND OF FAST DIDINTEGRATING TABLET OF SOLID DISPERSION OF SERTRALINE HCl [11, 12]

The powder blend was evaluated for its flow properties; the parameter like angle of repose, bulk density, tapped density, Compressibility Index and Hausner's ratio was calculated.

Angle of Repose

The flow characteristics are measured by angle repose. Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane

$$\Theta = \tan^{-1}(h/r) \quad \ldots Eq^{n}1$$

Table 3: Standards for Angle of Repose

Angle of Repose	Flowability
25-30	Excellent
30-35	Good
35-40	passable
>40	Very Poor

Bulk Density

Bulk density (ρ *b*) was determined by pouring blend into a graduated cylinder. The bulk volume (Vb) and weight of the powder (M) was determined. The bulk density was calculated using the formula.

BD = Weight of the powder / Volume of the powder …. $Eq^{n}2$

Tapped Density

The minimum volume (Vt) occupied in the cylinder and the weight (m) of the blend was measured. The tapped density (ρ t) was calculated using the following formula.

TBD=Weight of the powder/Tapped volume of the powder …$Eq^{n}3$

Hausner's Ratio

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula;

Hausner's ratio= ρ t/ρ b …. Eqn4

Were,

ρ **t** is tapped density

ρ **b** is bulk density

Table 4 : Standards for Hausner's Ratio

Hausner's Ratio	Flow
1.2-1.3	Excellent
1.3-1.4	Good
1.4-1.5	Fair
1.5-1.6	Poor

Compressibility Index

The simplest way for measurement of free flow of powder is compressibility, an indication of the case with which a material can be induced to how is given by compressibility index (I) which is calculated as follows

Carr's compressibility index (%) = [(TBD-BD)/ TBD x100 …Eq^{n}5

Table 5 : Standards for Compressibility Index

Carr's Index	Properties
5-15	Excellent
12-16	Good
18-21	Fair to Passable
23-35	Poor
35-38	Very Poor
>40	Extremely Poor

PREPARATION OF FAST DISINTEGRATING TABLET OF SERTRALINE HCl CONTAINING SOLID DISPERSION BY DIRECT COMPRESSION METHOD

Accurately weighed 250mg of powder blend was homogeneously mixed and was fed manually and compressed with constant compression force and hardness on 10 stations tablet compression machine on RIMEK MINIPRESS-IIMT. Total nine formulations were prepared.

EVALUATION OF FAST DISINTEGRATING TABLET [

1. Appearance

The tablets were visually observed for capping, chipping and lamination.

2. Thickness

Three tablets were selected randomly from each batch and thickness was measured by using Vernier Caliper.

3. Hardness

Hardness or tablet crushing strength (F^o) the force required to break a tablet in a diametric compression was measured using Pfizer Hardness Tester. For each formulation, the hardness of 6 tablets was determined using the Pfizer hardness tester. The tablet was held along its oblong axis in between the two jaws of the tester. At this point, reading should be zero kg/cm^2. Then constant force was applied by rotating the knob until the tablet fractured. The value at this point was noted in kg/cm^2.

4. Friability

Friability of the tablets was determined using Roche Friabilator. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and roping the tablets height of 6 inches in each revolution. preweighed sample of tablets was placed in the Friabilator and were subjected to 25 revolutions. Tablets were dedusted using a soft muslin cloth and reweighed, the friability (F) is given by the formula.

% Friability = (Initial wt. - Final wt. / Initial wt.) x 10 ….Eq^{n}7

5. Drug Content

Five tablets were taken randomly and individual tablet were crushed, an amount of the powder equivalent to 25 mg of drug was dissolved in the 100ml of phosphate buffer pH 6.8 was added. Stirred for 30 min in Sonicator. Then filtered, diluted suitably and analyzed for drug content at 273nm using UV-Visible spectrophotometer (JASCO-UV-730 Double beam spectrophotometer)

6. Weight Variation Method

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviates from the average weight.

Table 6: Specifications of % weight variation allowed in tablets

Average Weight of Tablet	% Deviation Allowed
80 mg or less	10
More than 80 mg but less than 250 mg	7.5
250 mg or more	5

7. Disintegration Time

The disintegration time of tablet was determined by using Disintegration test apparatus. Tablets were placed in disintegration test assembly and disc was placed was placed on tablets in each glass tube of assembly. The assembly was dipped in a vessel containing 900ml phosphate buffer pH 6.8 at 37^{0}C.The time for disappearance of tablet residue above mesh was noted as disintegration time.

8. Wetting Time

In that the tissue paper has been folded twice and placed in petri dish above that tabletis placed and 6 ml water was added. The time required to get the tablet completely wet was measured.

9. Water Absorption Ratio

In this method, a piece of tissue paper folded twice was placed in a small petri dish containing 6ml of water. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was then weighed. Water absorption ratio was determined using following equation

$$\text{Water absorption ratio} = Wa - Wb \backslash Wb \times 100 \quad \text{.....Eq}^{n}8$$

10. *In-vitro* Dissolution Studies

In vitro drug release studies were carried out using the USP Type II Dissolution test apparatus (Electrolab Model TDT-08L) set with a paddle speed of 50 rpm. Dissolution was performed in 900 ml of phosphate buffer pH 6.8 maintained at $37^0 \pm 0.5^0$C. The tablet of Sertraline HCl was taken in vessel of dissolution apparatus, the paddle was rotated at 50 rpm. The 5 ml sample was withdrawn at predetermined time interval and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced and the sample was diluted suitably with dissolution medium. The solution was filtered through Whatmann filter paper. The filtrate was analyzed by UV- Visible spectrophotometer. Three trials for each batch were performed and average percentage drug release was determined.

RESULTS AND DISCUSSION

Preformulation Studies

The results of physiochemical evaluation are as follows.

Identification and Characterization of Sertraline HCl

1. Organoleptic Properties

The Sertraline HCl was studied for physicochemical parameters such as colour, taste, odour and appearance. Sample of Sertraline HCl was found to be similar as in I.P. On the basis of physicochemical evaluation, it is concluded that the sample of Sertraline HCl complies with I.P.

Table 2.1 : Organoleptic Properties of Sertraline HCl

Test	Specification/ Limit	Observation
Appearance	Fine Powder	Complies as per I.P
Color	White	Complies as per I.P
Odour	Odourless	Complies as per I.P

2. Melting point of Drug

The melting point of Sertraline HC lwith the reported standards are shown in table 2.2

Table 2.2 : Melting point of drug

Test	Specification/ Limit	Observation
Melting point	243-249^{0}c	247 - 249^{0}c

3. Solubility Study of Drug

Sertraline HCl was found to be insoluble in water

UV Spectroscopic Analysis of Sertraline HCl

1. Determination of Absorption Maxima

The UV spectrum of Sertraline HCl was obtained in phosphate buffer pH 6.8 which shows absorbance maximum (λ max) at 273 nm.

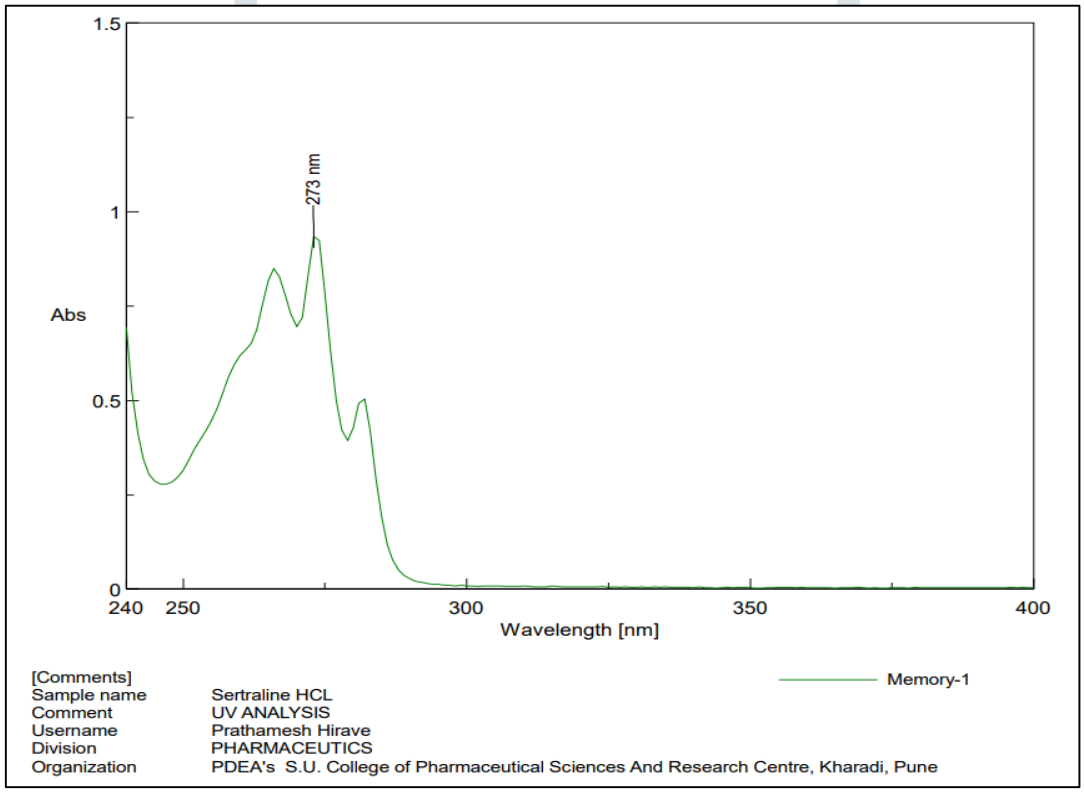


Figure 1: UV Spectra of Sertraline HCl in phosphate buffer pH 6.8

2. Determination of Standard Calibration Curve of Sertraline HCl

Standard Calibration Curve of sertraline HCl was determined by plotting Absorbance Vs Concentration at 273 nm using phosphate buffer pH 6.8. It was found that the dilutions of Sertraline HCl in phosphate buffer pH 6.8 show linearity (R^2 = 0.9982) and obeys Beer-Lambert law.

Table 2.3 : Standard Calibration Curve of Sertraline HCl

Sr.no.	Concentration (µg/ml)	Absorbance (nm)
1.	0	0
2.	10	0.0662
3.	20	0.1237
4.	30	0.1952
5.	40	0.2511
6.	50	0.3042
7.	60	0.3839

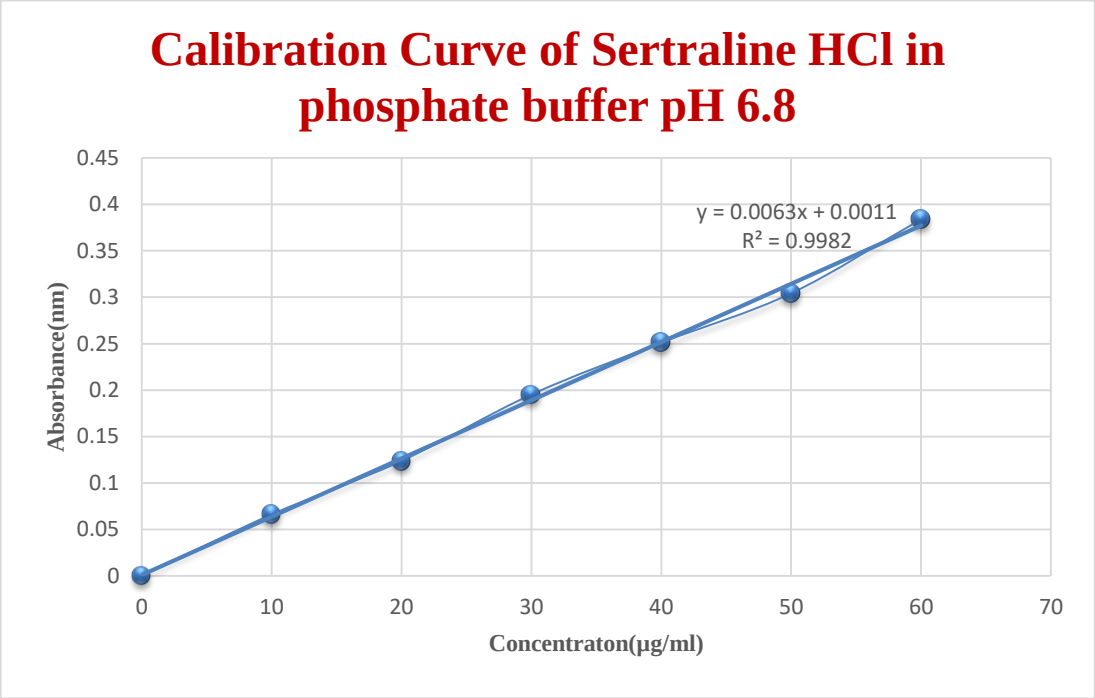
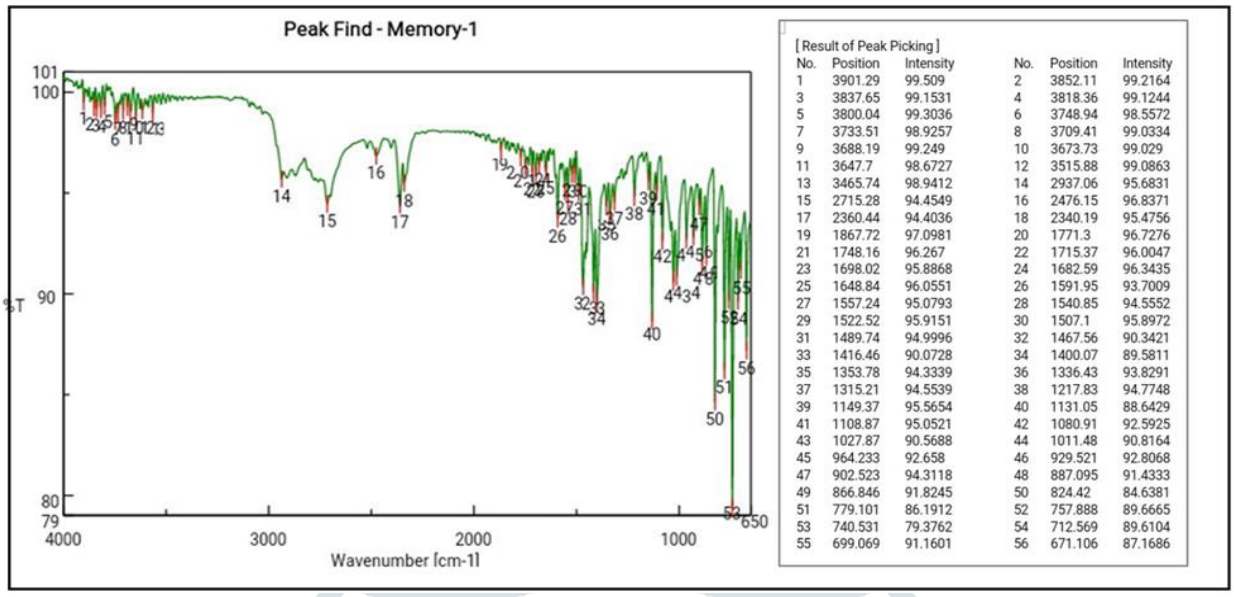


Figure 2: Standard Calibration Curve of Sertraline HCl

FT-IR Spectrum of Drug:

Major functional groups present in Sertraline HCl show characteristic peaks in IR spectrum. Table shows peaks observed at different wave numbers and the functional group associated with these peaks. The major peaks are identical to functional group of Sertraline HCl. Hence, the sample was confirmed as Sertraline HCl.



[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity
1	3901.29	99.509	2	3852.11	99.2164
3	3837.65	99.1531	4	3818.36	99.1244
5	3800.04	99.3036	6	3748.94	98.5572
7	3733.51	98.9257	8	3709.41	99.0334
9	3688.19	99.249	10	3673.73	99.029
11	3647.7	98.6727	12	3515.88	99.0863
13	3465.74	98.9412	14	2937.06	95.6831
15	2715.28	94.4549	16	2476.15	96.8371
17	2360.44	94.4036	18	2340.19	95.4756
19	1867.72	97.0981	20	1771.3	96.7276
21	1748.16	96.267	22	1715.37	96.0047
23	1698.02	95.8868	24	1682.59	96.3435
25	1648.84	96.0551	26	1591.95	93.7009
27	1557.24	95.0793	28	1540.85	94.5552
29	1522.52	95.9151	30	1507.1	95.8972
31	1489.74	94.9996	32	1467.56	90.3421
33	1416.46	90.0728	34	1400.07	89.5811
35	1353.78	94.3339	36	1336.43	93.8291
37	1315.21	94.5539	38	1217.83	94.7748
39	1149.37	95.5654	40	1131.05	88.6429
41	1108.87	95.0521	42	1080.91	92.5925
43	1027.87	90.5688	44	1011.48	90.8164
45	964.233	92.658	46	929.521	92.8068
47	902.523	94.3118	48	887.095	91.4333
49	866.846	91.8245	50	824.42	84.6381
51	779.101	86.1912	52	757.888	89.6665
53	740.531	79.3762	54	712.569	89.6104
55	699.069	91.1601	56	671.106	87.1686

Figure 3: FTIR Studies of Sertraline HCl

The IR spectrum of Sertraline HCl in figure 2.3 is characterized by Principal absorption peak at 3465.74 cm^{-1} (N-H Stretching), 2937.06 cm^{-1} (C-H Stretching), 1557 cm^{-1} (C=C Stretching), 1131.05 (C-N Stretching) and 1255 (C-Cl Stretching).

DRUG-EXCIPIENTS COMPATIBILITY STUDIES:

Sertraline HCl + Poloxamer 188

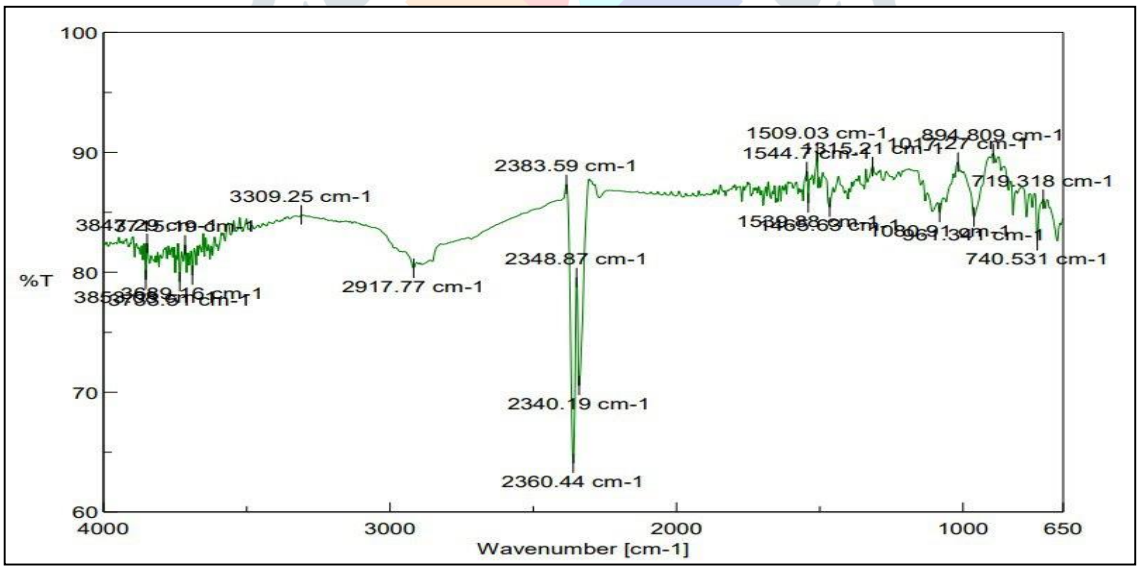


Figure 4: FTIR Studies of Sertraline HCl + Poloxamer 188

Sertraline HCl + Sodium Starch Glycolate

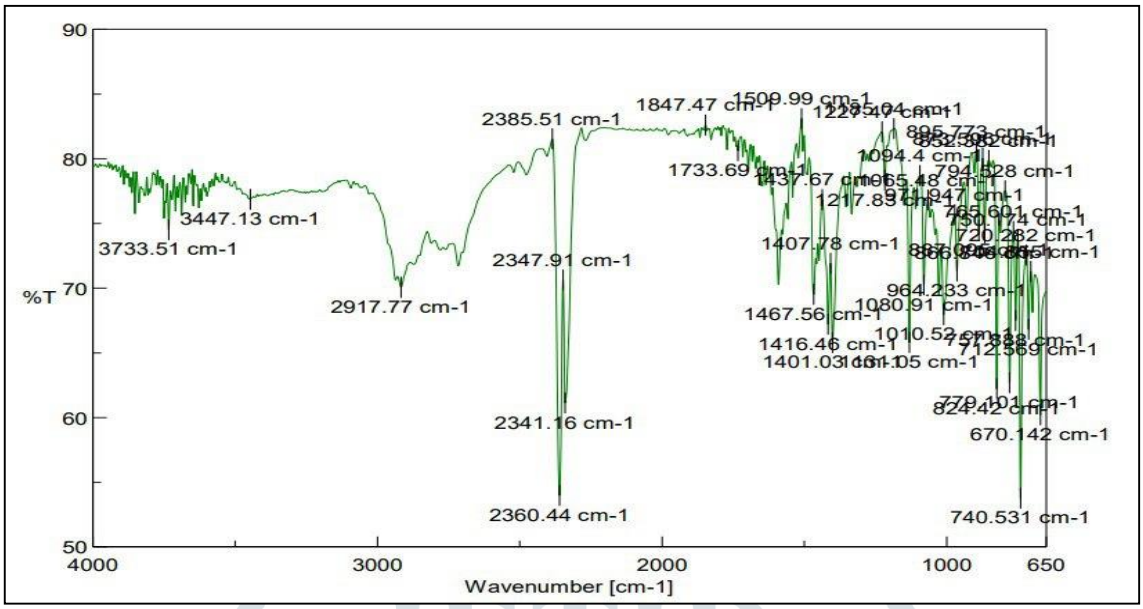


Figure 5: FTIR Studies of sertraline HCl + Sodium Starch Glycolate

Sertraline HCl + Crospovidone

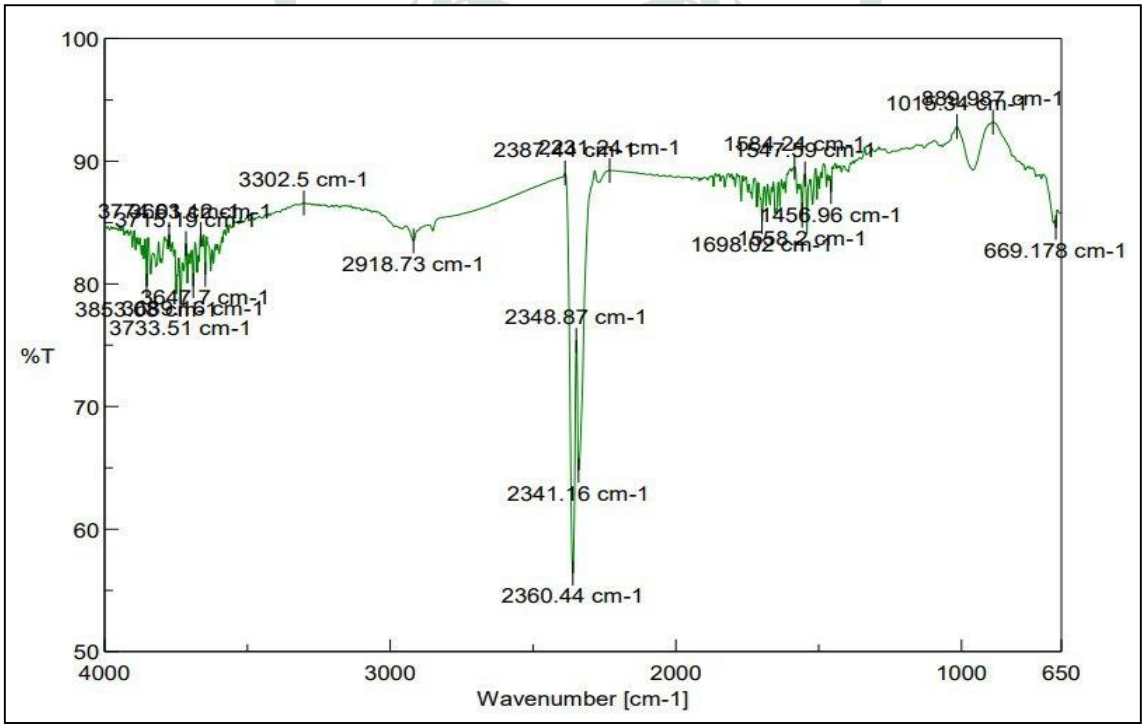


Figure 6: FTIR Studies of Sertraline HCl + Crospovidone

Sertraline HCl + Croscarmellose Sodium

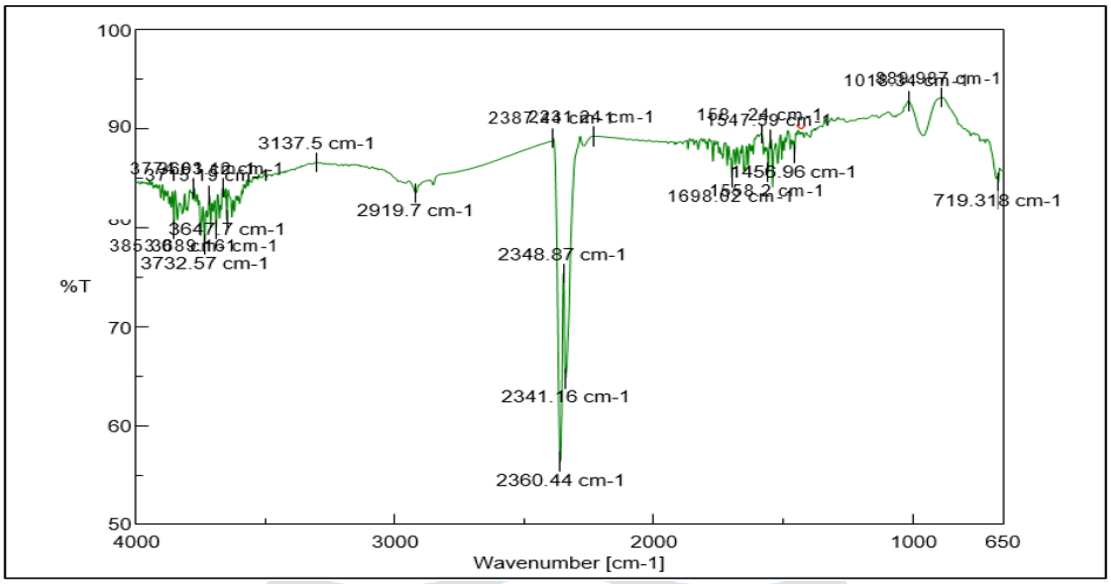


Figure 7: FTIR Studies of sertraline HCl + Croscarmellose Sodium

The FTIR spectrum of Drug and Excipient showed in figure 2.4 – 2.7. In IR spectra did not show any significant difference from those obtained for their physical mixture. The obtained results indicate that there was no positive evidence for interaction between Sertraline HCl and Excipients. These results clearly indicate that the above excipients can be used without any interaction for preparation of Solid Dispersion and Fast Disintegrating tablet of Sertraline HCl.

PREPARATION SOLID DISPERSION OF SERTRALINE HCl

The solid dispersion of Sertraline HCl was prepared by using different polymer ratios. Three formulations of Solvent Evaporation Method (S1-S3) were prepared and the composition is given in experimental work.

EVALUATION OF SOLID DISPERSION

The solid dispersion of Sertraline HCl prepared by Solvent Evaporation Method. These prepared formulations were evaluated for parameters like physical appearance, % practical yield, solubility study, drug content, in-vitro dissolution study, compatibility study.

1. Physical Appearance

All formulations of Sertraline HCl solid dispersion were evaluated for color and appearance. The physical appearance of each formulation is shown in Table 2.8

Table 2.4: Physical Appearance of Formulations Drug and Polymer

Formulations	Colour	Appearance	Odour
S1	White	Amorphous Powder	Odourless
S2	White	Amorphous Powder	Odourless
S3	White	Amorphous Powder	Odourless

2. Solubility Study of Solid Dispersion

Solubility study of various formulations of solid dispersion of Sertraline HCl prepared by Solvent evaporation

method was performed and shown in table 2.9

Table 2.5: Solubility Study of Solid Dispersion

Formulations	Drug: Carrier	Solubility*(mg/ml)
Pure drug	Pure drug	0.084±0.034
S1	Sertraline HCl+ Poloxamer 188(1:1)	0.169±0.010
S2	Sertraline HCl+ Poloxamer 188(1:3)	0.391±0.061
S3	Sertraline HCl+ Poloxamer 188(1:5)	0.512±0.011

Solubility study of various solid dispersion trial batches was performed. Solid dispersion prepared showed improved solubility of sertraline HCl as compared to pure drug and solid dispersions prepared by Solvent evaporation method. The solid dispersion from batch S3 was more soluble than pure drug and other formulation batches

3. Percentage Practical Yield Study of Solid Dispersion

Percentage practical yield was calculated to know about % yield or efficiency of any method which will help in selection of appropriate method. The practical yield for each batch is reported in Table 2.10

Table 2.6: Percentage Practical Yield Study of Solid Dispersion

Formulation	Ratio	Theoretical Yield (mg)	Practical Yield (mg)	% Practical Yield
S1	1:1	1000	901	90.10
S2	1:3	2000	1893	94.65
S3	1:5	3000	2918	97.26

Different trial batches of solid dispersions showed % practical yield from range 90.10 to 97.26%. The batch F3 Showed 97.26 % practical yield.

4. Drug Content of Solid Dispersion

The drug content of solid dispersion of Sertraline HCl of optimized formulation S3 Sertraline HCl + Poloxamer 188 (1:5) was found to be 98.53%, indicating good content in solid dispersion.

Table 2.7: Drug Content Study of Solid Dispersion

Formulation	Ratio	Drug content(%)*
S1	1:1	98.16±0.35
S2	1:3	97.06±0.12
S3	1:5	98.53±0.73

The drug content of solid dispersion of Sertraline HCl was found to be 97.06 to 98.53%, it indicating good content in Solid Dispersion.

5. *In vitro* Drug Release Study

The dissolution study of pure drug and all formulations were carried out to calculate the % drug release.

1. Dissolution Study of Pure Drug

Dissolution study of pure drug in phosphate buffer pH 6.8 was carried out and absorbance was taken in UV spectrophotometer which is reported Table 3.2

Table 2.8: Dissolution Study of Pure Drug

Time (min)	Cumulative % drug release*
0	00
5	15.39±0.13
10	23.37±0.45
15	29.63±0.29
20	33.24±0.38
25	42.53±0.93
30	52.04±0.75

*Results are the mean of three determinations

The % drug release of pure drug after 30 min was 52.04% each reading is taken was triplicate and then mean values were calculated.

Dissolution Profile of Solid Dispersions Prepared by Solvent Evaporation Method

The formulations of solid dispersions prepared by Solvent evaporation method(S1-S2) were subjected to dissolution study. The percentage drug release of formulations is showed in Table 3.3 and accordingly the graph was plotted to calculate the percentage drug release of formulations in phosphate buffer pH 6.8 and it is shown in Figure 2.8.

Table 2.9 : Dissolution Profile of Solid Dispersions Prepared by Solvent Evaporation Method

Time (min)	Cumulative % of Drug Release*		
	S1	S2	S3
0	00	00	00
5	23.75±0.13	29.70±0.59	36.15±0.10
10	32.80±0.10	41.29±0.21	51.10±0.25
15	48.30±0.40	56.95±0.30	66.75±0.34
20	63.25±0.65	73.38±0.70	81.35±0.60
25	70.22±0.78	80.24±0.88	88.37±0.79
30	83.41±0.56	90.10±0.10	95.48±0.31

*Results are the mean of three determinations

Out of three formulations S3 showed maximum drug release i.e. 95.48 %. Solid dispersion (S3) of Sertraline HCl with Poloxamer 188 prepared by Solvent evaporation method showed significant improvement in solubility and dissolution rate. Increased wetting and solubilizing effect of Poloxamer 188 as well as the molecular dispersion of drug in solid dispersion and alteration of surface properties of drug particle may be responsible for the enhanced dissolution rate of Sertraline HCl from solid dispersion compared to pure Sertraline HCl.

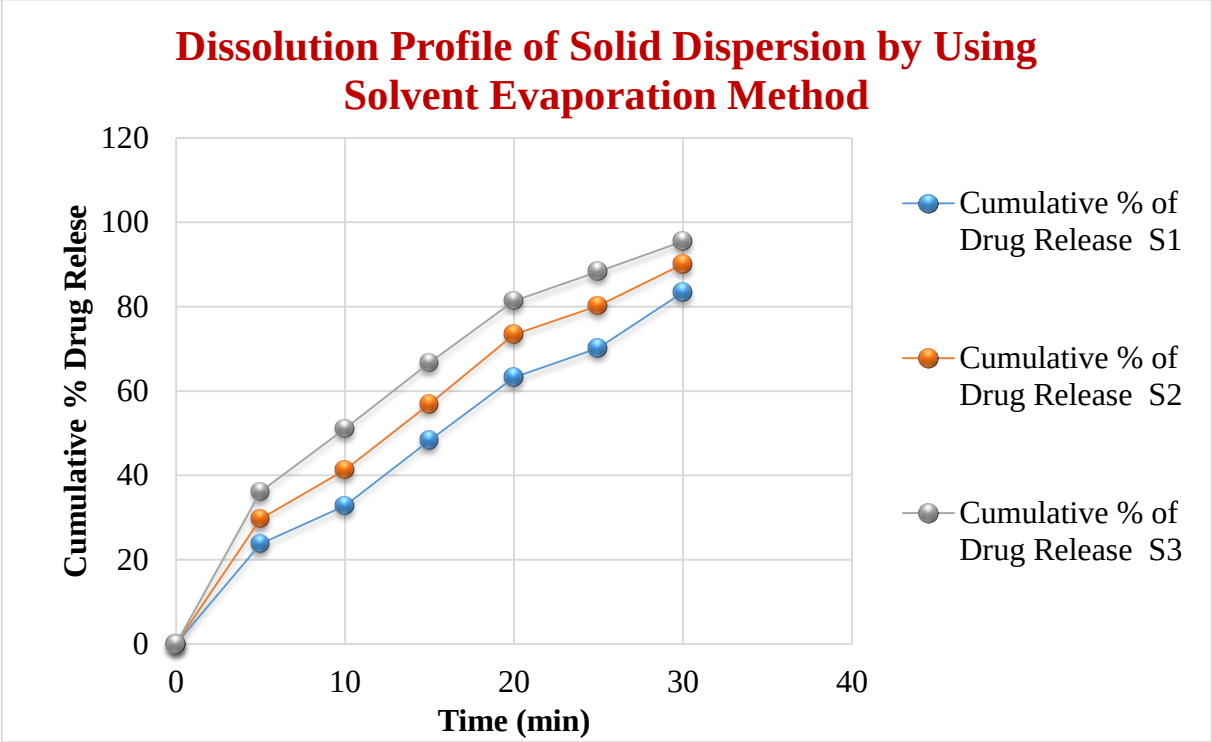


Figure 2.8: Dissolution Profile of Solid Dispersions Prepared by Solvent Evaporation Method

FT-IR Study of Solid Dispersion

1. Fourier Transform Infrared Spectroscopy (FTIR) Interpretation Solid Dispersion (S3) Prepared by Solvent evaporation method

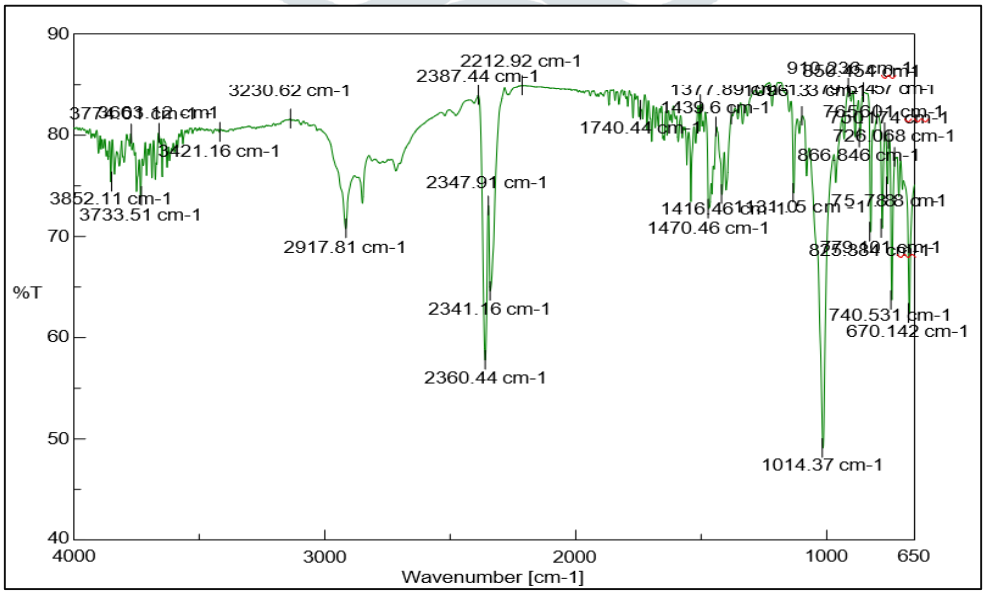


Figure 8: FTIR Studies of Solid Dispersion

In IR spectrum of solid dispersion of Solvent evaporation method showe2 in figure 3.9. In above IR spectra the peak of drug and polymer are showed in Table 3.4. All principal peaks have appeared in formulation it indicating no chemical interaction between Sertraline HCl and polymer.

FORMULATION OF FAST DISINTEGRATING TABLET OF SERTRALINE HCl

According to comparative dissolution study showed in figure 2.8 it is concluded that the solid dispersion prepared by Solvent evaporation method containing Sertraline HCl + PEG (1:5) was shown maximum percent drug release as compared to other solid dispersion. Hence the solid dispersion S3 Formulation was selected for preparation of fast disintegrating tablets

EVALUATION OF TABLET BLEND FOR FAST DISINTEGRATING TABLETS [6,

The tablet blend was evaluated for various precompression parameter like are angle of repose, bulk density, tapped density, hausner's ratio and compressibility index. Results are as follows.

Table 2.10: Evaluation of Tablet Blend for Fast Disintegrating Tablets

Formulation	Angle of Repose (θ˚)*	Bulk Density (gm/ml)*	Tapped Density (gm/ml)*	Hausner's Ratio (HR)*	Compressibility Index (%)*
F1	26.67 ± 0.33	0.41±0.11	0.45±0.22	1.09±0.03	8.6±0.27
F2	29.39 ± 0.15	0.42±0.34	0.46±0.39	1.09±0.11	8.3±0.39
F3	28.07 ± 0.38	0.41±0.05	0.44±0.05	1.07±0.18	8.6±0.22
F4	27.14 ± 0.40	0.35±0.03	0.38±0.42	1.08±0.08	7.8±0.27
F5	27.29 ± 0.26	0.40±0.34	0.43±0.37	1.02±0.15	6.9±0.42
F6	26.14 ± 0.35	0.42±0.10	0.46±0.25	1.09±0.25	8.6±0.10
F7	27.44 ± 0.21	0.45±0.03	0.49±0.03	1.08±0.03	8.1±0.21
F8	28.71 ± 0.84	0.42±0.23	0.45±0.30	1.09±0.05	8.8±0.22
F9	28.39 ± 0.11	0.35±0.11	0.38±0.10	1.08±0.20	7.8±0.30

*Results are the mean of three determinations

1. Angle of Repose

Table 3.5. indicates the results obtained for angle of repose of all the formulations. The values were found to be in the range of 26.14 θ˚ to 29.39 θ˚ all formulations showed the angle of repose within 30˚. It indicates that all formulations showed good flow properties.

2. Bulk Density

Bulk density is reported in Table 3.5. The bulk density of mixed blend varies between 0.35 to 0.42 gm/ml, indicating good packaging capacity of tablets.

3. Tapped Density

The tapped density results are reported in table 3.5. The tapped density of mixed blend was found in the range of 0.38 to 0.49 gm/ml, indicating good packing capacity of tablets.

4. Compressibility Index

The percent compressibility of powder mixture was determined. Table 3.5. indicates result obtained for percentage compressibility. The percent compressibility for all the six formulations lies within the range of 6.9 – 8.88 %. all the formulations showing good compressibility

5. Hausner's Ratio

Hauser's ratio of the powder was determined from bulk density and tapped density. Hauser's ratio of all the formulation lies within the acceptable range. The Hauser's ratio of all the formulations in the range of 1.02 – 1.09. All the formulations showed good flow property.

From the results of precompression studies of the blend from formulations F1-F9 it is concluded that all the formulations blend possesses good flow property and compressibility.

EVALUATION OF FAST DISINTEGRATING TABLETS

All the formulations were subjected to post compression evaluation in which various parameters like weight variation, thickness, hardness, friability, drug content, in vitro disintegration time, and in vitro dissolution studies were evaluated. The results obtained are as follows.

Table 2.11: Evaluation of Fast Disintegrating Tablets

Formulation	Thickness (mm)*	Hardness (kg/cm^2)*	Weight Variation(mg)*	Friability (%)*	Disintegration time (Sec)*	Wetting Time(Sec)*	% Water Absorption Ratio*	Drug Content*
F1	3.51±0.25	3.6±0.34	250.20±1.22	0.36±0.02	52±0.16	48±1.02	52.50±0.22	96.35±1.22
F2	3.40±0.10	3.5±0.80	251.75±1.14	0.52±0.05	43±0.19	32±1.04	62.31±0.48	97.63±2.08
F3	2.81±0.15	3.7±0.10	248.10±1.01	0.36±0.12	30±0.16	42±1.08	55.55±0.67	97.21±1.45
F4	2.90±0.45	3.7±0.83	247.90±1.50	0.40±0.11	37±0.14	30±1.05	62.56±0.82	98.53±2.56
F5	3.62±0.20	3.4±0.45	251.10±1.30	0.44±0.03	54±1.05	45±1.04	53.50±0.89	99.41±1.30
F6	3.58±0.11	3.2±0.57	250.15±1.02	0.36±0.05	28±0.14	21±1.01	70.50±0.56	99.51±1.89
F7	3.30±0.25	3.6±0.90	249.15±2.10	0.60±0.04	45±0.16	35±1.02	60.10±0.65	96.28±1.32
F8	3.80±0.14	3.5±0.52	251.45±1.01	0.40±0.03	39±0.16	38±1.07	58.50±0.74	97.24±2.34
F9	3.39±0.37	3.4±0.11	250.20±1.20	0.24±0.05	30±0.19	39±1.01	56.56±0.35	99.38±1.21

*Results are mean of three determinations

1. Appearance

The tablets were visually observed for capping, chipping and lamination.

2. Thickness

The measured Thickness of tablets of each batch ranged between 2.81–3.80mm. This ensures good handling and transportation of all tablets.

3. Weight Variations

All the formulated (F1 to F9) tablets passed weight variation test as the % Weight variation was within the pharmacopeia limit of ±7.5 of the weight. The weight of all the tablets were found to be uniform with low standard deviation values.

4. Hardness

The measured hardness of tablets of each batch ranged between 3.2 to 3.7 Kg/cm^2. This ensures good handling and transportation of all tablets.

5. Friability

The % Friability was less than 1% in all formulations ensuring that the tablets were mechanically strong.

6. Drug Content

The percentage of Drug content for F1 to F9 was found to be between 96.28 – 99.51% of Sertraline HCl, it complies with official specifications.

7. Disintegration Time

The measured disintegration time of tablets of each batch ranged between 28 to 52 seconds This ensures as concentration of superdisintegrants increased, decreased in disintegration time. The formulation batch F6 containing Crospovidone showed less disintegration time i.e. 28 seconds. So, formulation batch F6 was optimized batch.

8. *In vitro* Drug Release of Drug from Tablet

All the nine formulations were subjected for the *in vitro* dissolution studies using tablet dissolution apparatus (USP). The phosphate buffer pH 6.8 was used as dissolution medium. The sample were withdrawn at different time intervals, Filtered, diluted and analyzed at 273 nm. Cumulative % drug release was calculated on the basis of mean amount of tablet present in respective table. The results obtained in the *in vitro* drug release for all formulations F1 to F9 are as follows.

Table 2.12: *In vitro* Cumulative % Drug Release of Drug from Tablets

Time (min)	Cumulative % Drug Release*								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	00	00	00	00	00	00	00	00	00
5	28.25 ±0.30	28.96 ±0.03	30.91 ±1.40	29.58 ±0.98	31.25 ±1.22	34.67 ±1.35	28.06 ±1.35	29.25 ±1.23	31.71 ±1.45
10	36.61 ±1.27	38.71 ±1.38	42.09 ±1.55	37.93 ±1.26	40.09 ±1.49	42.54 ±1.42	36.51 ±1.50	37.76 ±1.46	43.61 ±1.58

15	48.10 ±1.32	51.35 ±1.56	58.72 ±1.69	51.70 ±1.35	54.13 ±1.56	60.84 ±1.56	49.85 ±1.65	50.26 ±1.55	56.91 ±1.70
20	65.91 ±1.50	65.21 ±1.72	71.94 ±1.75	67.79 ±1.55	70.03 ±1.78	75.03 ±1.70	63.12 ±1.72	69.79 ±1.67	72.21 ±1.82
25	72.26 ±1.65	79.21 ±1.85	87.84 ±1.86	75.18 ±1.79	82.79 ±1.86	92.52 ±1.87	73.52 ±1.85	80.28 ±1.85	89.36 ±1.92
30	88.02 ±1.85	90.75 ±1.96	92.99 ±1.98	91.10 ±1.92	93.41 ±1.94	98.18 ±1.95	90.12 ±1.90	89.17 ±1.92	94.14 ±1.98

*Results are mean of three determinations

The rapid dissolution was observed in formulation F6 releases 98.18% at the end of 30 minutes. Formulations F1-F9 released 88.02 to 98.18% at the end of 30 min. Rapid dissolution might be due to fast breakdown of particles and rapid absorption of drugs. The drug release was completely achieved in shorter duration of time. In all the formulations the drug release within 30 minutes. High dissolution may occur due to faster breakdown.

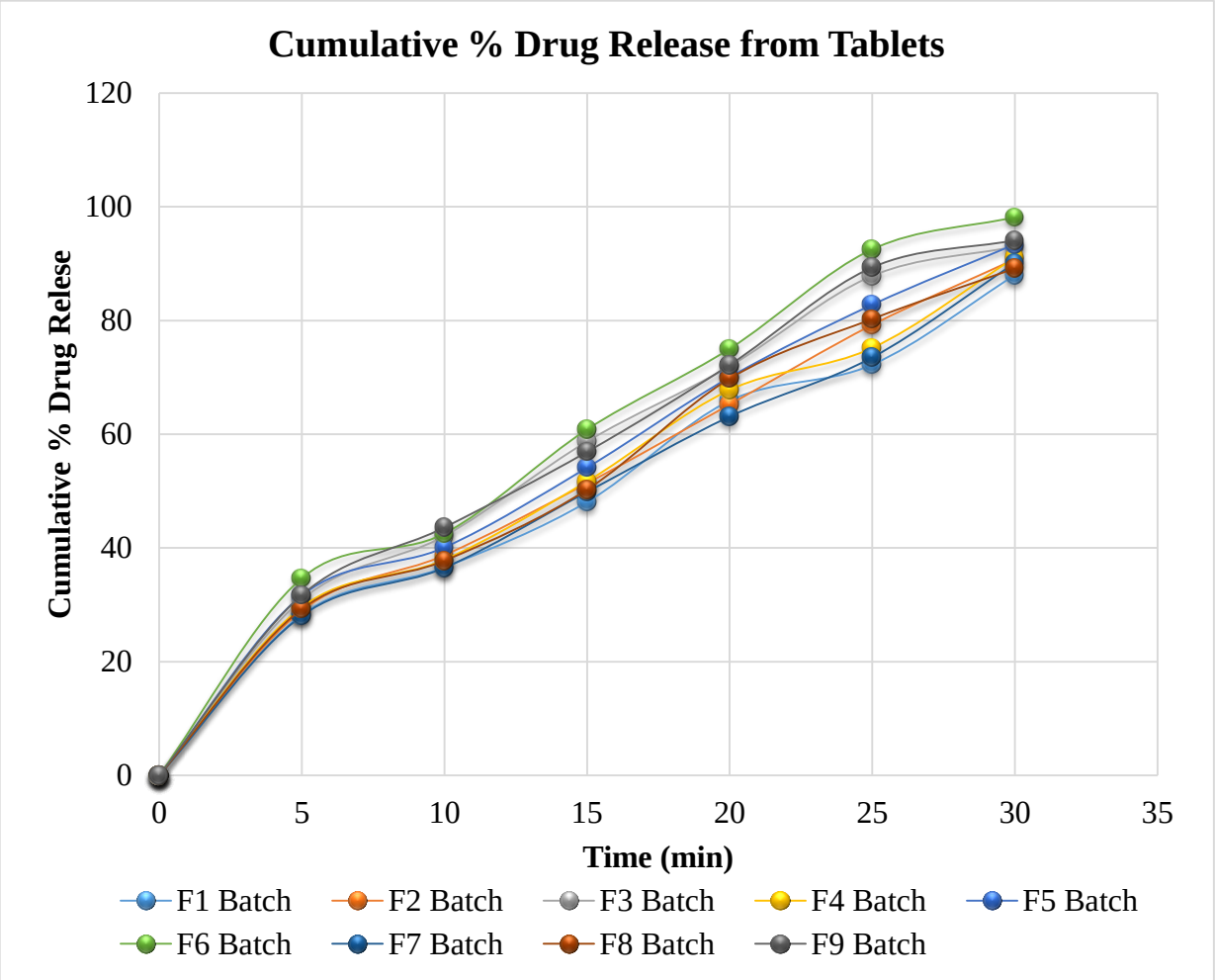


Figure 9: Cumulative % drug releases of F1-F9 formulations

CONCLUSION: Overall, the results showed that the solubility and dissolution rate of Sertraline HCl were increased by a suitable ratio of solid dispersion of S3 with Poloxamer 188 generated by Solvent evaporation method. When compared to pure Sertraline HCl, the rate at which Sertraline HCl dissolves from solid dispersion may be increased due to changes in the drug's surface properties. It was selected to use the direct compression method to formulate a fast disintegrating tablet of Sertraline HCl in a solid dispersion. Sodium Starch Glycolate, Crospovidone, Crosscarmellose Sodium were used as super disintegrants in the tablet formulation. Angle of repose, bulk and tapped densities, compressibility index, and Hausner's ratio of the powder blend were all assessed before compression. The weight variation, hardness, friability, drug content, disintegration time, wetting time, in vitro drug release, and stability investigations of the compressed tablets was also assessed. The F6 formulation produced encouraging results in the experiments mentioned above. FTIR study, which demonstrated that F6 had no interaction with excipients, provided additional support for it. The optimized batch F6 underwent stability studies for 90 days, and the findings were satisfactory. Therefore, the F6 formulation was regarded as the optimal formulation. Among all of the created solid dispersions, it was discovered that S3 was optimal. The study demonstrates that employing a solid dispersion approach and Solvent evaporation method can significantly increase the rate at which Sertraline HCl dissolves. Thus, formulations for fast disintegrating Sertraline HCl tablets using the Sodium Starch Glycolate, Crospovidone, Croscarmellose sodium systems could be taken into consideration. When compared to other formulations, Sertraline HCl (F6) fast disintegrating tablets showed a greater medication release. The solid dispersion technique can be used to increase the solubility, dissolution rate, and oral bioavailability of medications that are not water soluble, according to the results above.

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