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SOLUBILITY ENHANCEMENT OF SERTRALINE HYDROCHLORIDE-FORMULATION & COMPARATIVE EVALUATION OF LIQUID SOLID COMPACTS WITH SOLID DISPERSIONS

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ABSTRACT

Sertraline hydrochloride belongs to the class of antidepressants known as selective serotonin reuptake inhibitors (SSRIs). It is poorly water soluble drug comes under BCS Class II,having only 46% oral bioavailability. The poor dissolution rate is major problem in pharmaceutical manufacturing hence for enhancing the solubility, dissolution and to avoid hepatic metabolism fast dissolving tablets of Sertraline hcl were prepared. The aim and objective of present research study was to formulate and evaluate the fast dissolving tablets of Sertraline hcl by solid dispersion & liquid solid compact techniques. Solid dispersions were prepared by using PVPK30 & urea as carriers. Liquid solid compacts were prepared by using Tween 80 and PEG 400 as non volatile solvents, Avicel PH102 and Aerosil as carrier and coating materials simultaneously. Drug and exciepients are characterized by FT-IR studies. Various formulations were prepared incorporating superdisintegrants such as Crosspovidone, Crosscarmellose Sodium and Sodium Starch Glycolate in different concentrations by direct compression method. The formulated Fast Dissolving Tablets were evaluated for various physicochemical parameters like hardness, friability, thickness, weight variation, disintegration time, drug content and % Cumulative drug release. The results of the evaluation tests indicated that the optimized formulation F20 showed desired release along with good disintegration time and desired release rate for the Sertraline hcl. Different

formulations were prepared among the formulations the best formulation shows maximum amount of drug release with in10 mins of time period. With this liquid solid compact method was selected as best method for solubility enhancement of Sertraline hcl.

KEYWORDS: Sertraline hcl, liquid solid compacts, solid dispersions, fast dissolving tablets.

INTRODUCTION

About 45% of new chemical entities coming from the discovery are poorly bioavailable. This exerts strong limits to the performance of a drug by necessitating administering a much higher dose than strictly required from the pharmacological point of view. This can induce harmful side-effects or create problems related to cost of treatment. Due to poor bioavailability the formulator may have to select the injection route instead of the oral route.[1] Most widely discussed but still not completely resolved point in pharmaceutical research is, solubility or dissolution enhancement. As a result, more than 40% of new candidates entering drug development pipeline fail because of non optimal biopharmaceutical properties.[2]

Solubility behavior of a drug is one of the key determinants of its oral bioavailability. A great number of newly developed, beneficial chemical entities do not reach the public merely because of their poor oral bioavailability due to inadequate dissolution. Although salt formation, solublization, particle size reduction have commonly used to increase dissolution rate and thereby oral absorption and bioavailability of low water soluble drugs[3,5], The BCS class II drugs for which the dissolution profile must be clearly defined and reproducible shows high absorption number (An) and low dissolution number (Dn). Drugs in this class are expected to have a variable dissolution profile due to the formulation and in vivo variables that, in turn, affect the absorption.[6] The use of water-soluble salts and polymorphic forms, reducing particle size to increase surface area, the formation of water soluble molecular complexes, solid dispersion, co-precipitation, lyophilization, microencapsulation, and the inclusion of drug solutions or liquid drugs into soft gelatin capsules are some of the major formulation tools which have been shown to enhance the dissolution characteristics of water-insoluble drugs.[7,8]

Several researchers have shown that the liquid solid technique is the most promising method for promoting dissolution rate of poorly water soluble drugs.[9,10] The technique of 'liquid solid compacts' is a new and promising addition towards such a novel aim for solubility and

dissolution improvement.[11] Liquisolid compact is one of low cost, simple formulation technique and capability of industrial production and serves to be advantageous for this technique. Liquid solid system refers to formulations formed by conversion of drug suspensions or solution in non-volatile solvents into dry, non adherent, free flowing and compressible powder mixtures by blending the suspension or solution with selected carriers and coating materials. They are prepared by simple blending with selected powder excipients referred to as the carriers and the coating materials. Various grades of cellulose, starch, lactose, etc., may be used as the carrier, whereas very fine particle size silica powder may be used as the coating material. The compression of these latter systems resulted in a significant 'Liquid Squeezing Out' phenomenon.[12,14]

Sertraline is primarily a serotonin reuptake inhibitor (SRI) used as major therapeutic advances in psychiatry and is drug of choice for treatment of major depressive disorders which is lipophilic (log P [octanol/water], 5.1), poorly water soluble (3.5 mg/L),. Therapeutic doses of sertraline (50-200 mg/day) taken by patients for four weeks resulted in 80-90% inhibition of serotonin transporter (SERT) in striatum as measured by positron emission tomography. Sertraline is also a dopamine reuptake inhibitor with 1% of its SRI potency and sigma-1 receptor agonist with 5% of its SRI potency.[15] Sertraline weakly blocks α1-adrenoreceptors with 1-10% of its SRI potency.[16] Its half-life in the body is 13-45 hours and is about 1.5 times longer in women (32 hours) than in men (22 hours), resulting in the proportionally 1.5 higher exposure of women and its bioavailability is 44%.[17] In order to improve the bioavailabilty of sertraline hydrochloride and to reduces its side effects.

Also, Sertraline Hcl has large value of Tmax about 6 hours. So from all the discussion, the ideal delivery route for Sertraline Hcl is one by which we can modify its Tmax and Cmax to a better side. With this we can achieve two targets with one arrow. First, we can increase bioavailability (more Cmax) as there is no first pass metabolism in fast dissolving route. At salivary pH, fewer drugs gets ionized compare to stomach, so rapid absorption is there (less Tmax). Although oral administration is the most popular route many patient find in difficulties with solid dosage swallow solid unit dosage form and do not take their medication as prescribed .it is estimated that 50% of the population is affected by the problem of difficulties in swallowing which result in high incidence of patient compliance and ineffective therapy.[18]

MATERIALS AND METHODS

1. Materials

The following gift samples were received: Sertraline hydrochloride (Dr. Reddy laboratories hyd); Avicel PH 102 (Qualigens fine chemicals, Mumbai); Aerosil 200 (Colorcon Ltd, Goa). The following samples were purchased: Tween 80, polyethylene glycol 400 & 6000 (PEG400 & 6000), PVPK30, Cross Povidone, Cross carmelose sodium, Sodium starch glycolate (Hetero drugs Pvt Ltd, kottur.), methanol (Research lab), All reagents used were of analytical grade.

2. Equipments

Electronic balance (Shimadzu, A×200, Japan), u.v/visible spectrophotometer (Elico SL 159), Rotary tablet machine (Cadmach, Ahmedabad), Tablet Dissolution test apparatus (VEEGO Disso 2000,Navi,Mumbai), Disintegration test apparatus (Labindia Disso 2000, Navi, Mumbai), Melting point apparatus (Cintex Mumbai),

3. Experimental

3.1. Solubility studies of Sertraline hcl

The solubility studies of Sertraline hcl were carried out as described by Spireas et al., (1998); Spireas and Sadu, (1998); Nokhodchi et al., (2005). In this study, the solubility of Sertraline hcl was determined in different solvents including: PEG 400, glycerin, propylene glycol, DMSO, Ethanol, Tween 80 and distilled water. Preparing saturated solutions of the drug in these solvents and analyzing its drug content spectrophotometrically performed the test. The mixture was stirred using magnetic bead for 48 hours and then cooled to 25°C. The solutions were filtered and their concentration was determined by UVspectrophotometer (Jasco V530, Japan) at 238 nm. The results were extrapolated to determine the percent w/w of Sertraline hcl in its saturated solution with the solvent under investigation.

3.2 Solubility enhancement of Sertraline hydrochloride by using solid dispersion technique.

(I) Preparation of Physical Mixture

Preparation of Physical Mixture Accurately weighed amount of Sertraline hcl and carriers (PVP K-30 and PEG 6000) in various drug-to-carrier weight ratios (1:1, 1:3 & 1:5) were thoroughly blended in glass mortar for 5 min. The products were kept in desiccator for further study

(II) Preparation by solvent evaporation method

The solid dispersions of Sertraline hcl and carriers (PVP K-30 and PEG 6000) in various drug-to-carrier weight ratios (1:1, 1:3 & 1:5) were prepared by solvent evaporation method. The desired quantity of CC was dissolved in 20 ml of Ethanol in a beaker then the carrier was added and mixed to dissolve at 40°C on a hot plate to get a clear solution. Then the solvent was allowed to evaporate in hot air oven at 40°C ± 5°C. The process of evaporation was continued until the constant weight was obtained. The prepared samples were crushed, pulverized and sifted through mesh number 80 and stored in desiccators

Table 1: Preparation of solid dispersions of drug by using PVPK30 &PEG400 as Carriers

Solid dispersion by solvent evaporation method			Solid dispersion by Physical Mixing method		
Formulation Code	**Drug: carrier**	**Carrier**	**Formulation Code**	**Drug: carrier**	**Carrier**
SD1	1:1	PVPK30	SD7	1:1	PVPK30
SD2	1:3		SD8	1:3	
SD3	1:5		SD9	1:5	
SD4	1:1	PEG6000	SD10	1:1	PEG6000
SD5	1:3		SD11	1:3	
SD6	1:5		SD12	1:5	

3.3 Solubility studies in nonvolatile solvents for liquid solid compact manufacturing

In this study excess amount of pure drug was added to the non volatile liquid vehicle shaken it for 48 hrs at 25^0C on a rotary shaker. After 48 hours stirring the saturated solution was filtered through milli pore filter paper and analyzed by UV spectrophotometer Another method to determine the solubility is that take 1-40mg of drug into a screw cap vial to which solvent is added in increasing amounts and was shaken until a clear solution was formed. Then finally determine the solubility of drug in the nonvolatile solvent by the following formula,

Solubility= Amount of drug taken(mg)/volume of liquid added

Prior to the selection of suitable non volatile solvent in the formulation there is a need to check the saturation solubility with the selected list of non volatile solvents. From the values of solubility the drug solubility in which liquid is high is taken as solvent for the liquid solid system for the improvement of dissolution rate and with least solubility retard the drug release rate.

a. Determination of angle of slide[19]

Required amount of the carrier material was weighed and placed on one end of the glass slide and the slide was raised slowly till the slide is angular to the horizontal surface. This angle is called as angle of slide. This is useful for the measuring the flow behavior of the material. It is the ideal angle for the good flow.

b. Liquid load factor (Lf)[20]

For the formulation of liquid solid compact powder mixture (Carrier and Coating material requires good flow ability and compact ability .Powder mixture retain only come amount of liquid to produce good flow able and compactable powder. A mathematical approach is needed to calculate the required quantities of carrier and coating materials was proposed by spireas et.al. This approach is based on the Parameters like liquid load factor, flowable liquid retention potential (φ) value and compressible liquid retention potential (ψ) value.

Lf is defined as the ratio of weight of liquid medication to that of carrier. Depending upon the ratio of carrier to coating material (i.e excipients ratio, R) an acceptable flowing and compressible liquid solid system can be produced.

R = Q/q

= Weight of the carrier /weight of the coating material

LF = W/Q

Lf = weight of the liquid medication/weight of the carrier

φ value indicates that the maximum amount of a given non volatile liquid that can be retained by the powder mixture in order to get acceptable flow ability. The flow ability of material can be measured by the angle of repose, compressibility index and Hausner's ratio. Ψ number indicates that the maximum amount of a given non volatile liquid that can be retained by the powder or the powder mixture in order to get the good compact ability.

Liquid load factor ensures good flow ability and good compact ability can be determined by φLf or ψLf which is having the low value.

φLf = φ +φ (1/R) ψLf = ψ + ψ (1/R)

ψ ,φ =are the φ and ψ number of carrier material and ψ ,φ are the φ and ψ number of coating material. Some ψ and φ values of powder excipients or powder materials with a particular ration and with particular non volatile solvents commonly employed in the liquidsolid system.

Table 2: Liquid-solid formulation standard and observed parameters of various powder excipients with commonly used liquid vehicles powder.

Excipient or System	Standard values			
	Φ-values		ψ-values	
	Tween 80	PEG-400	Tween 80	PEG-400
Avicel pH 102(carrier)	0.16	0.005	0.224	0.242
Aerosil (coat)	3.31	3.26	0.560	0.653
	Observed values			
Avicel pH 102(carrier)	0.14	0.003	0.264	0.272
Aerosil (coat)	3.32	3.15	0.572	0.612

4. Preformulation studies

Flow behavior

In the tablet formulations flow properties measurement is very important and essential. Flow properties can be studied by measurement of some properties like Angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio.

a. Angle of repose

It can be determined by fixed funnel, free standing cone method and open end cylinder methods. A funnel is placed at a height (H) of 2.5cm with its tip above the graph paper placed on a horizontal flat surface. The sample powder to be analyzed is poured through the funnel until the conical pile is formed on the paper. The diameter (2r) of the cone is measured. The tangent of the angle of repose is given by

$$\text{Tan } \theta = H/r \quad \text{(or) Tan } \theta = H/0.5D$$

Where,

θ=Angle of repose,

H=Height of the heap,

D& r=Diameter & radius of the cone,

b. Bulk density and tapped density

A weighed quantity of powder was taken to determine the bulk and tapped densities.

Bulk density=mass/volume

Tapped density= Mass /Tapped volume

Hausner ratio and carr's index were calculated from bulk and tapped densities. Hausner's ratio=Bulk density/Tapped density

Carr's index = (Tapped density- bulk density/ tapped density) x 100

Table 3: Effect of Carr's Index and Hausner's Ratio on flow properties

S.No	Carr's Index	Flow Character	Hausner's Ratio
1	<10	Excellent	1.00-1.11
2	11-15	Good	1.12-1.18
3	16-20	Fair	1.19-1.25
4	21-25	Passable	1.26-1.34
5	26-31	Poor	1.35-1.45
6	32-37	Very poor	1.46-1.59
7	>38	Very very poor	>1.60

Formulation of sertraline hydrochloride by solid dispersion technique

From the solubility studies of prepared solid dispersions SD3 has shown better solubility and drug content profiles. Hence SD3 was selected among all the solid dispersions prepared. The amount of complex equivalent to 25 mg of drug per tablet were taken and mixed with directly compressible diluents and superdisintegrants in mortar with help of pestle. Then finally aspartame as sweetener and magnesium stearate as a lubricant was added. The blend was than compressed using 8 mm punch using Rimek tablet machine. The total weight of tablet maintains 400 mg.

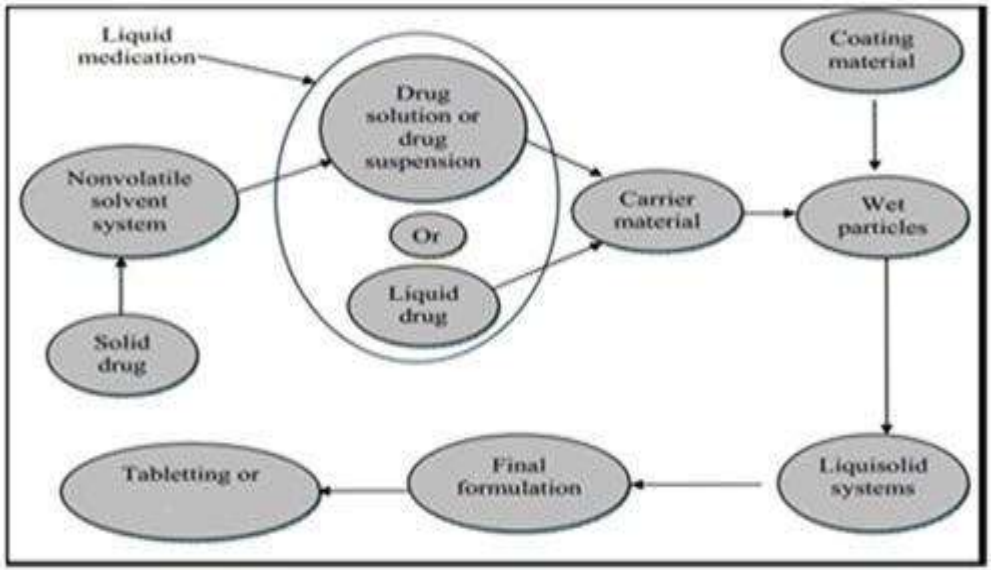

Fig 1. Steps involved in the preparation of liquid solid system

The formulation table of Sertraline Hcl by solid dispersion technique was enlisted below.

Table 4: Formulation of solid dispersion with different conc of Super Disintegrants

S.No	Ingredients	Formulation Code								
		SF1	SF2	SF3	SF4	SF5	SF6	SF7	SF8	SF9
1	SD3 (DRUG+PVPK30)	Equivalent weight of 25mg of drug								
2	Avicel PH102	150	150	150	150	150	150	150	150	150
3	PVP	2%	2%	2%	2%	2%	2%	2%	2%	2%
4	Cross povidone (CP)	2.5%	5%	7.5%	-	-	-	-	-	-
5	Cross carmelose sodium (CCS)	-	-	-	2.5%	5%	7.5%	-	-	-
6	Sodium starch glycolate (SSG)	-	-	-	-	-	-	2.5%	5%	7.5%
7	Mannitol	20	20	20	20	20	20	20	20	20
7	Lactose	50	40	30	50	40	30	50	40	30
8	Aerosil	2%	2%	2%	2%	2%	2%	2%	2%	2%
9	Magnesium stearate	2%	2%	2%	2%	2%	2%	2%	2%	2%
Total tablet Weight		400	400	400	400	400	400	400	400	400

(VII) Formulation of sertraline hydrochloride by using liquid solid compact technique with direct compression method

25mg of sertraline hydrochloride was dissolved in non volatile solvents (poly ethylene glycol 400 & tween80) by using magnetic stirrer. The solution was then sonicated for 10 min until a homogeneous drug solution was obtained. Next, the calculated weights (W) of the resulting liquid medications (equivalent to 25 mg drug) were incorporated into the calculated quantities of the carrier material (cellulose micro crystalline) and mixed thoroughly. The resulting wet mixture was then blended with the calculated amount of the coating material (colloidal silicon dioxide) using a standard mixing process to form simple admixture. Two factors to be considered in manufacturing of liquid solid compacts are, concentration of the drug in liquid vehicle (PEG400, Tween 80) and carrier: coating ratios. Different liquid load factors (Lf) were calculated for these liquid solid compacts. To this, above 2.5%, 5%,7.5% w/w of cross povidone,cross carmelose sodium, sodium starch glycolate were added in different formulations and mixed with the above mixture for 10 min. Finally lactose, magnesium stearate and talc was added The final blend of liquid solid powder system was compressed into rotary tablet machine.

Table 5: Liquid solid compact formulations of F1to F9 with PEG 400

S.No	Ingredients	Formulation code									
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	Sertraline hcl+ Liquid medication(PEG)	Equivalent weight of 25mg of drug									
2	Cellulose Micro Crystalline (Carrier)	250	250	250	250	250	250	250	250	250	250
3	Colloidal Silicon Dioxide (Coating material)	125	125	125	125	125	125	125	125	125	125
4	Cross Povidone (CP)	-	2.5%	5%	7.5%	-	-	-	-	-	-
5	Cross Carmellose Sodium (CCS)	-	-	-	-	2.5%	5%	7.5%	-	-	-
6	Sodium starch Glycolate (SSG)	-	-	-	-	-	-	-	2.5%	5%	7.5%
7	Mannitol	5	5	5	5	5	5	5	5	5	5
8	Lactose	55	42	28	14	42	28	14	42	28	14
9	Magnesium stearate	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
10	Talc	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
Total tablet weight			550	550	550	550	550	550	550	550	550

Table 6: Liquid Solid Compact Formulations F11-F20 with Tween80

S.No	Ingredients	Formulations									
		F11	F12	F13	F14	F15	F16	F17	F18	F19	F20
1	Sertraline hcl+ Liquid medication (tween80)	Equivalent weight of 25mg of drug									
2	Cellulose MicroCrystalline (Carrier)	250	250	250	250	250	250	250	250	250	250
3	Colloidal Silicon Dioxide (Coating material)	125	125	125	125	125	125	125	125	125	125
4	Cross povidone (CP)	-	2.5%	5%	7.5%	-	-	-	-	-	-
5	Cross carmelose sodium (CCS)	-	-	-	-	2.5%	5%	7.5%	-	-	-
6	Sodium starch glycolate (SSG)	-	-	-	-	-	-	-	2.5%	5%	7.5%
7	Mannitol	5	5	5	5	5	5	5	5	5	5
8	Lactose	56	42	28	14	42	28	14	42	28	14
9	Magnesium stearate	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
10	Talc	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
	Total tablet weight	550	550	550	550	550	550	550	550	550	550

Table 7: Different Parameters Of Liquid Solid Compact Formulations

Formulation Code	Weight of carrier (Q)	Weight of coating material (q)	Weight of liquid medication (W)	Excipients ratio (R)	Loading Factor (Lf)
F1	250	125	74	2	0.296
F2	250	125	69	2	0.276
F3	250	125	67	2	0.268
F4	250	125	72	2	0.288
F5	250	125	74	2	0.296
F6	250	125	64	2	0.256
F7	250	125	74	2	0.296
F8	250	125	73	2	0.292
F9	250	125	70	2	0.280
F10	250	125	72	2	0.288
F11	250	125	74	2	0.296
F12	250	125	62	2	0.248
F13	250	125	60	2	0.240
F14	250	125	65	2	0.256
F15	250	125	66	2	0.264
F16	250	125	67	2	0.268
F17	250	125	70	2	0.283
F18	250	125	68	2	0.272
F19	250	125	69	2	0.276
F20	250	125	71	2	0.284

Post compressional studies

Hardness

Tablets require certain amount of strength, or hardness and resistance to friability, to withstand mechanical shocks of handling in manufacture, packaging and shipping. The monitoring of tablet hardness is especially important for the drug products that possess real or potential bioavailability problems or that are sensitive to altered dissolution release profiles as a function of the compressive force employed. The hardness was tested for 6 tablets from each formulation using Monsanto hardness tester.

Friability testing

The tablet friability test is the method to determine physical strength of uncoated tablets upon exposure to mechanical shock or attrition. A six number of tablets were weighed and placed in the Roche friabilator apparatus where they were exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus at a rate of 25 rotations per minute. After four minutes of this treatment or 100 revolutions, the tablets were weighed and the weight compared with the initial weight. The loss due to abrasion is a measure of the tablet friability. The value is expressed as a percentage.

Weight variation

With a tablet designed to contain a specific amount of drug in a specific amount of tablet formula, the weight of the tablet being made is routinely measured to help ensure that a tablet contains the proper amount of drug. The IP weight variation test was run by weighing 20 tablets. Individually, calculating the average weight, and comparing the individual tablet weights to the average. The tablets meet the IP test if not more than 2 tablets are outside the percentage limit and no tablet differs by more the twice the percentage limit.

Thickness

Thickness is a dimensional test done during the production. The thickness of tablet was done using Mitutoyo digital Vernier calipers. The total thickness was found and followed by scrapping the immediate release.

Drug content

Ten tablets were individually weighed and crushed. A quantity of powder equivalent to the mass of one tablet was extracted in 100 mL of pH 6.8 phosphate buffer. The solution was centrifuged at 3000 rpm for 15 min. The drug content was analyzed at 246 nm using a UV/ Visible spectroscopy after suitable dilution with pH 6.8 phosphate buffers.

In-vitro Disintegration test

The USP device to test disintegration uses 6 glass tubes with a 10 mesh screen at the bottom. To test for disintegration time, one tablet is placed in each tube, and the basket rack is positioned in a 1L beaker of medium at 37 + 20C. The standard motor driven device is used to move the basket assembly containing the tablets up and down through a distance of 5 to 6cm at a frequency of 28 to 32 cycles per minute. Perforated plastic discs were placed on top of the tablets.

In-vitro drug release studies

In-vitro dissolution studies were performed in a USP XXIII dissolution test apparatus, type II (paddle method) (Disso 2000, Labindia, India) at 37 ± 0.5^{0C} and with a paddles rotation speed of 50rpm. The tablets were placed into 900ml of 6.8 phosphate buffer solution was as dissolution medium. The tablets were placed in sinkers which kept them in sink condition during the dissolution study. Dissolution studies were carried out in triplicate. 10 ml aliquots of samples were collected at 10min interval up to 60min. They were filtered and estimated for Sertraline hydrochloride released using UV-visible spectrophotometer at 273nm. At each

time of withdrawal, 10ml of fresh medium was replaced into the dissolution flask. The concentration was calculated by using the standard curve prepared using 6.8 phosphate buffer as solvent. The cumulative percentage of Sertraline hydrochloride released from tablets was also calculated.

RESULTS AND DISCUSSION

6.1-Preformulation

6.1.1. Identification of Sertraline hcl

The reports of identification were showed in table 18. In Identification of API it was found that Sertraline hcl was soluble in organic solvents like Acetone, Methanol and Alcohol. Melting point of Sertraline hcl was 242ºc and it exhibits wave length is 273nm.

6.1.2. Solubility Study of Sertraline hcl.

Solubility data of drug Sertraline hcl in various liquid vehicles is shown in Table 2. Sertraline hcl appears to be more soluble in Tween 80 than other vehicles. The solubility is an important factor in liquisolid systems, as higher solubility of drug in liquid vehicle can lead to higher dissolution rates since the drug will be more molecularly dispersed and more surface of drug will be exposed to the dissolution media.

Table 8: Solubility study of Sertraline HCl in different solvents

S.no	Solvent	Solubility (mg/ml) ±S.D
1	DMSO	25±4.1
2	Ethanol	10±0.3
3	Tween80	57.14±3.9
4	PEG 400	10.6±1.2
5	Isopropyl Alcohol	4.3±0.3
6	Water	3.2±1.7
7	Propylene Glycol	8.2±0.2
8	pH 6.8 buffer	0.017±0.0018

6.1.4. Characterization of Micromeritic parameters of Sertraline hcl.

Characterization of Sertraline hcl was conducted by different parameters and the reports were shown in the above table 19.The studies on angle of repose showed that Sertraline hcl was 42.91º this value indicated passable flow property. On analyzing for density it was found that Sertraline hcl showed bulk density value 0.39 gm/cc and tapped density value 0.52gm/cc. The value of Carr's Index for Sertraline hcl was 22 indicated that two drugs showed passable flow properties. The value of Hausner's ratio for Sertraline hcl was 1.28 indicated that drug shows

passable flow characteristics. Based on results i found poor flow characteristics. So need to improve the flow of the powder.

6.2-Stability studies

FTIR SPECTRAL STUDIES

IR spectra analysis

The IR spectrum showing percentage transmission (T%) versus wave number of Sertraline hcl is shown in Fig. 1 with characteristic peaks of C-N-H stertching and C-N stretching at 3853 cm^{-1} and 1018 cm -1 , respectively. Also C-C Stretching group at 824 cm -1.From the figure it is evident that there was no chemical interaction between the drugs and excipients used**.** The IR Spectra of Sertraline hcl with cellulose micro crystalline, aerosil, Crospovidone, CCS& SSG were shown in fig.8-17. The following peaks were observed in Sertraline hcl with excipients.

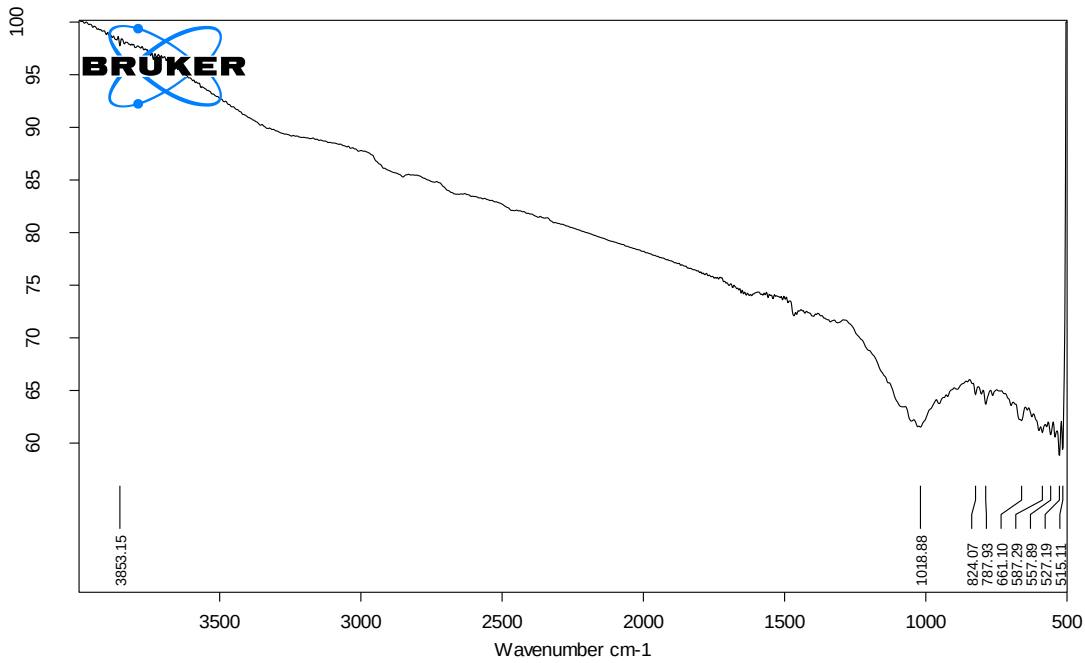

Fig 2: FT-IR spectra of Sertraline hydrochloride

Table 9: FT-IR spectra details of Sertraline hydrochloride

S.NO	Wave length	Specification
1	3853 cm^{-1}	N-H Stretching
2	1018 cm^{-1}	C-N Stretching
3	824 cm^{-1}	C-C Stretching

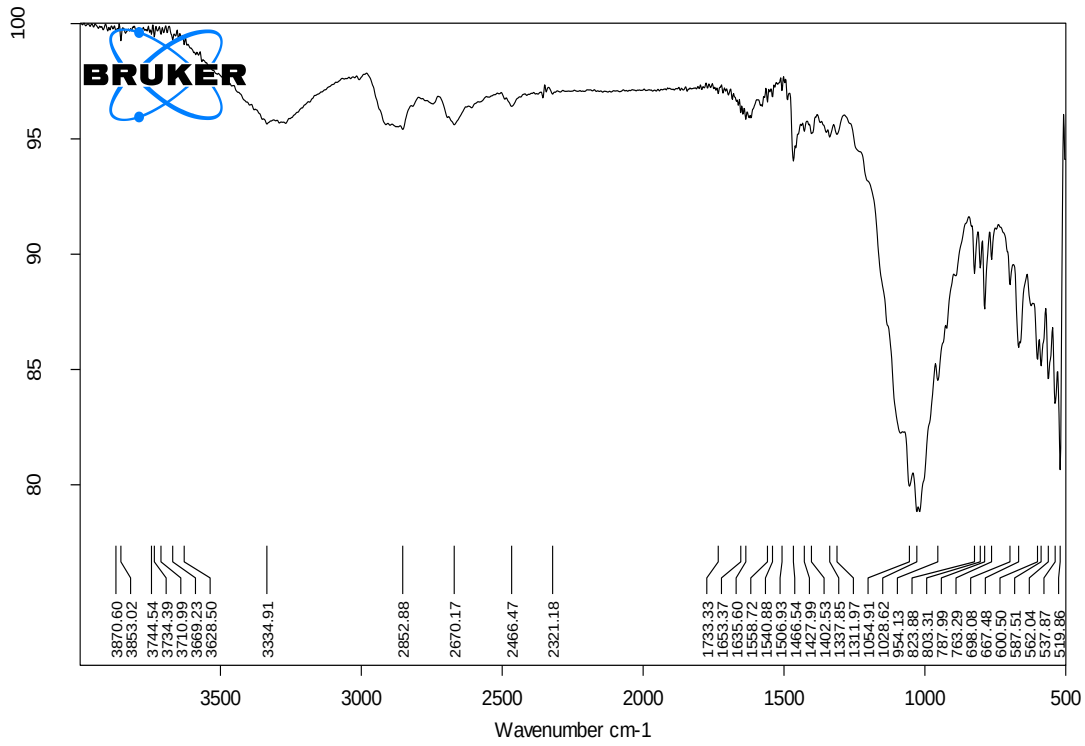

Fig.3: FT-IR spectra of Liquid Solid Compact Formulation with Tween80 as solvent

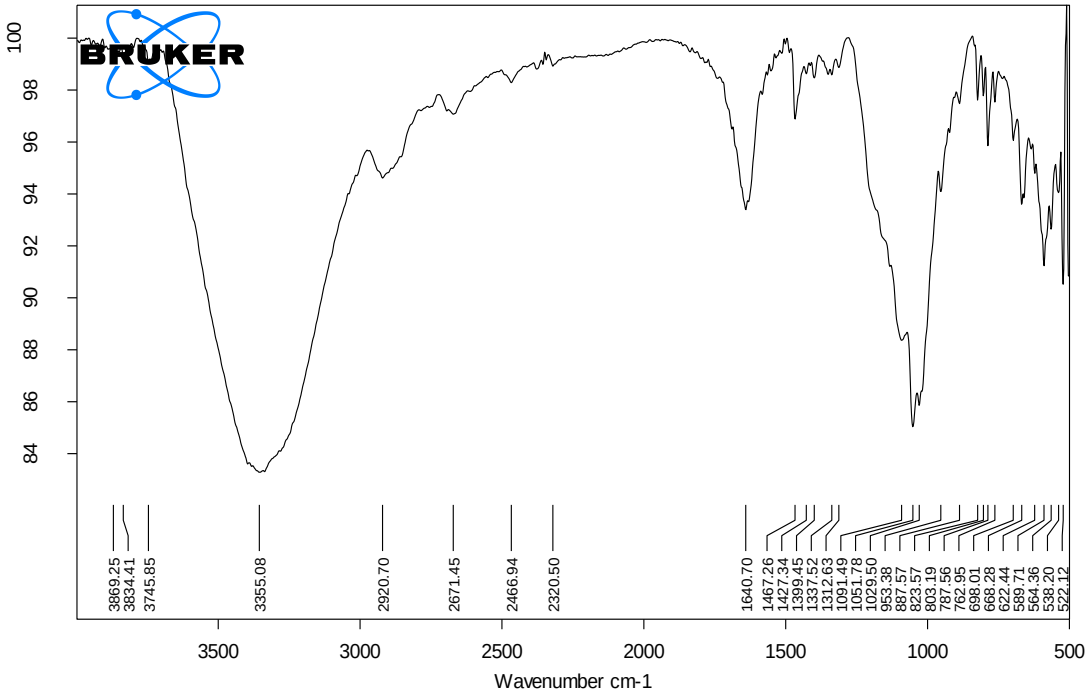

Fig. 4: FT-IR spectra of Liquid Solid Compact Formulation with PEG 400 as solvent

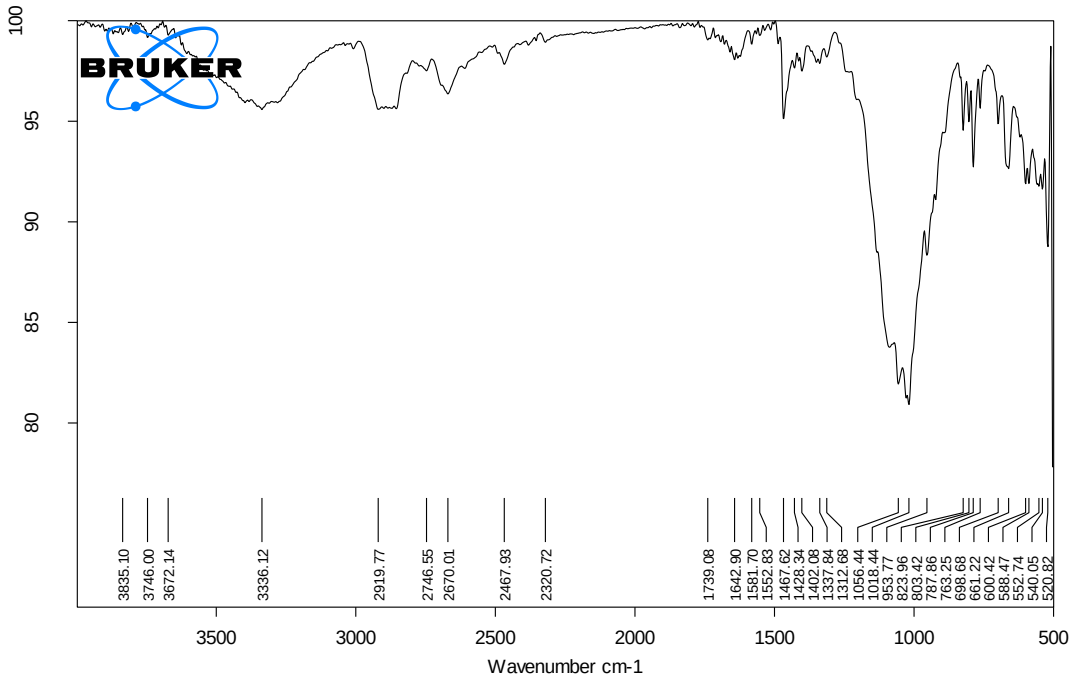

Fig. 5: X-Ray diffraction of pure Sertraline hydrochloride

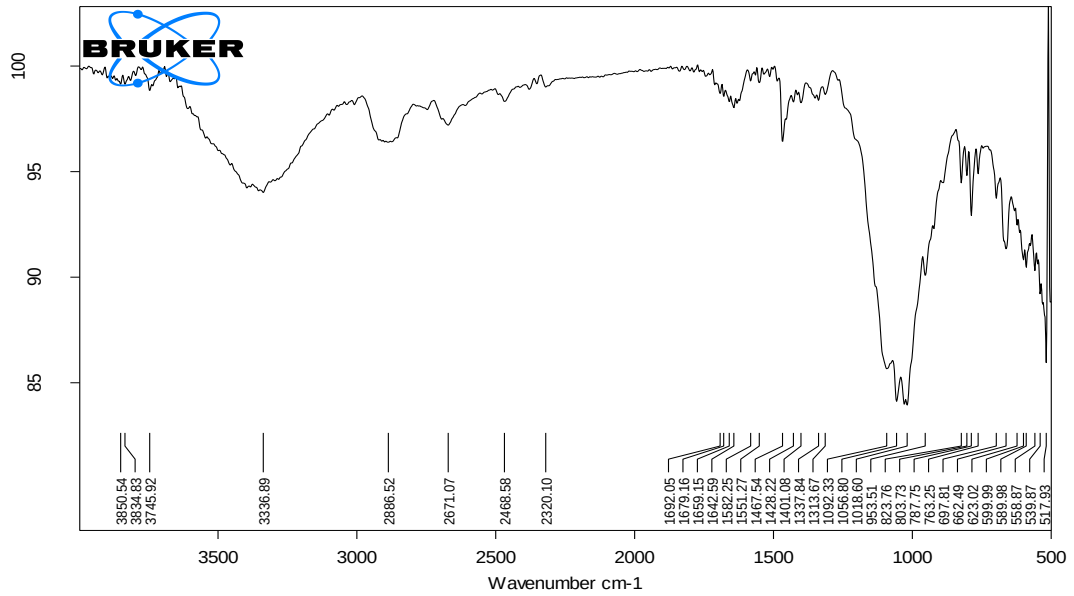

Fig. 6: X-ray diffraction of liquid solid compact powder with Tween80 as solvent

6.3- Analytical method

Sertraline hcl was estimated using UV/VIS Spectrophotometric method. It was found that under UV/VIS Spectrophotometer Standard absorbance of the peak of Sertraline hcl was 0.1557 for 60 µg/ml of standard weight. The reports of the analytical method were shown in table 20 & fig 25.

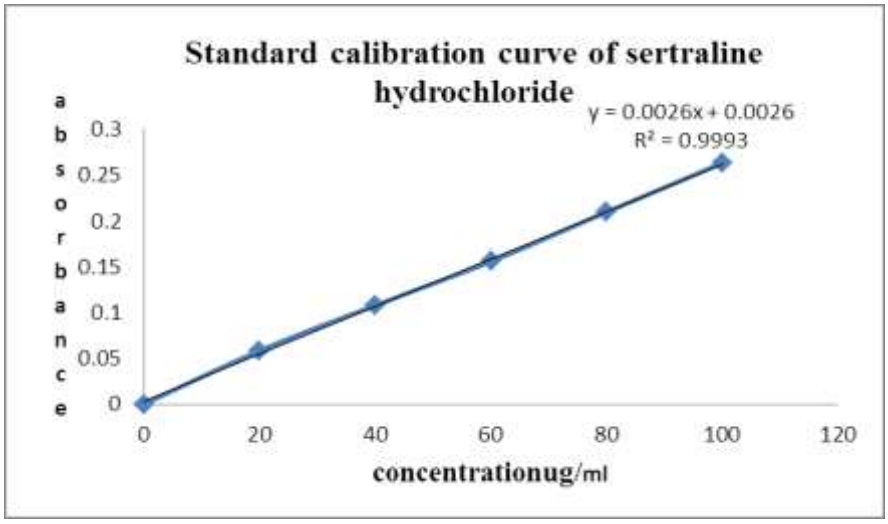

Fig 7: Standard calibration curve of sertraline hydrochloride

Solubility study of Sertraline hcl in solid dispersions:

Solid dispersions of Sertraline hcl were prepared by both solvent evaporation and physical mixing methods. Solubility data of these solid dispersions was plotted in fig .With this data maximum solubility was observed with SD3 and its drug content is also 100.3±1.6. From these values SD3 was selected as best solid dispersion. Then the formulations of solid dispersion with different superdisintegrant concentrations as SF1-SF9 were formulated.

Solubility pattern of Sertraline hcl in Solid Dispersions

Table 10: Solubility & drug content of Sertraline hcl in Phosphate Buffer (pH 6.8) ± S.D

Solid dispersion by solvent evaporation method			Solid dispersion by Physical Mixing method		
Formulation Code	**Solubility (mg/ml) ±S.D**	**Drug content (%)**	**Formulation Code**	**Solubility (mg/ml) ±S.D**	**Drug content (%)**
SD1	0.141	97.1±2.3	SD7	0.031	92.89±1.4
SD2	0.214	98.52±1.2	SD8	0.034	94.35±2.6
SD3	**0.279**	**100.3±1.6**	SD9	0.035	99.73±1.4
SD4	0.152	95.8±2.3	SD10	0.024	95.8±1.7
SD5	0.208	96.14±1.7	SD11	0.026	96.86±1.2
SD6	0.226	99.2±2.3	SD12	0.028	98.82±2.3

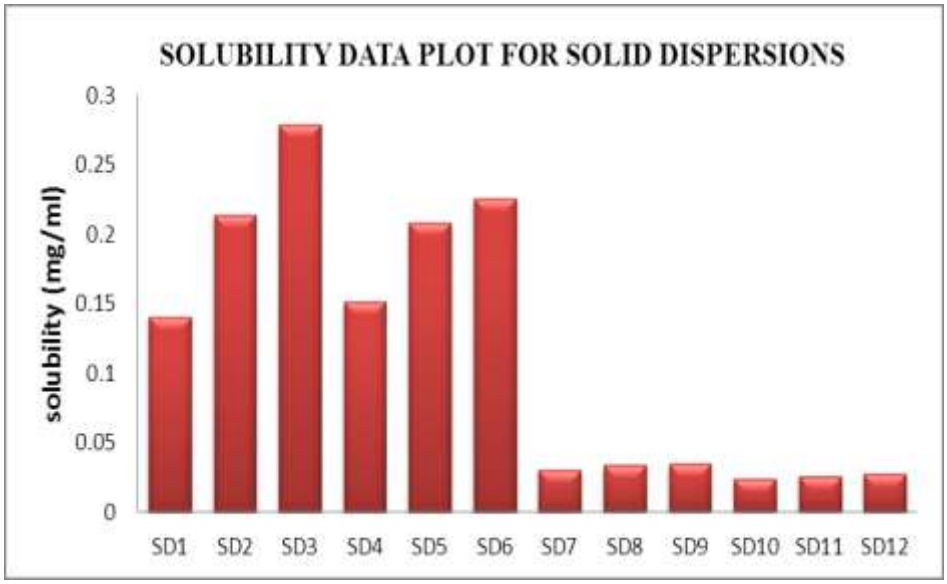

Fig.8: solubility data

6.1.3. Measuring Angle of Slide for Determination of Flowable Liquid Retention Potential.

Angle of slide determination is an important step in the formulation of liquid solid tablets. The relationship of angle of slide with corresponding φ of Avicel, and φCo of Aerosil for liquid vehicle are shown in Figures 2(a), 2(b), and 2(c), respectively. The Lf was then used to decide the optimum amount of carrier and coating materials required to ensure dry-looking, free-flowing and compactible powdered systems. The highest liquid factor was obtained for Avicel, and accordingly, the amount of carrier was lower than other formulations.

Φ value of Carrier and Coat materials in Poly Ethylene Glycol and Tween 80 were cited in the literature & found to be 0.005, and 3.26, respectively. According to mathematical model proposed by Spireas et. al. equation for Avicel PH-102 and Aerosil 200 in poly ethylene glycol and tween 80 was calculated by using R values as

$$\mathbf{Lf = 0.005 \pm 3.26\ (1/R)}$$

Liquid solid powder systems were prepared & their flow properties were calculated. These liquid solid powder systems were blended with different super disintegrant ratios & exciepients.

6.4-Evaluation of pre-compression and post compression Parameters

The preliminary studies were carried out by preparing various formulations with different process variable and subjecting the formulation to all pre-compression and post-compression parameters.

6.4.1-Characterisation of Liquid Solid Compacts &solid dispersions

The study of organoleptic properties for all batches was done and reported. The study of angle of repose, density, compressibility index was done for all formulations. Characteristics of Sertraline hcl fast dissolving tablets of liquid solid compacts with PEG 400 & Tween 80 and solid dispersions with PVPK30 & PEG 6000 prepared with Crosspovidone, CCS, SSG by direct compression method were reported in tables 21-27.

Density

From the results it was observed that the bulk density of Sertraline hcl in liquid solid compacts was found between 0.58 & 0.66 gm/cc and that of solid dispersions was found between 0.58 & 0.65 gm/cc. The Tapped density of Sertraline hcl in liquid solid compacts was found between 0.63 & 0.75 gm/cc and that of solid dispersions was found between 0.68 &0.74 gm/cc.

Compressibility index

The compressibility Index of Sertraline hcl in liquid solid compacts was found between 8.5 &15.9 and that of solid dispersions was found between 11.12 & 13.20.

Angle of repose

The Angle of repose of Sertraline hcl in liquid solid compacts was found between 27.3º & 35.2º and that of solid dispersions was found between 31.2º & 35.6º.

From the above investigational reports, it indicates that excellent flow property for liquid solid compacts and good flow property for solid dispersions of the direct compression powders.

5.5 Evaluation of pre-formulation Parameters

Table 11: Flow properties for solid dispersion formulations of Sertraline hcl

S.No	Angle of repose	Bulk Density gm/cc	Tapped density gm/cc	Carr's index	Hausner'sratio
SF1	31.2±1.379	0.65±0.031	0.73±0.010	11.1±1.185	1.12±0.031
SF2	33.3±1.286	0.59±0.016	0.69±0.025	14.4±1.085	1.16±0.012
SF3	31.6±1.131	0.65±0.038	0.74±0.050	12.16±1.10	1.13±0.021
SF4	33.16±1.181	0.63±0.045	0.72±0.025	12.15±1.12	1.14±0.016
SF5	34.9±1.163	0.64±0.024	0.74±0.018	12.6±1.130	1.13±0.016
SF6	34.6±1.210	0.59±0.041	0.68±0.020	13.2±1.185	1.15±0.018
SF7	33.17±1.126	0.62±0.035	0.71±0.019	12.6±1.140	1.14±0.019
SF8	35.6±1.168	0.58±0.025	0.69±0.025	15.9±1.121	1.18±0168
SF9	34.18±1.120	0.61±0.051	0.70±0.026	12.8±1.201	1.14±0.012

Table 12: Flow properties for liquid solid compact formulations

S.No	Angle of repose	Bulk Density gm/cc	Tapped Density gm/cc	Carr's index	Hausner' sratio
F1	35.23±0.63	0.58±0.02	0.69±0.12	15.9±0.78	1.18±0.05
F2	33.16±0.71	0.63±0.03	0.72±0.09	12.5±0.79	1.14±0.03
F3	34.18±0.75	0.61±0.02	0.70±0.15	12.8±0.88	1.14±0.04
F4	29.7±0.69	0.64±0.04	0.71±0.12	9.8±0.81	1.10±0.06
F5	30±0.88	0.62±0.08	0.73±0.23	15.06±0.88	1.17±0.03
F6	31.6±0.79	0.66±0.05	0.75±0.31	12±0.79	1.13±0.05
F7	29.5±0.85	0.65±0.04	0.72±0.24	9.7±0.83	1.10±0.03
F8	30.3±0.67	0.63±0.06	0.7±0.26	10±0.91	1.1±0.02
F9	33.3±0.86	0.59±0.07	0.69±0.18	14.4±0.86	1.16±0.04
F10	31.5±0.68	0.65±0.03	0.73±0.15	10.9±0.85	1.12±0.03
F11	27.3±0.82	0.63±0.04	0.63±0.13	10±0.86	1.11±0.05
F12	25.6±0.67	0.64±0.06	0.7±0.28	8.5±0.79	1.0±0.06
F13	32.1±0.85	0.6±0.02	0.7±0.26	14.2±0.76	1.16±0.04
F14	33.3±0.83	0.59±0.06	0.68±0.19	13.2±0.82	1.15±0.06
F15	28.30±0.73	0.65±0.04	0.72±0.18	9.7±0.83	1.10±0.01
F16	33.6±0.78	0.62±0.06	0.71±0.25	12.6±0.85	1.14±0.06
F17	32.1±0.76	0.65±0.07	0.74±0.26	12.16±0.89	1.13±0.04
F18	30.5±0.68	0.63±0.03	0.72±0.18	12.5±0.79	1.14±0.07
F19	26.31±0.69	0.62±0.04	0.69±0.19	10.14±0.81	1.11±0.04
F20	25.1±0.33	0.63±0.02	0.69±0.23	8.6±0.63	1.0±0.02

Physical characterization of Sertraline hcl tablets

Tablet hardness

Hardness of the developed formulations varies from 3.7±0.43 kg/cm^2 to 4.5±0.46 kg/cm^2 for liquid solid compacts and from 3.5±0.125 kg/cm^2 to 4.5±0.142 kg/cm^2 for solid dispersions.

Tablet thickness

Thickness of the Sertraline hcl liquid solid compacts varied from 4.99±0.52 to 5.80±0.64 mm and for solid dispersions varies from 3.98±0.12 to 4.52±0.14 mm.

Weight variation

The average weight of twenty tablets of Sertraline hcl was calculated for each formulation which varied from 5.9±0.38 to 7.3±0.34 for liquid solid compacts and from4.8±0.142 to 5.5±0.192 for solid dispersions, which Complies the official requirement as per IP.

% Friability

Friability of the developed formulations varied from 0.37±0.023% to 0.49±0.024% loss for liquid solid compacts and varied from 0.65±0.026 % to 0.91±0.025% loss for solid dispersions which was less than 1% as per official requirement of IP.

Drug content

The drug content was estimated for all the formulations the results obtained between the range 91.5 to 99.9 %. All the formulations were found within the limits.

Disintegration time

The most important parameter that needs to be optimized in the development of fast disintegrating tablets is the disintegration time of tablets. In the present study disintegration time of all batches were found. Among them, formulations with super disintegrants disintegrate in the range of 1min 20sec (80 sec) to 5 min 9sec (309 sec) and for the formulation without super disintegrants shows disintegration with in 9 min 5sec, fulfilling the official requirements.

5.6 Evaluation of Post compression Parameters

Table 13: Post compression studies of Sertraline hcl solid dispersions

S.No	Hardness ± S.D	Thickness ± S.D	Weight variation ± S.D	%Friability ± S.D	Drug content	Disintegration time
SF1	3.9±0.154	3.98±0.12	5.5±0.192	0.79±0.031	95.5	4min2sec
SF2	3.5±0.125	4.33±0.52	4.9±0.158	0.85±0.035	93.6	3min45sec
SF3	3.7±0.123	4.42±0.31	5.1±0.129	0.81±0.032	95.9	1min53sec
SF4	4.1±0.132	4.16±0.15	4.6±0.121	0.91±0.025	98.3	3min1sec
SF5	4.5±0.142	4.52±0.14	5.3±0.153	0.83±0.023	96.8	3min58sec
SF6	3.8±0.138	4.25±0.16	4.9±0.154	0.65±0.026	97.12	2min and 52sec
SF7	4.3±0.123	4.50±0.17	5.2±0.135	0.83±0.032	96.3	3min55sec
SF8	4.0±0.182	4.47±0.14	4.8±0.142	0.074±0.025	94.6	3min2sec
SF9	3.9±0.152	4.11±0.016	5.1±0.132	0.72±0.033	99.9	2min59sec

Table 14: Post compression studies of Sertraline hcl liquid solid compact formulations

S.No	Hardness ± S.D	Thickness ± S.D	Weight variation ± S.D	%Friability ± S.D	Drug content	Disintegration time
F1	3.9±0.37	5.23±0.85	7.3±0.34	0.45±0.026	97.16	12min25sec
F2	4.2±0.41	5.22±0.77	6.4±0.42	041±0.021	93.88	7min2sec
F3	3.8±0.38	5.31±0.65	5.9±0.36	0.39±0.25	95.3	4min35sec
F4	4.5±0.45	5.00±0.68	6.3±0.32	0.46±0.02	91.44	2min50sec
F5	3.8±0.39	4.99±0.52	7.2±0.41	0.47±0.015	96.5	6min3sec
F6	4.0±0.48	5.66±0.45	6.8±0.34	0.38±0.012	98.3	4min20sec
F7	4.2±0.45	5.45±0.51	5.9±0.38	0.42±0.024	96.64	2min3sec
F8	4.4±0.38	5.80±0.64	6.4±0.42	0.46±0.025	97.32	6min2sec
F9	4.5±0.46	5.21±0.53	6.7±0.32	0.49±0.024	95.08	3min 29sec
F10	3.8±0.38	5.64±0.52	6.3±0.36	0.37±0.023	98.1	2min5sec
F11	4.3±0.45	5.25±0.45	7±0.43	0.41±0.016	92.88	9min59sec
F12	4.1±0.46	5.55±0.65	6.6±0.39	0.48±0.022	96.32	6min25sec
F13	4.4±0.41	5.68±0.98	6.5±0.41	0.38±0.023	91.32	3min58sec
F14	4.3±0.47	5.25±0.85	7.1±0.36	0.45±0.015	98	2min9sec

F15	3.8±0.45	5.42±0.65	6.4±0.41	0.43±0.013	97.6	5min3sec
F16	3.7±0.43	5.15±0.72	6.3±0.39	0.48±0.017	94.4	3min25sec
F17	4.0±0.41	5.65±0.45	7.2±0.37	0.46±0.012	96.5	1min59sec
F18	4.3±0.43	5.12±0.33	6.8±0.42	0.43±0.019	93.23	4min45sec
F19	3.9±0.42	5.88±0.45	7.1±0.39	0.38±0.023	96.9	2min56sec
F20	4.5±0.39	5.00±0.25	6.9±0.36	0.45±0.019	99.9	1min 20sec

S.D =Standard deviation.

In-Vitro Dissolution studies of Sertraline hcl

The formulations F1 to F10 liquid solid compacts containing PEG 400 as non volatile solvent and super disintegrants (CP,CCS &SSG) in 2.5%, 5% & 7.5% concentration prepared by direct compression method. These formulations were subjected to drug release studies in dissolution media namely, 6.8 pH buffer.

The formulation F1 which was formulated without superdisintegrants shows, maximum amount of the drug release(97.24%) in .60mins and the formulation F2 that containing 2.5 % Crosspovidone , maximum amount of the drug release (93.88 %) in 50 min, The formulation F3 that containing 5 % Crosspovidone shows, maximum amount of the drug release(95.88 %) in 30 min, The formulation F4 that containing 7.5% Crosspovidone shows, maximum amount of the drug release(95.62 %) in 20 min , The formulation F5 that containing 2.5 % CCS shows, maximum amount of the drug release (96.64 %) in 50min. The formulation F6 that containing 5 % CCS shows, maximum amount of the drug release (97.68 %) in 30min The formulation F7 that containing 7.5 % CCS, maximum amount of the drug release (97.28 %) in 20min, The formulation F8 that containing 2.5 % SSG, maximum amount of the drug release (96.42 %) in 40min The formulation F9 that containing 5 % SSG, maximum amount of the drug release (96.98 %) in 30min The formulation F10 that containing 7.5 % SSG, maximum amount of drug release(99.12 %) in 20min.

From the above release studies with increase in superdisintegrants concentration the release time decreases and formulation containing 7.5 % SSG shows highest release time 20min.

The formulations F11 to F20 liquid solid compacts containing Tween 80 as non volatile solvent and superdisintegrants (CP,CCS &SSG) in 2.5%, 5% & 7.5% concentration prepared by direct compression method. These formulations were subjected to drug release studies in dissolution media namely, 6.8 pH buffer.

The formulation F11 which was formulated without superdisintegrants shows, maximum amount of the drug release (95.1%) in 40mins, the formulation F12 that containing 2.5% Crosspovidone shows, maximum amount of the drug release (95.6%) in 30 min, The formulation F13 that containing 5 % Crosspovidone shows, maximum amount of the drug release (96.2%) in 20 min, The formulation F14 that containing 7.5% Crosspovidone shows, maximum amount of the drug release (96.9%) in 10 min, The formulation F15 that containing 2.5 % CCS shows, maximum amount of the drug release (95.82%) in 30min. The formulation F16 that containing 5% CCS, shows maximum amount of the drug release (96.86%) in 20min. The formulation F17 that containing 7.5 % CCS shows, maximum amount of the drug release (98.22 %) in 10min, The formulation F18 that containing 2.5 % SSG shows, maximum amount of the drug release (98.56%) in 30min. The formulation F19 that containing 5 % SSG, shows maximum amount of the drug release (99.6%) in 20min. The formulation F20 that containing 7.5 % SSG, shows maximum amount of drug release (99.76 %) in 10min.

From the above release studies with increase in superdisintegrants concentration the release time decreases and formulation containing 7.5 % SSG shows highest release time 10min.

The solid dispersion formulations SF1 to SF9 containing PVPK30 as carrier and superdisintegrants (CP, CCS &SSG) in 2.5%, 5% & 7.5% concentration were prepared by direct compression method. These formulations were subjected to drug release studies in dissolution media namely, 6.8 pH buffer.

The formulation SF1 that containing 2.5 % Crosspovidone, maximum amount of the drug release (93.88 %) in 50 min, The formulation SF2 that containing 5 % Crosspovidone shows, maximum amount of the drug release (95.88 %) in 30 min, The formulation SF3 that containing 7.5% Crosspovidone shows, maximum amount of the drug release (95.62 %) in 20 min, The formulation SF4 that containing 2.5 % SSG shows, maximum amount of the drug release (96.42%) in 40min. The formulation SF5 that containing 5 % SSG shows, maximum amount of the drug release (98.28 %) in 30min The formulation SF6 that containing 7.5 % SSG, maximum amount of the drug release (96.42 %) in 20min, The formulation SF7 that containing 2.5 % CCS, maximum amount of the drug release (96.42 %) in 40min The formulation SF8 that containing 5 % CCS, maximum amount of the drug release (96.98 %) in 30min The formulation SF9 that containing 7.5 % SSG, maximum amount of drug release(97.65 %) in 20min.

From the above release studies with increase in superdisintegrants concentration the release time decreases and formulation containing 7.5 % SSG shows highest release time 20min. The reports of the release were shown in tables 35 to 38 and the graphs were shown in fig 26 to 37.

Table 15: % drug release data of solid dispersion formulations

S.NO	TIME (MIN)	Formulation code								
		SF1	SF2	SF3	SF4	SF5	SF6	SF7	SF8	SF9
1	5	10.14	18.16	26.28	18.16	28.16	50.6	12.16	24.16	39.62
2	10	20.36	35.42	62.36	29.48	40.12	78.36	25.48	38.12	71.32
3	20	40.28	73.24	94.52	52.22	72.24	98.28	47.64	72.24	97.65
4	30	47.92	95.88	-	80.88	96.98	-	80.88	96.98	-
5	40	70.28	-	-	96.42	-	-	96.42	-	-
6	50	93.88	-	-	-	-	-	-	-	-
7	60	-	-	-	-	-	-	-	-	-

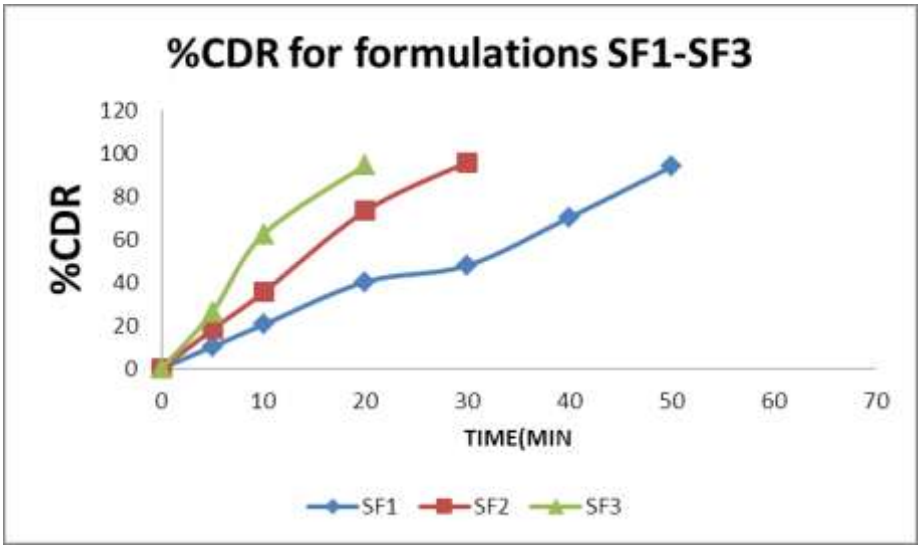

Fig 9: % Release graph of sertraline hcl with Crospovidone (SF1-SF3).

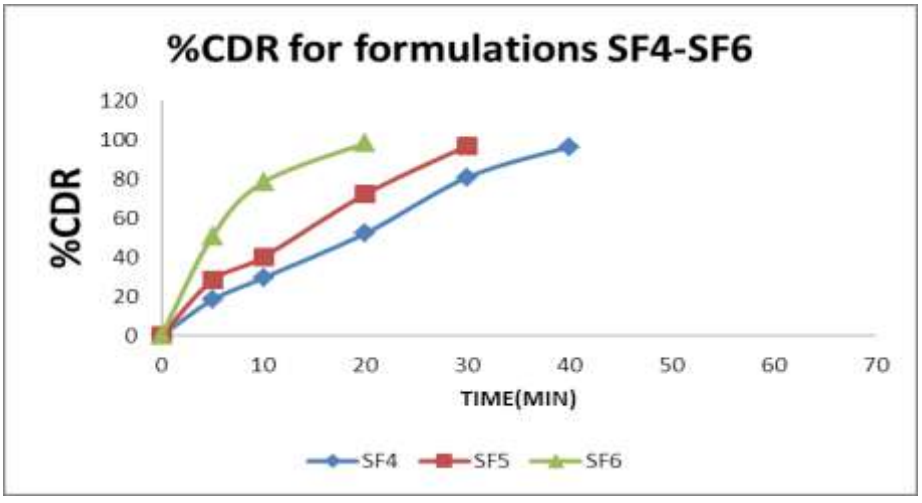

Fig 10: % Release graph of sertraline hcl with sodium starch glycolate (SF4-SF6).

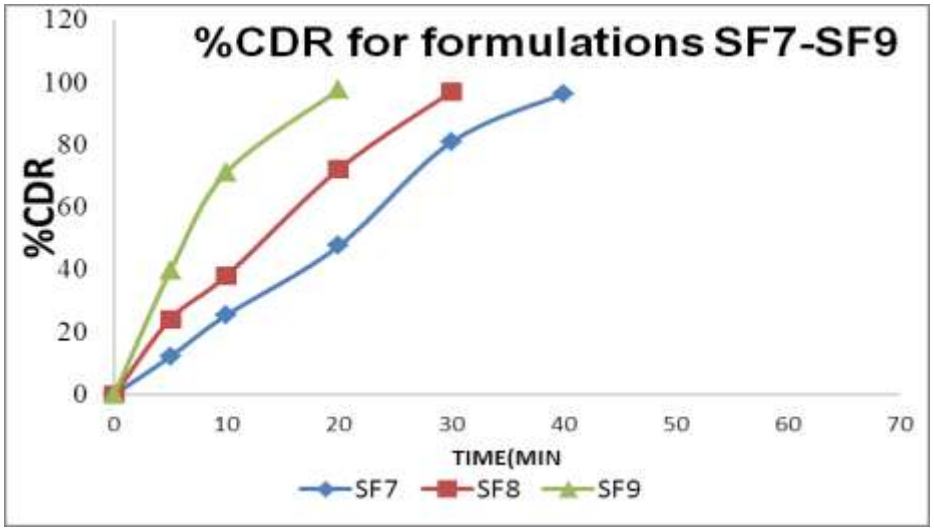

Fig 11: % Release graph of sertraline hcl with cross carmellose sodium(SF7-SF9).

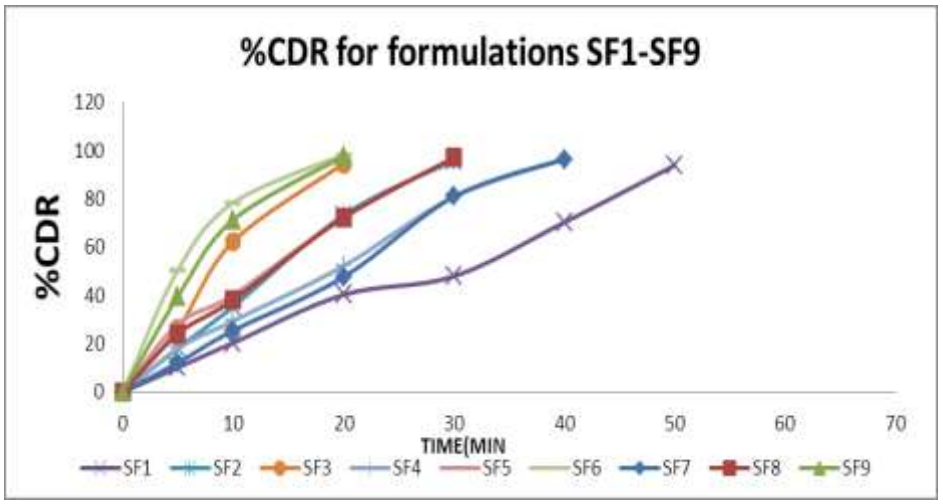

Fig12: % Release graph of sertraline hcl with solid disperssion (SF1-SF9).

%DRUG RELEASE STUDIES

Table 16 :% Drug release data of liquid solid compacts of Sertraline hcl (PEG400)

S.NO	TIME (MIN)	Formulation code									
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	5	9.82	16.14	26.16	33.28	10.36	30.18	32.26	18.16	28.16	50.6
2	10	18.26	20.36	35.42	62.36	18.24	40.04	45.68	25.48	36.12	74.32
3	20	29.32	40.28	73.24	95.62	42.42	80.52	97.28	47.64	72.24	99.12
4	30	40.56	47.92	95.88	-	62.52	97.68	-	80.88	96.98	-
5	40	61.76	70.28	-	-	74.12	-	-	96.42	-	-
6	50	81.76	93.88	-	-	96.64	-	-	-	-	-
7	60	97.24	-	-	-	-	-	-	-	-	-

Table 17: % Drug release data of liquid solid compacts of Sertraline hcl (Tween 80)

S.NO	TIME (MIN)	Formulation code									
		F11	F12	F13	F14	F15	F16	F17	F18	F19	F20
1	5	13.21	20.1.8	29.1	50.5	17.25	34.26	54.6	19.25	35.23	87.8
2	10	26.38	47.32	75.23.	96.9	55.76	59.4	98.22	39.6	77.01	99.76
3	20	35.12	74.16	96.2		77.6	96.86		77.5	99.6	
4	30	70.3	95.6			95.82	-	-	98.56	-	-
5	40	95.1		-	-		-	-	-	-	-
6	50		-	-	-	-	-	-	-	-	-
7	60		-	-	-	-	-	-	-	-	-

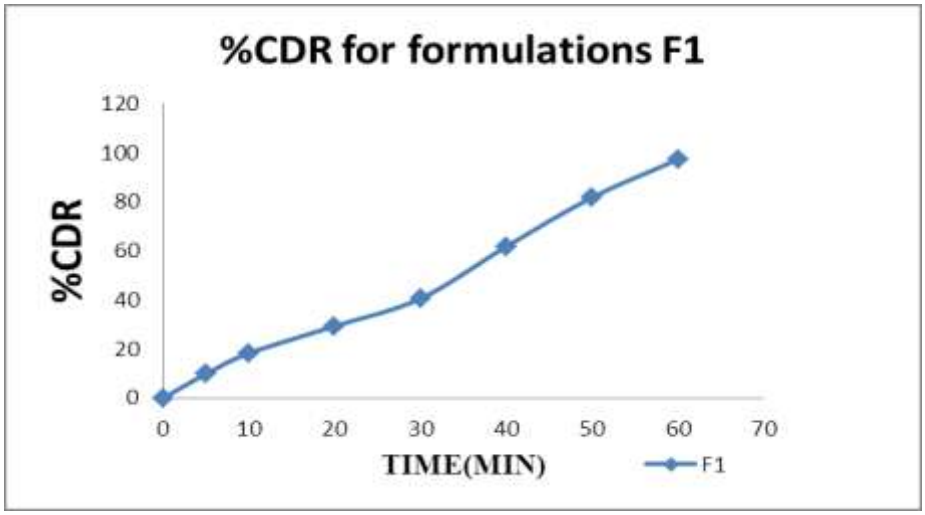

Fig 13: % Release graph of sertraline hcl without super disintegrant (F1).

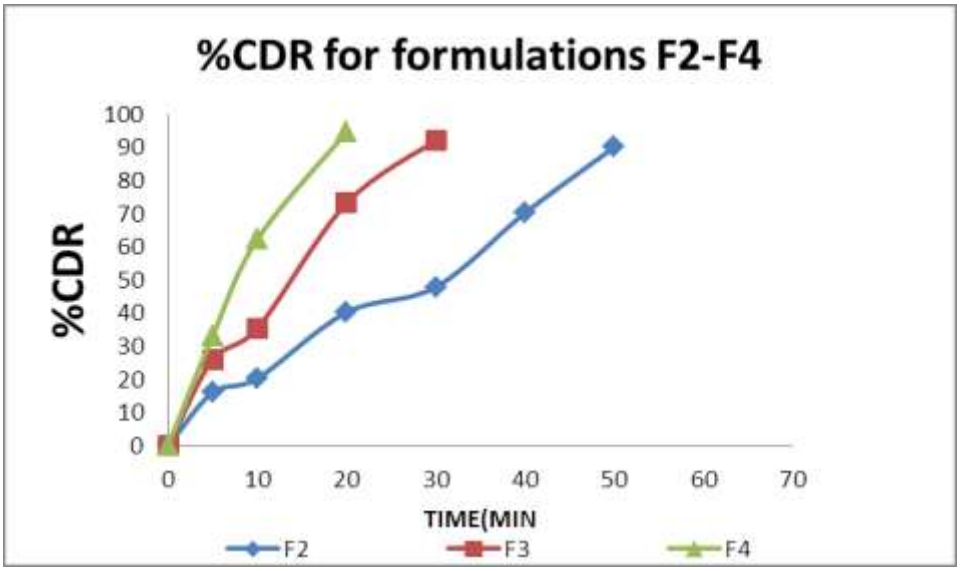

Fig 14: % Release graph of sertraline hcl with Crospovidone (F2-F4).

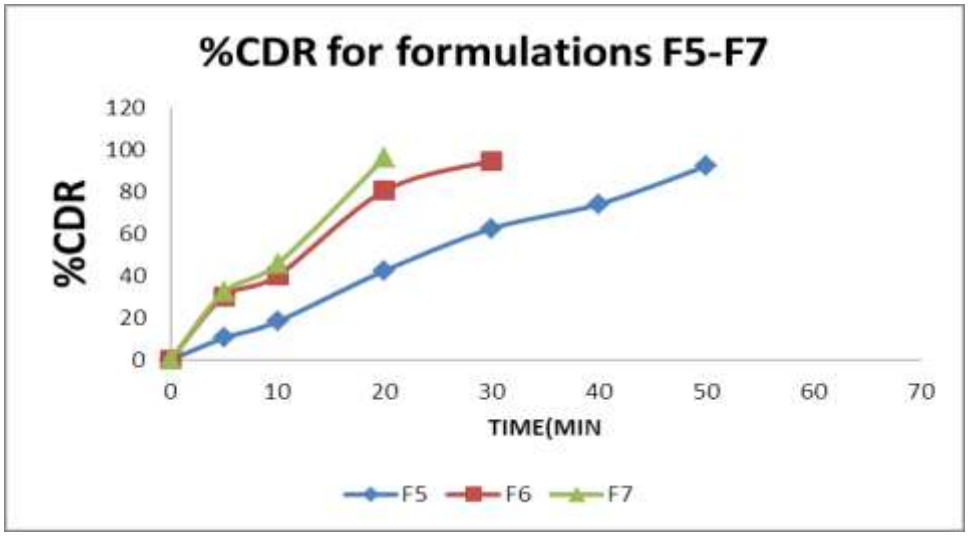

Fig 15: % Release graph of sertraline hcl with Croscarmellose sodium (F5-F7).

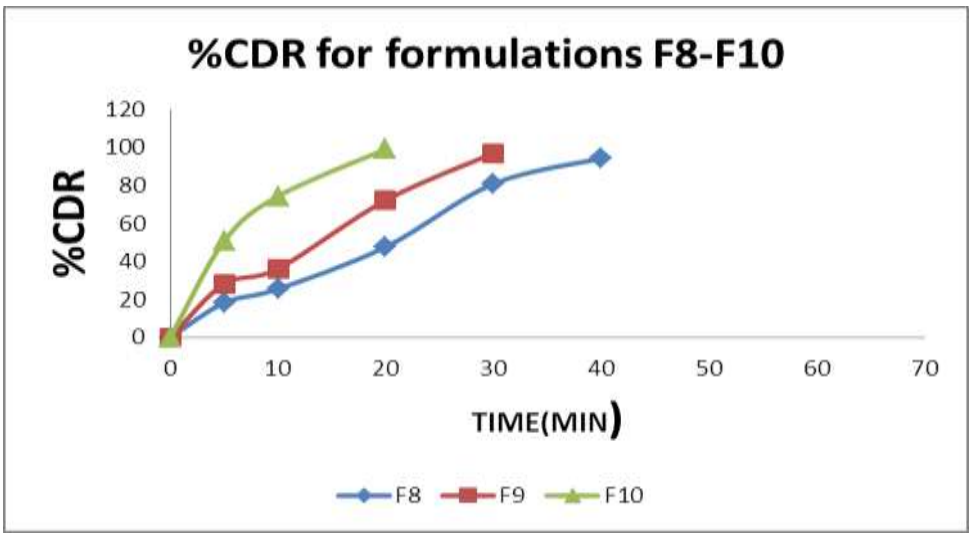

Fig 16: % Release graph of sertraline hcl with Sodium Starch Glycolate (F8-F10).

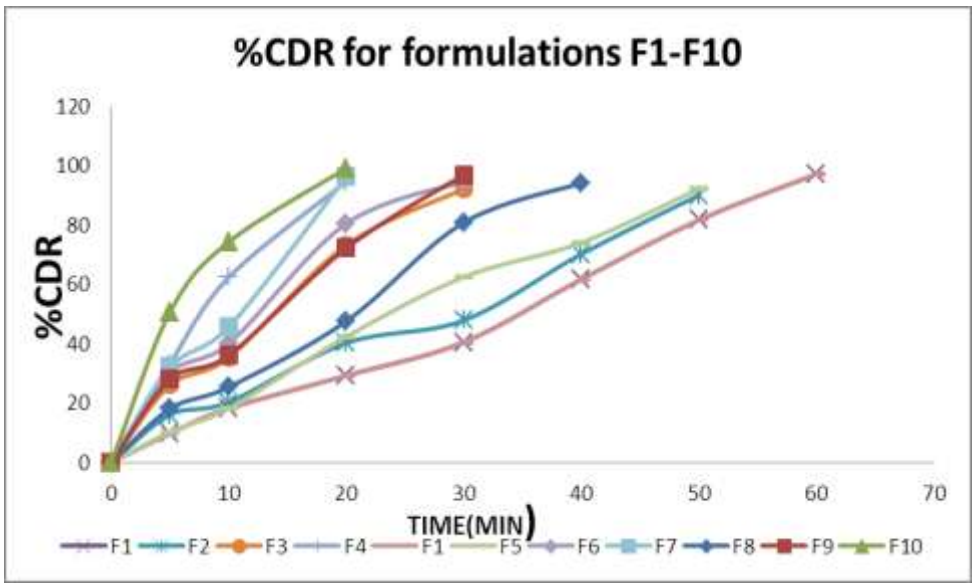

Fig 17: % Release graph of sertraline hcl with PEG 400 as solvent (F1-F10).

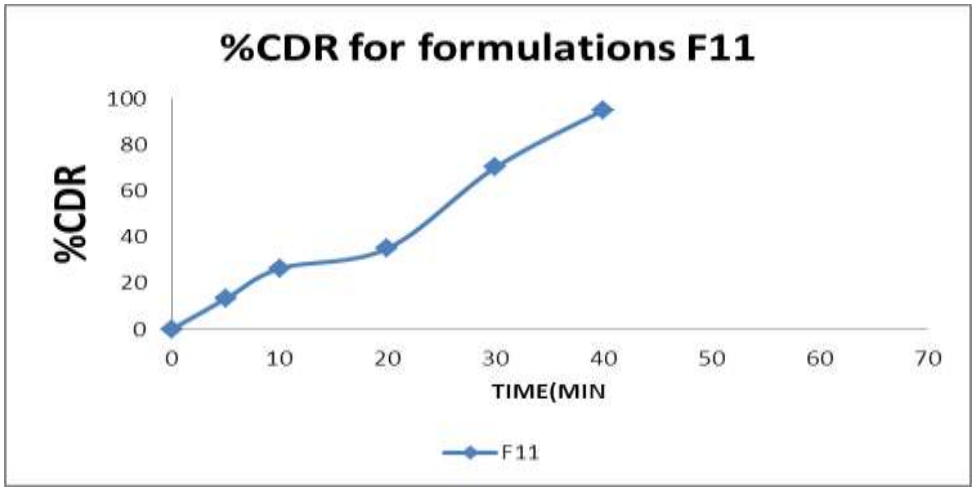

Fig 18: % Release graph of sertraline hcl without Super Disintegrants (F11).

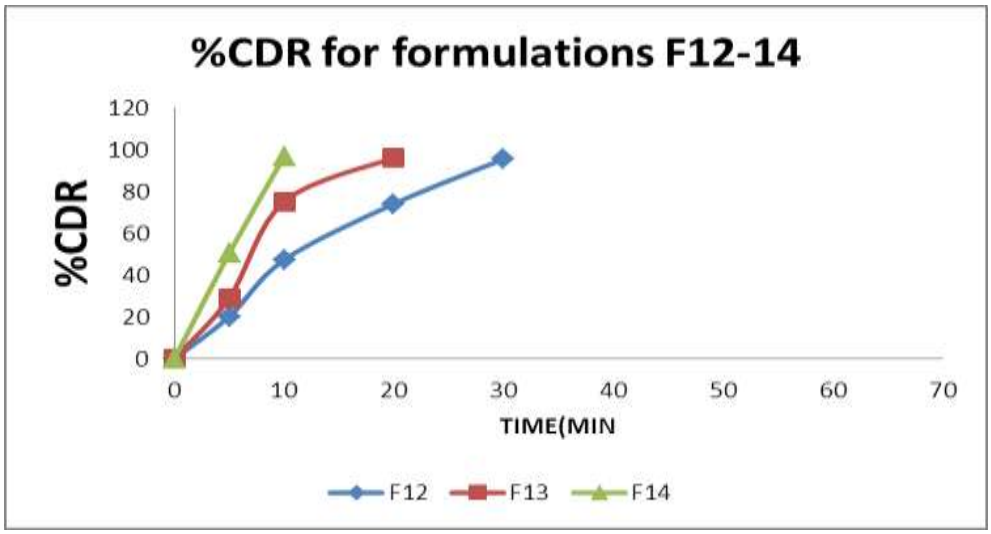

Fig 19: % Release graph of sertraline hcl with Cross povidone (F12-F14)

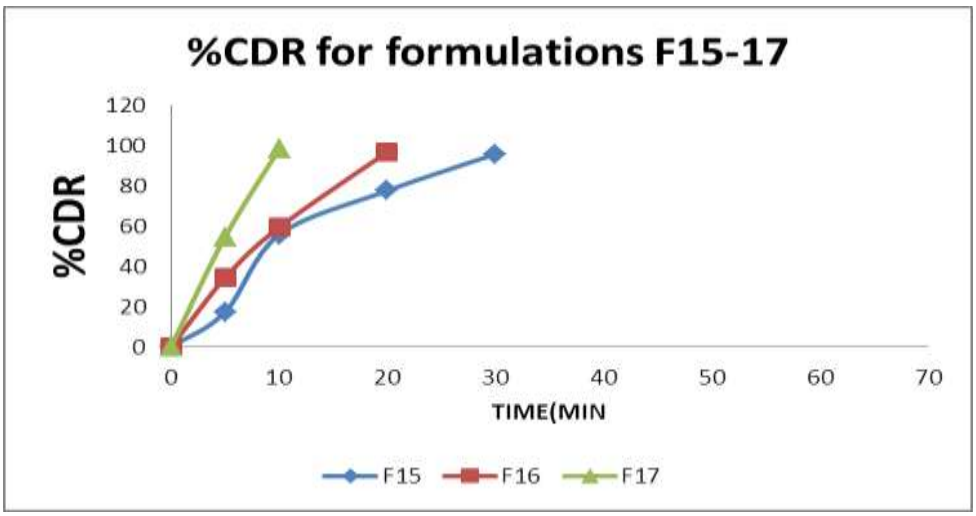

Fig 20: % Release graph of sertraline hcl with Croscarmellose sodium (F15-F17).

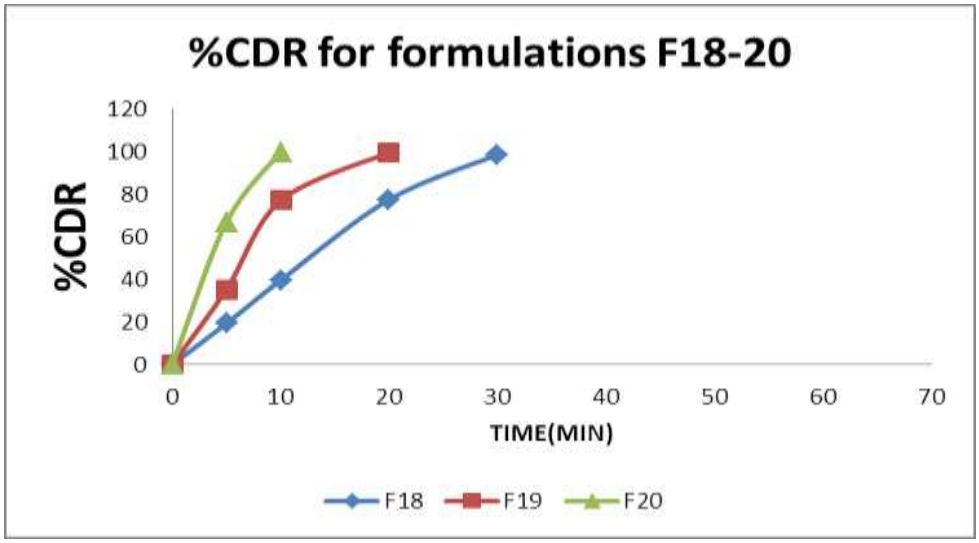

Fig 21: % Release graph of sertraline hcl with Sodium Starch Glycolate (F18-F20).

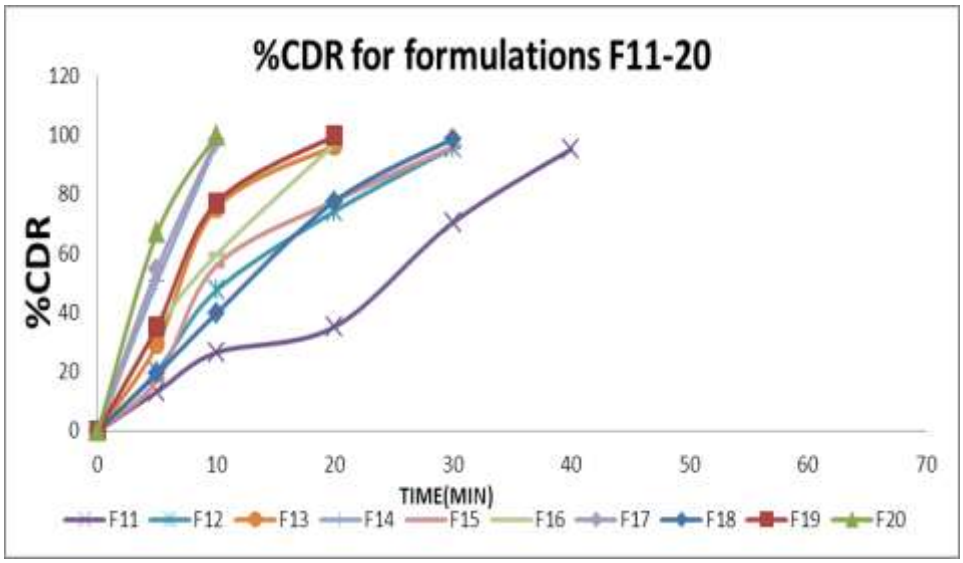

Fig 22: % Release graph of sertraline hcl with Tween80 as solvent (F11-F20).

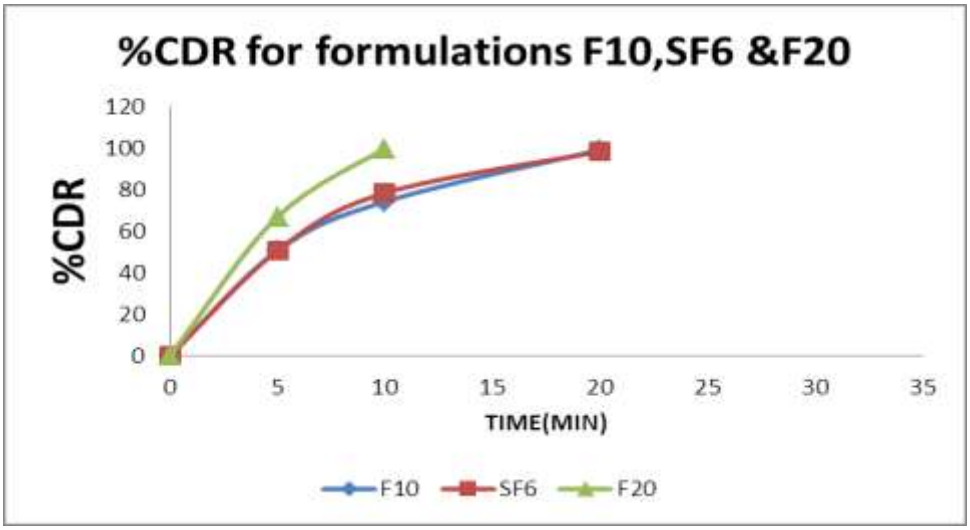

Fig.23: % Release graph of sertraline hcl with Best formulations (F10, SF6, F20).

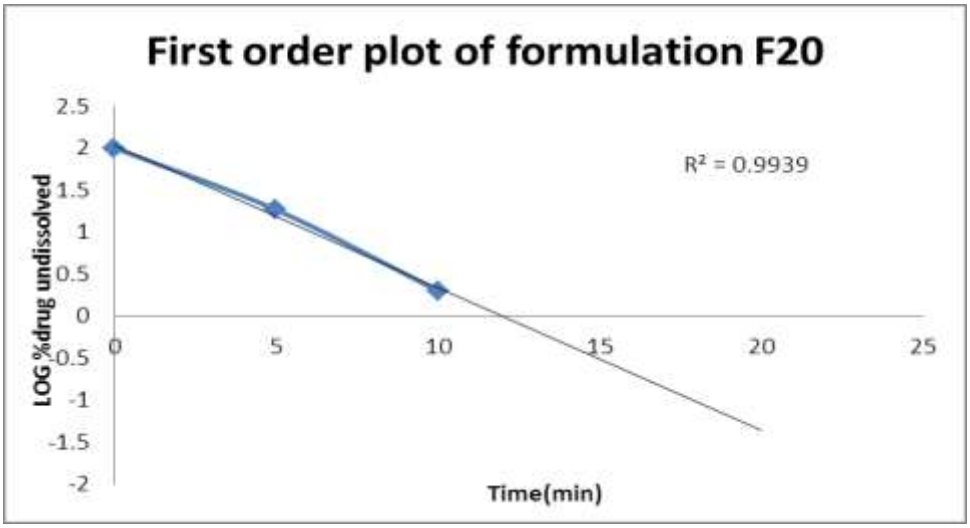

Fig.24: % Release graph of sertraline hcl with Best formulations For first order

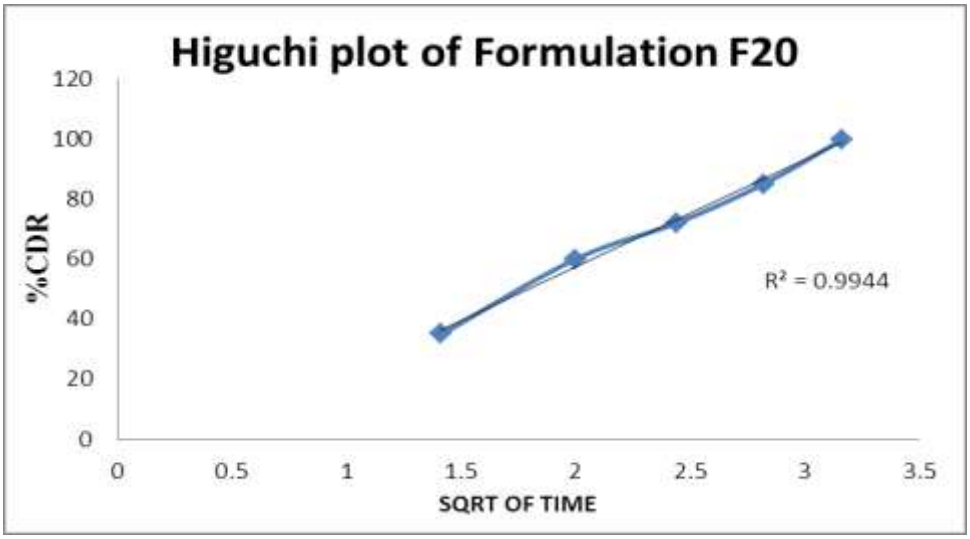

Fig.25: % Release graph of sertraline hcl with Best formulations For Higuchi

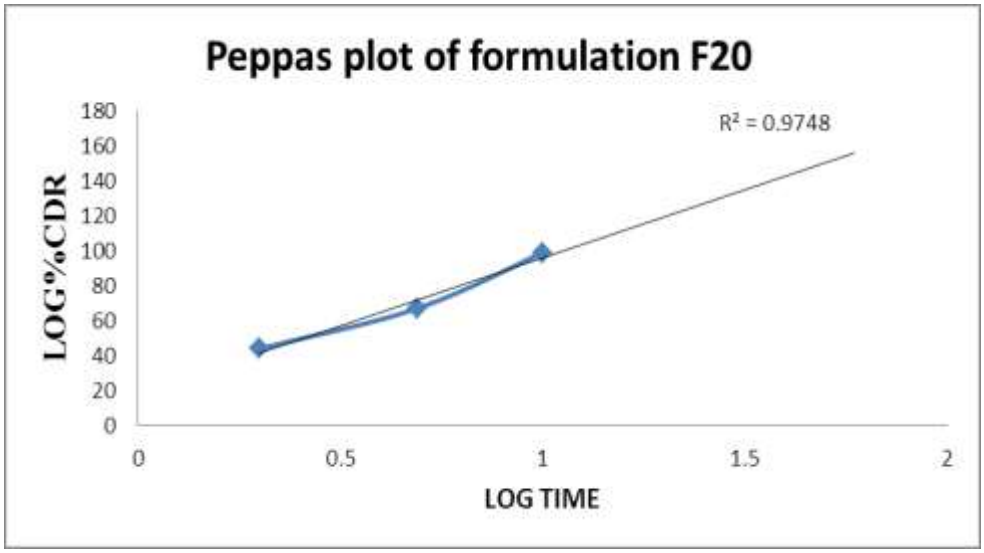

Fig.26: PEPPA'S plot for Sertraline Hcl for formulation F20

Table 18: Kinetics of drug release for best formulation

Formulation code	Correlation co-efficient (R^2)				k	n
	Zero order	First order	Higuchi	Peppa's		
F20	0.865	0.985	0.962	0.897	0.052	0.765

DISCUSSION

From above all the studies, enhancement of solubility was done by using liquid solid compacts and solid dispersions. Drug release was increased with an increase in concentration of superdisintegrants Crospovidone, Croscarmellose and SSG used in this investigation. Among These three different formulations it was found to be liquid solid compacts with Tween 80 as non volatile solvent shows best release of Sertraline hcl. It shows 99.77% drug release with in 10min. The release exponent 'n' for optimized formulation F20 was found to be 0.765 ($0.5<n<1$) that indicate a coupling of diffusion and erosion, so called as anomalous diffusion.

Effect of solid dispersions on solubility enhancement of Sertraline hcl shows satisfactory results, but not up to the mark. Due to significantly increased wetting properties and surface area of the drug particles liquid solid formulations significantly improved drug dissolution compared to solid dispersion formulations and, consequently, improved oral bioavailability.

SUMMARY & CONCLUSION

Sertraline hcl was serotonin reuptake inhibitor (SSRI) used to treat depression, obsessive-compulsive disorder, panic disorder, and post traumatic stress disorder, which is highly permeable drug and is having poor solubility limitation thus having poor bioavailability (46%). So it was logically decided to enhance its solubility and design fast dissolving tablets by different solubility enhancement techniques such as liquid solid compacts and solid dispersions. Among all these formulations, after comparing the solubility and dissolution profile it was found F20 give desired dissolution profile of Sertraline hcl more than 98% release in 10 min. Kinetics of in vitro drug release of optimized formulation F20 found to follow Peppa's kinetic model having highest R^2 value with drug release mechanism as anomalous diffusion coupled with erosion. The formulations were found to possess excellent flow characteristics as well as satisfactory compressibility with desired dissolution profiles. Improved drug solubility and dissolutions could be achieved by formulating Sertraline hcl as liquid solid compact with the superdisintegrant SSG. Finally it was concluded that liquid solid compacts is an promising technology enhance the solubility, dissolution and subsequent

bioavailability of Sertraline Hcl compared with that of solid dispersions of Sertraline Hcl and the solubility enhancement was achieved by increasing the surface area and wetting properties by liquid solid compact technique.

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