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Research Article

FORMULATION AND EVALUATION OF FAST DISINTEGRATING TABLETS OF SERTRALINE HCL BY USING NATURAL SUPER DISINTE-GRANTS

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Abstract

The speed of onset of action of antidepressant is clinically important for several reasons. Objective of this research was to formulate fast disintegrating tablets of sertraline hydrochloride by using natural superdisintegrants so that it will minimize time of onset of action and also become economic. Direct compression method is use to prepare fast disintegrating tablets. Paper describes impact of different concentration of natural superdisintegrants like gelatinized starch, treated agar on various parameters of fast disintegrating tablets of sertraline Hcl. All formulation were evaluated for various parameters such as hardness, friability, drug content, wetting time, dissolution study, disintegration test. An optimized formulation (GS-6) was found to have good hardness of 3.10 kg/cm^2, disintegration time of 22.37 second and dissolution of 95 % in 12 min.The conclusion is results obtained clearly indicate that optimized batch GS-6 having remarkable increase in disintegrating and dissolution time for the treatment of depression.

Key Words: Sertraline Hcl, FDT, Direct compression techniques, Superdisintegrants, FTIR

Introduction:

The concept of fast disintegrating drug delivery system emerged from the desire to provide patient with conventional means of taking their medication. Because of physiological changes associated with especially elderly and pediatric are quite unable to swallow (Dysphagia); rather, this is commonly problem of all age groups patients. Solid dosage forms that can be disintegrated, dissolved or suspended by saliva in mouth resulting in easy swallowing can provide significant benefits to the pediatric and geriatric population, as well as other peoples who prefer the convenience of easily swallowable dosage form. This tablet disintegrates instantaneously when placed on tongue, releasing the drug that dissolves or disperses in the saliva. Fast disintegrating tablets are upon introduction into mouth dissolve or disintegrate in in absence of water in fraction of seconds. Fast disintegrating tablets are solid dosage form which does not need to chew. Fast disintegrating tablets are placed in mouth, allowed to disperse in saliva.[1]

As the oral mucosa is highly vascularized, drugs that are absorbed through the oral mucosa can directly enter into systemic circulation, bypassing the GIT and hence first pass metabolism in liver. These results to rapid onset of action & greater bioavailability of drug than hose observed from conventional tablets. There are ease of administration to patient who can't swallow such as pediatric, geria-

tric & psychiatric, bedridden patients. There is no need of water to swallow these tablets which is highly conventional feature for patient during travelling. [2]

The FDT is also known as fast melting, fast dispersing, rapid dissolving, rapid melt and quick disintegrating tablets. All FDTs approved by Food and Drug Administration are classified as orally disintegrating tablets. Recently, the European Pharmacopoeia adopted the term orodispersible tablets for tablets that disperse or disintegrate in less than 3 Min in the mouth before swallowing. Such tablet disintegrates into smaller granules or melts in mouth from solid to gel like structure, allowing easy swallowing by patients. The disintegration time for good FDT varies from several seconds to about a minute. [3]

MATERIALS AND METHOD

Materials

Sertraline hydrochloride was obtained as gift sample from Dr. Reddys Lab (Hyderabad).Microcrystalline cellulose, Lactose, Sodium Saccharine, Magnesium Stearate, and Talc were obtained as gift sample from Lobachem Mumbai. All other chemicals& reagents were analytical grade.

Preparation of Fast disintegrating tablets by direct compression method

Fast disintegrating tablets of Sertraline Hcl were prepared by direct compression using natural superdisintegrants like gelatinized starch & treated agar using direct compressionmethod according to the formula given in (Table 1& 2). All ingredients shown in table 1 were co-ground in a pestle and motor and then talc and magnesium stearate were added and mixed for 10 min. The mixed blend of drug-excipient was compressed using a single punch tablet machine to produce tablets of 4mm diameter. The total weight of tablet is kept 125 mg.

Flow properties of powder blend

Prepared natural superdisintegrants and powder blend was evaluated for various parameters like angle of repose, bulk density, tap density, cars index, hausner ratioand result was shown in table no.3.

Evaluation of Fast disintegrating tablets of Sertraline Hcl

Weight uniformity

Twenty tablets were taken & their weight was determined individually &collectively on digital weighing balance. The average weight of one tablet was determined from collective weight.[4]

Table 1: Formulation of sertraline HclFast disintegrating tablets using gelatinized starch (mg)

S. No	Content	GS-1	GS-2	GS-3	GS-4	GS-5	GS-6
1	Sertraline Hcl	25	25	25	25	25	25
2	Gelatinized Starch	02	04	06	08	10	12
3	Microcrystalline cellulose	35	35	35	35	35	35
4	Lactose	49	47	45	43	41	39
5	Sodium saccharine	5	5	5	5	5	5
6	Magnesium stearate	4	4	4	4	4	4
7	Talc	5	5	5	5	5	5
TOTAL		125 mg					

Table 2: Formulation of sertraline HclFast disintegrating tablets using treated agar(mg)

S. No	Content	TA-1	TA-2	TA-3	TA-4	TA-5	TA-6
1	Sertraline Hcl	25	25	25	25	25	25
2	Gelatinized Starch	02	04	06	08	10	12
3	Microcrystalline cellulose	35	35	35	35	35	35
4	Lactose	49	47	45	43	41	39
5	Sodium saccharine	5	5	5	5	5	5
6	Magnesium stearate	4	4	4	4	4	4
7	Talc	5	5	5	5	5	5
TOTAL		125 mg					

Hardness test

The hardness of the tablets was determined using Monsanto Hardness tester. The hardness was measured in terms of Kg/cm^2.[5]

Friability test

The friability of tablets was determined by using Rolex Friabilator.Twenty tablets were initially weighed and transferred into friabilator. The friabilator was operated at 25 RPM for 4 min. tablets were reweighted after removal of fines (Dusted) and percentage of weight loss was calculated. Friability below 1 % was considered acceptable.[6]

Drug content uniformity

Six tablets were weighed and taken in mortar and crushed to make powder. A quantity of powder weighing equivalent to 25 mg of sertraline Hcl was taken in 100 ml volumetric flask. Then 1 ml from this solution was taken and diluted up to 10ml with ethanol and absorbance was measured at 274.5 nm. The amount of sertraline Hcl was estimated by standard calibration curve of drug.

Water absorption Ratio

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured. The wetted tablet was then weighed.

$$\text{Water absorption Ratio [R]} = \frac{Wa - Wb}{Wb} \times 100$$

Where, Wa is weight of tablet after water absorption & Wb is weight of tablet before water absorption.

Wetting time

Tissue paper folded in a six-inch diameter petridish. The tablet was placed on tissue paper near the centre of petridish and 6 ml water was added. The tissue paper wicks the water and tablet begins to water uptake. At the complete wetting of tablet, time recorded as wetting time. [7]

***In vitro* disintegration time**

Tablet was added to 10 ml of 0.1 N Hcl maintained at 37°±2 °C as the immersion liquid. Time required for complete dispersion of tablet was measured.

***In vitro* dissolution studies**

Dissolution rate was studied by using USP type-II apparatus using 900 ml of Phosphate buffer pH 6.8 as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5 °C; aliquot of dissolution medium was withdrawn at every 2 min interval and filtered. The absorbance of filtered solution was measured by UV spectrophotometric method at 273.5 nm and concentration of the drug was determined from standard calibration curve. [8]

Drug polymer interaction studies

FTIR studies: IR spectra for pure drug, formulations Sertraline Hcl, gelatinized starch and Treated agar, and optimized batch were recorded in a Fourier transform infrared (FTIR) spectrophotometer with KBr pellets.[9]

Stability study

The purpose of stability testing is to provide evidence on how quality of drug substance varies with time under influence of variety of environmental factors such as temperature, humidity, light and enables recommended storage condition retest period and shelf lives to be established. Short-term stability (accelerated) studies was carried out by storing the tablets at 40°C±2°C/ 75±5% RH over a 3 month period for selected formulation in an amber colored rubber stoppered bottle. At intervals of every one month, the tablets were visually examined for any physical changes, friability, hardness, *in vitro* disintegration time and *in vitro* dissolution time.[10]

RESULTS AND DISCUSSION

Table 3: Powder evaluation for Sertraline Hcl Formulations & prepared Superdisintegrants

S. No	Batch	Angle of repose (O) *	Bulk density (g/cm³) *	Tap density (g/cm³)*	Cars index %*	Hausner ratio*
1	GS-1	27.15±0.88	0.53±0.12	0.67±0.89	14 ±0.21	1.264±0.06
2	GS-2	28.49±0.83	0.52±0.45	0.65±0.76	13 ±0.69	1.25±0.11
3	GS-3	26.62±0.72	0.55±0.13	0.69±0.14	14 ±0.14	1.254±0.19
4	GS-4	26.12±0.63	0.54±0.81	0.68±0.52	14 ±0.11	1.259±0.17
5	GS-5	27.26±0.93	0.51±0.18	0.64±0.38	13 ±0.15	1.254±0.82
6	GS-6	27.35±0.78	0.50±0.17	0.64±0.16	14 ±0.51	1.28±0.19
7	TA-1	26.32±0.85	0.53±0.55	0.68±0.34	15 ±0.14	1.283±0.07
8	TA-2	26.31±0.47	0.54±0.29	0.69±0.11	15±0.13	1.277±0.79
9	TA-3	28.15±0.17	0.52±0.12	0.66±0.87	14±0.39	1.269±0.14
10	TA-4	28.16±0.12	0.54±0.14	0.68±0.19	14±0.18	1.259±0.12
11	TA-5	28.95±0.39	0.52±0.59	0.66±0.15	14±0.62	1.269±0.69
12	TA-6	26.66±0.14	0.51±0.15	0.66±0.35	15±0.11	1.294±0.12
10	GS	27.15±0.34	0.55±0.38	0.68±0.14	13±0.64	1.236±0.11
11	TA	27.71±0.19	0.50±0.13	0.65±0.19	15±0.09	1.3±0.57

*** mean ± SD, n=3**

Table 4: Post compression parameters for sertraline Hcl formulations

S. No.	Batch	Wt. variation in mg *	Hardness in Kg/cm²*	Friability % *	Average content (%)
1	GS-1	125.04±1.52	3.32±012	0.3184	98.29±0.175
2	GS-2	125.5±1.6	3.29±0.28	0.4803	96.08±0.19
3	GS-3	125.05±0.56	3.4±0.09	0.1592	98.02±0.179
4	GS-4	126.5±0.75	3.45±0.19	0.1587	97.74±0.436
5	GS-5	126.3±0.23	3.46±0.27	0.2377	98.63±0.354
6	GS-6	124±1.4	3.10±0.21	0.1581	99.92±0.154
7	TA-1	125.4±0.95	3.28±0.15	0.4815	95.03±0.265
8	TA-2	126.15±0.32	3.41±0.31	0.4796	97.10±0.241
9	TA-3	125.2±0.45	3.36±0.24	0.4792	98.75±0.154
10	TA-4	125.5±0.78	3.34±0.29	0.48	97.91±0.123
11	TA-5	124.8±1.8	3.4±0.17	0.5608	96.04±0.432
12	TA-6	124.9±1.03	3.23±0.09	0.5604	95.16±0.141

*** mean ± SD, n=3**

Table 5: Physicochemical evaluation of tablets

S. No	Batch	Water absorption ratio*	Wetting Time (sec) *	Disintegration Time (sec) *
1	GS-1	54.12±1.3	55.32±1.24	60.66±2.4
2	GS-2	55.46±1.8	49.19±2.1	54.33±1.5
3	GS-3	57.39±2.16	41.84±3.14	47.66±1.8
4	GS-4	58.89±0.98	37.32±1.65	43±1.96
5	GS-5	60.43±1.65	30.02±1.55	35.33±2.4
6	GS-6	61.19±1.45	18.69±2.15	22.37±1.53
7	TA-1	53.72±1.30	56.02±2.01	64.23±1.19
8	TA-2	54.26±2.35	51.48±1.35	55.13±2.41
9	TA-3	56.68±1.6	48.30±2.03	50.6±2.97
10	TA-4	57.37±2.14	44.01±1.05	49.62±1.92
11	TA-5	59.78±2.31	41.41±1.36	48.36±2.79
11	TA-6	62.14±1.12	38.15±1.65	45.12±2.63

*** mean ± SD, n=3**

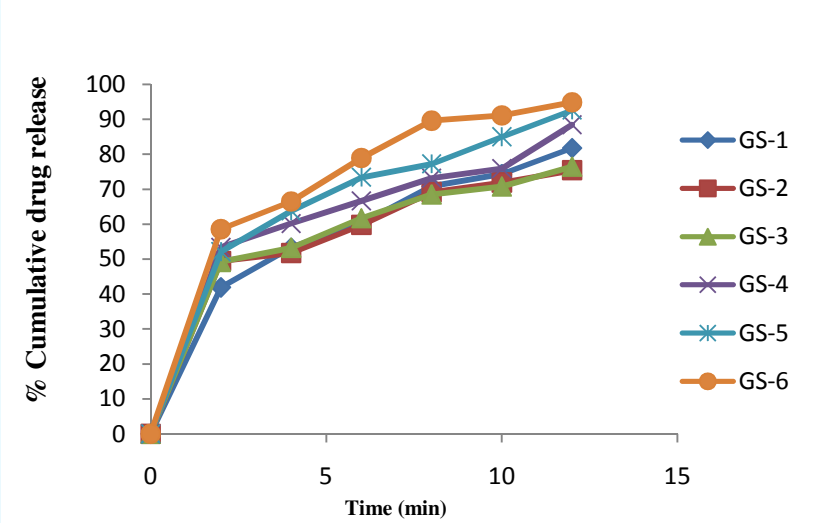

Fig. 1: % cumulative drug release of batch GS-1 to GS-6

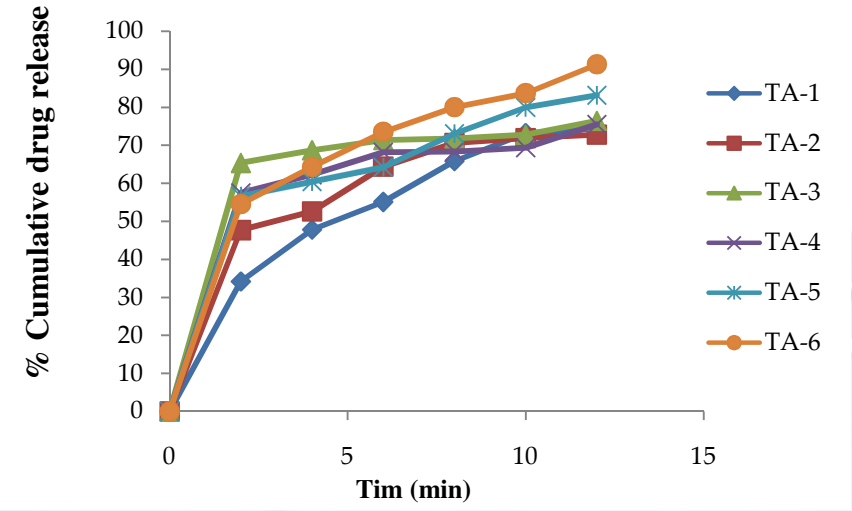

Fig. 2: % cumulative drug release of batch TA-1 to TA-6

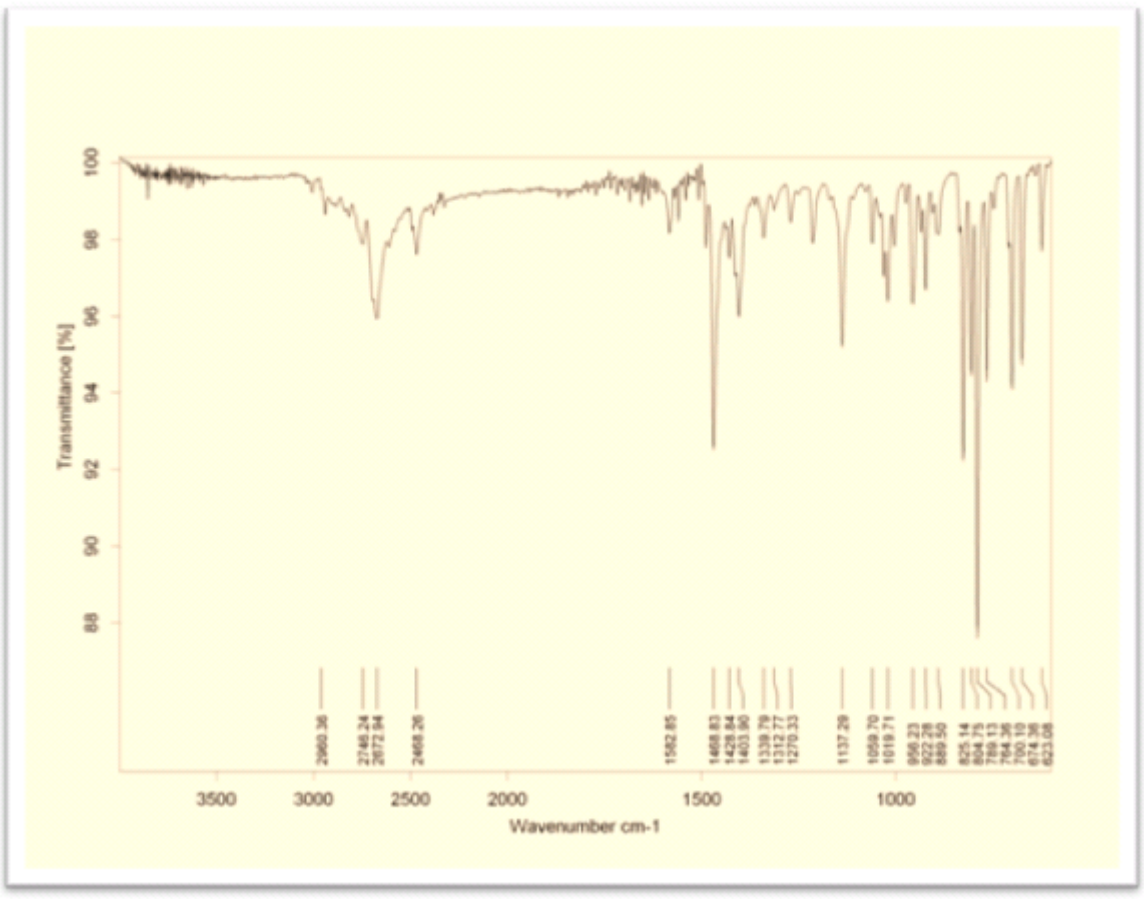

Fig. 3: IR Spectrum of Sertraline Hcl

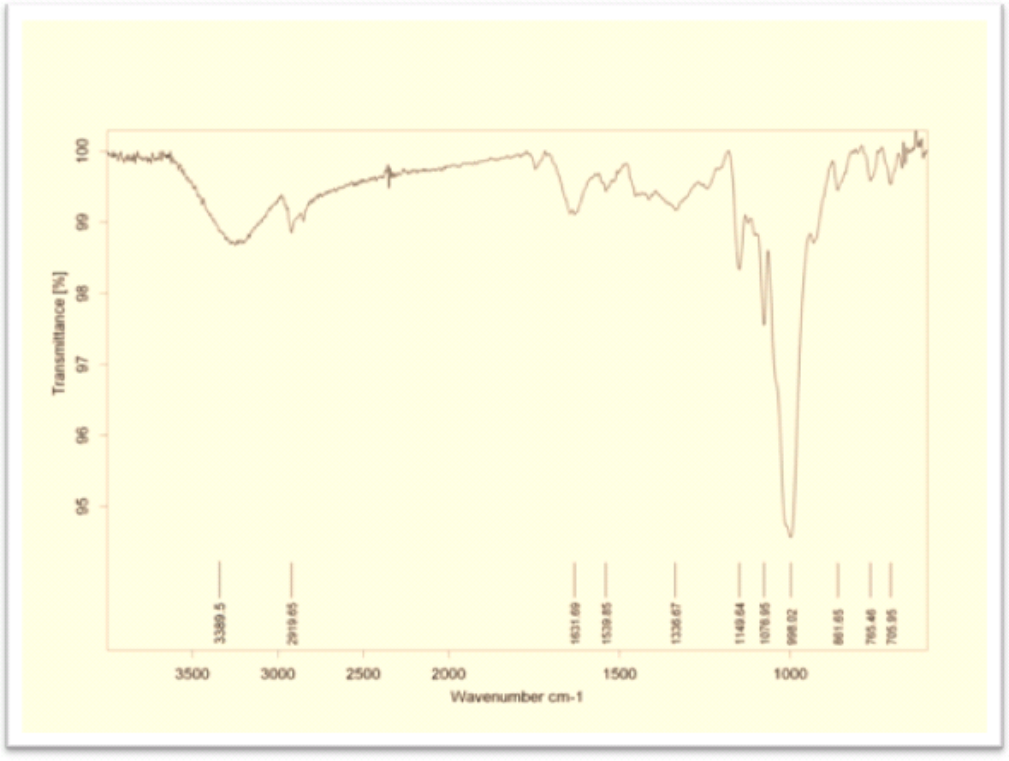

Fig. 4: IR Spectrum of gelatinized starch

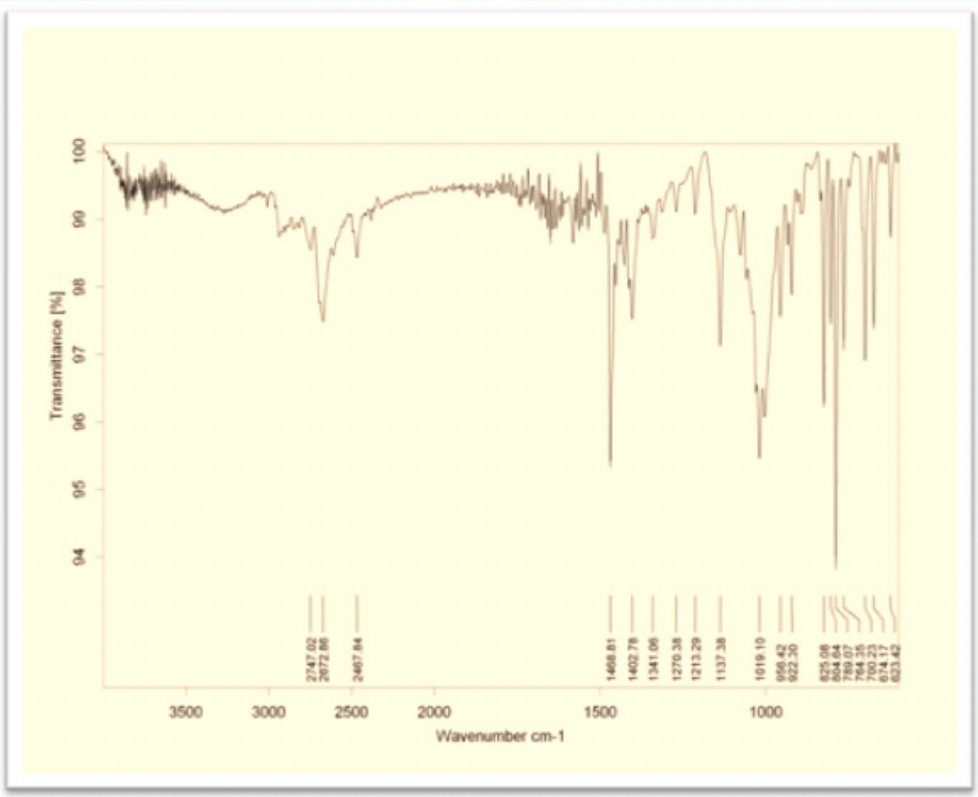

Fig. 5: IR Spectrum of optimized batch (GS-6)

Table 6: IR Spectral interpretation data

S.	Compound	Frequency (cm^{-1})	Type of vibration
1	Sertraline Hcl	3010 (w) 1582 (m),1468 (m) 2960 (m) 789 (s) 3430 (w) 2810 (m) 1428 (w)	Ar-CH- Str. -C=C Str. Aliphatic –CH Str. of CH_3 C-Cl Str. C-NH str. CH Str of Tetrahydro napthaline CH Bending of Tetrahydro napthaline
2	Gelatinized starch	1336(w) 2960(m),2875(m) 3320(w) 998 (s) 1631(m)	-C-O-C- CH Str. of CH_2 OH Str. C-O Str. OH Bending
3	Optimized batch	3020 (w) 1590 (m),1468.81 (s) 2940 (m) 789.07 (m) 3490 (w) 2747.02 (m) 1428 (w) 1341.06(w) 2980 (m), 2895(m) 3340(w) 980 (m) 1645(w)	Ar-CH- Str. -C=C Str. Aliphatic –CH Str. of CH_3 C-Cl Str. C-NH str. CH Str. of Tetrahydro napthaline CH Bending of Tetrahydro napthaline -C-O-C- CH Str. of CH_2 OH Str. C-O Str. OH Bending

Table 7: Stability study data of batch GS-6

Parameter	Initial	After 1 month	After 2 month	After 3 month
% friability	0.1581	0.1550	0.1523	0.1500
Hardness (Kg/cm^2)	3.10±0.21*	3.9±0.25*	3.5±0.36*	3.2±0.85*
Disintegration time(sec)	22.37±1.53*	19±0.22*	18±0.52*	16±0.30*
% drug content	99.92±1.32*	98.20±0.41*	99±0.85*	98.25±0.43*

*** mean ± SD, n=3**

CONCLUSION

Fast disintegrating tablets of Sertraline Hcl were prepared by direct compression method by using gelatinized starch and treated agar as a superdisintegrants in different concentrations. Prepared formulations of both superdisintegrantspassed all pharmacopoeia tests. FTIR study revealed that there was no shift in peaks, indicating there is no interaction between Sertraline Hcl and other excipients.*In-vitro*dissolution and disintegration study shows that GS-6 hasgreater drug release than other batches.Among the 2 superdisintegrants used gelatinized starch shows better dissolution and disintegration result.The stability of Sertraline Hcl tablets has showed that there is no remarkable influence evaluation result. So the GS-6 formulation was found to be best among all other formulation because it has exhibited greater wetting time, hardness, friability, *In-vitro*dissolution and disintegration rate. So Gelatinized Starchwas found to be best among other superdisintegrants used.

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