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Advances in Bioresearch

ORIGINAL ARTICLE

Formulation and Optimization of Fast Disintegrating Tablets of Sertraline Hydrochloride: An Anti-Depressant Drug

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ABSTRACT
The Present study aimed to develop of Fast Disintegration Dosage Form of the Antidepressant drug of Sertraline Hydrochloride has significant impact on patient compliance it causes increase in bioavailability of dosage from rapid onset and so quicker action. The aim of this study is to prepare and optimize Fast Disintegration Tablets of Sertraline Hydrochloride to improve patient compliance, enhance dissolution rate, and required rapid therapeutic action. Sertraline Hydrochloride is a selective serotonin reuptake inhibitor (SSIR) widely prescribed for depression and anxiety disorders. Obsessive-compulsive disorder, panic disorder, post -traumatic stress disorder, Premenstrual dysphoric disorder and general anxiety disorder. However, conventional oral tablets of sertraline hydrochloride exhibit delayed inset of action and reduced bioavailability due to extensive first-pass metabolism. Fast Disintegration Tablets were prepared by direct compression method using various concentration of Crospovidone and sodium starch glycolate as superdisintegrants. Pre-compression parameters including angle of repose, bulk density, Tapped density, Carr's index and Hausner ratio for satisfactory flow characteristics suitable compression. Prepared tablets were evaluated for hardness, thickness, friability, weight variation, drug content, wetting time, water absorption ratio, disintegration time in-vitro dissolution study, MTT Assay showed concentration-dependent cytotoxicity for Sertraline HCL. The formulation exhibited excellent mechanical strength, uniformity, and rapid drug release across batches. The optimized batch of Sertraline Hydrochloride FDT offers a clinically promising dosage from with rapid onset, east to administration and increased the solubility.
Keywords: *Sertraline Hydrochloride, Fast Disintegrating Tablets, Super-disintegrants, Direct Compression Method, FTIR, DSC, Dissolution, Drug Release, MTT Assay.*

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INTRODUCTION

Depression and anxiety disorders are among the most common mental health conditions affecting millions of people worldwide and contribute significantly to reduced quality of life, disability, and social burden [1,2]. According to the World Health Organization, depression is a leading cause of illness globally, affecting people of all age groups, while anxiety disorder frequently occurs along with depression and require long-term pharmacological treatment [3]. Many pediatric, geriatric patients, patients with dysphagia, mentally retarded patients, uncooperative or nauseated have difficulty in swallowing tablets. Swallowing of conventional tablets will be inhibited by conditions such as unavailability of water, this problem can be overcome by formulating rapidly dissolving or fast disintegrating dosage from for oral administration that dissolves rapidly in the saliva and does not require water for swallowing [4,5]. Sertraline Hydrochloride is a selective serotonin reuptake inhibitor (SSRI) commonly used in the treatment of major depressive disorder, anxiety disorder, obsessive-compulsive disorder, and panic disorder [6–8]. Chemically, Sertraline Hydrochloride a naphthylamine derivative, is (1S,4S)-4-(3,4-Dichlorophenyl)-1,2,3,4 tetrahydro-1 naphthyl(methly)amine chloride. This drug possesses good therapeutic efficacy and is widely prescribed due to its safety and tolerability profile. Sertraline Hydrochloride absorption from the gastrointestinal tract is almost complete, but rather slow with a maximum time plasma concentration (Cmax) reaching 8.4 hr after ingestion [9,10]. The reason for may be

contributed to extensive first-pass metabolism in the liver. The fast disintegration of FDTs was using same superdisintegrants, which enhance saliva penetratin and facilitate quick drug release. Recant advances in excipients technology and direct compression techniques have enabled the development of mechanically stable tablets with rapid disintegration properties.

The present study aims to formulate and optimize fast disintegrating tablets of Sertraline Hydrochloride tablet which will improve both therapeutic outcomes and patient medicine adherence. The primary goal development through the direct compression method and evaluation of compression stage for dissolution rate analysis and drug release. Therefore, the aim of our work is to prepare Sertraline Hydrochloride of Fast Disintegration Tablets.

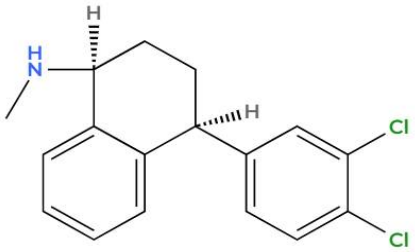


Figure 1: Structure Sertraline Hydrochloride

MATERIAL AND METHODS

Materials

Sertraline Hydrochloride is from Yellow Chem Products Pvt, Ltd., Mumbai. Crospovidone obtained was from Rajesh Chemicals, Mumbai Pvt, Ltd., Sodium Starch Glycolate was obtained from Corel Pharma Chem., Microcrystalline Cellulose was obtained from Modern Industries Pvt, Ltd., Aspartame was obtained from Yellow Chem Products Pvt, Ltd., Mannitol is obtained from Dolphine Chemicals, Mumbai. Magnesium Stearate was obtained from J. P Fine Chemicals Pvt. Ltd., Talc was obtained from Loba Chemie, Palghar., All other chemicals and studied were of analytical or HPLC AND NMR grade.

Equipment uses

The digital weigh balance from Shimadzu, Japan; the fluidised bed dryer and double cone blender from Cad Mach, Ahmadabad, Gujarat; the rapid mixture granulator from Remi, Mumbai; the single rotary compression machine from Lab Press, eight stations; the disintegration tester from Electro Lab, Chennai; the dissolution apparatus from Electro Lab, TDT 08L; the UV-VIS Spectrophotometer from Jasco, v-630; the hot air oven from Tempo Instruments, Mumbai; and glass wares from Borosil were all purchased commercially.

Method of Preparation of fast disintegrating tablets by direct Compression Method

Sertraline Hydrochloride Fast Disintegrating Tablets (FDTs) were made using directly compressible excipients and the Direct Compression Method. To guarantee a consistent distribution of particle sizes, each ingredient was precisely weighed and run through sieve number 60. Using the geometric dilution technique, the medication was combined with mannitol and microcrystalline cellulose. Superdisintegrant like Sodium Starch Glycolate and Crospovidone were added and evenly blended. Finally, Talc and Magnesium Stearate were added as glidants and lubricants, respectively. Weight 400 mg prepared powder put into the die cavity of compression machine, then compressed with 6 mm concave punches. A rotary tablet compression machine was used to compress the prepared powder blend into tablets after it had been assessed for pre-compression parameters. The hardness, friability, weight fluctuation, wetting time, disintegration time, homogeneity of drug content, and in vitro dissolving study of the compressed tablets were further assessed.

Formulation of Fast Disintegrating Tablets of Sertraline Hydrochloride

Table 1: Composition of RF1-RF9 Runs with different composition and Different Concentration of Super-disintegrants.

Sr. No.	Ingredient	RF1	RF2	RF3	RF4	RF5	RF6	RF7	RF8	RF9
1	Sertraline Hydrochloride (mg)	50	50	50	50	50	50	50	50	50
2	Crospovidone	8	8	8	14	14	14	20	20	20
3	Sodium Starch Glycolate	8	20	32	8	20	32	8	20	32
4	Mannitol	206	194	182	200	188	176	194	182	170
5	Microcrystalline Cellulose	80	80	80	80	80	80	80	80	80
6	Magnesium Stearate	4	4	4	4	4	4	4	4	4
7	Talc	8	8	8	8	8	8	8	8	8
8	Aspartame	20	20	20	20	20	20	20	20	20
9	Peppermint	16	16	16	16	16	16	16	16	16

Drug-Excipients Compatibility

Drug-Excipients Compatibility Study, to determine potential physical or chemical interactions between the active pharmaceutical ingredient (API) and excipients used in the formulation of fast disintegrating tablets (FDTs), a drug–excipient compatibility research is a crucial pre-formulation experiment was performed using Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimeter (DSC).

FTIR Analysis

FTIR analysis was performed to evaluate the compatibility between Sertraline Hydrochloride and selected excipients i. e Crospovidone and Sodium Starch Glycolate used in fast disintegrating tablets. The characteristic peaks of the drug were retained in the physical mixtures without significant shifting or disappearance, indicating absence of chemical interaction and confirming compatibility of formulation components [11–13].

DSC Analysis

Differential Scanning Calorimetry (DSC) analysis was carried out to investigate the thermal compatibility of Sertraline Hydrochloride with selected excipients used in fast disintegrating tablets. The characteristic endothermic peak of the drug 250^0C, corresponding to the melting point of the sample and melting point endotherm indicates a high degree of crystallinity and purity of the material and interactions with polymer such as Crospovidone, Sodium Starch Glycolate was retained in the physical mixtures with minor variations, indicating absence of significant drug–excipient interaction and confirming formulation stability [14–16].

Pre- Compression Evaluation of Powder

Angle of Repose

Angle of repose such as the free-standing cone and fixed funnel can be used to calculate the angle of repose. In the fixed funnel method, graph paper is placed on a level, horizontal surface, and a funnel is fastened with its tip at a predetermined height (H). Carefully pour powder or grains through the funnel until the top of the conical pile just touches the tip of the funnel. Tan θ = H/R, where H is the height and R is the radius of the powder cone, is the formula for calculating the angle of repose (θ) if R is the radius of the base of the conical pile. By measuring the height and radius of the created powder pile, you can determine the angle of repose using this relationship [17,18].

Bulk Density

Bulk density of the powder blend was determined by transferring a weighed quantity of powder into a graduated measuring cylinder and measuring the untapped volume occupied by the powder. Bulk density was calculated to evaluate the packing ability and flow characteristics of the blend used for preparation of Sertraline Hydrochloride fast disintegrating tablets [19].

Bulk Density = Weight of the Powder / Volume of the Powder

Tapped Density

A weighted amount of powder blend was transferred into a measuring cylinder, and then the measuring cylinder was mechanically tapped until a consistent volume was achieved in order to calculate the tapped density. In order to assess the blend's compressibility and packing qualities for making Sertraline Hydrochloride fast-disintegrating tablets, the tapped volume was measured [19].

Tapped Density = Weight of the Powder / Tapped Volume of the Powder

Compressibility Index

Compressibility index was determined from bulk density and tapped density to evaluate the flowability and compressibility characteristics of the powder blend used for preparation of Sertraline Hydrochloride

fast disintegrating tablets. Lower values of Carr's index indicate better flow properties of the powder blend suitable for direct compression [20].

% Compressibility = (Tapped density - Bulk density/ Tapped Density) x 100

Hausner Ratio

Hausner's ratio was determined using bulk density and tapped density to assess the flow property of the powder blend used in the preparation of Sertraline Hydrochloride fast disintegrating tablets. Powder blends floe property is crucial for Sertraline Hydrochloride Tablets. A lower Hausner's ratio indicates better flowability and compressibility of the powder blend suitable for direct compression.

Hausner Ratio = Tapped Density / Bulk Density

Post Compression Evaluation of Fast Disintegrating Tablets

Weight Variation

Twenty Tablets were selected randomly and individually weighted using a Digital Electronic Balance. The average weight was calculated according to the limits of IP.

Tablet Thickness

Tablets thickness was measured using a vernier calliper at different points to ensure uniformity in tablet size and appearance.

Tablet Hardness

A Monsanto hardness tester was used to measure tablet hardness in order to assess the tablets mechanical strength.

Friability Test

The "Roche Friabilator" was used to assess the friability of tablets. The percentage (%) is used to express it. Ten pills were put into a friabilator after being first weighed (W initial). For four minutes, the friabilator ran at 25 rpm. Once more, the tablets were weighed (W final). Tablet friability of less than 1% is regarded as acceptable.

% Friability: (Initial Weight - Final Weight / Initial Weight) x 100

Drug Contant

Three tablets were taken randomly and individual tablet were crushed, an amount of the powder equivalent to 50 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).

Wetting Time

The tablet was placed on a twice folded of tissue paper or whatmann filter paper in a petri dish containing 6 ml of distilled water and allowed to tablet complete wet. The time required for the tablet to completely wet was measured.

Water Absorption Ratio

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

Water absorption ratio: Wa – Wb / Wb x 100

Dis-integration Test

The Disintegration time of tablets was determined by using a USP Disintegration Apparatus. Tablets were placed in each assembly tubes. The assembly was dipped in a vessel containing 900ml phosphate buffer pH 6.8 at 37^0C. The time required for complete disintegration of tablets was recorded.

***In-vitro* Dissolution Study**

Dissolution study was carried out using USP Dissolution Apparatus Type 2 set with a paddle speed of 50 rpm [21,22]. Dissolution media using 900 ml of phosphate buffer pH 6.8 maintained at 37^0C. The sample was withdrawn at the intervals of 5,10,15,20,25,30,35,40,45 min according to preprogrammed manner. A sample 5 ml of the solution was withdrawn from the dissolution apparatus at specific time intervals, and the sample were replaced with fresh dissolution medium. This samples were filtered through Whatman filter paper. The filtrate was analyzed by UV- Visible Spectrophotometer at 273 nm.

Cell Cyto-toxicity Study

SH-SY-5Y cells were maintained in modified eagle medium (MEM) supplemented with NEAA and fetal bovine serum under standard culture conditions of 37^0C and 5%CO_2. The cells were seeded into 96-wll plates and incubated for 24 hours. After incubation, different concentrations of the test sample were added to the wells, while untreated cells were kept as control. The plates were again incubated for 24 hours. After treatment, cell morphology was observed under a microscope. Then, MTT reagent was added to each well and incubated for 4 hours for formation of purple formazan crystals by living cells. After that, solubilization solution was added to dissolve the crystals. The absorbance was measured at 570 nm using

a microplate reader. The percentage cell viability and IC50 value were calculated from the obtained absorbance values.

Optimization of Fast Disintegration Tablet of Sertraline Hydrochloride

The optimization of Fast Disintegration Tablet formulation of sertraline hydrochloride 50 mg was done by using design expert software. A central Composite Design (CCD) using Design-Expert software (Version 13, Stat-Ease Inc., USA) was employed to optimize Sertraline Hydrochloride Fast Disintegration Tablets. Crospovidone (X_1) and Sodium Starch Glycolate (X_2) were selected as independent variables, while disintegration time (Y_1) and Drug Release (Y_2) were considered as dependent responses. The relationship between variables and responses was evaluated using polynomial regression analysis.

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2$$

Table 2: Levels of Independent Variables

Sr. No.	Independent Variables	Low level (-1)	High level (+1)
1	Crospovidone	2	5
2	Sodium Starch Glycolate	2	8

Drug Release Kinetic Study

Drug Release kinetic study shoe different kinetic model i.e Zero order, Hixson order, Higuchi model and Korsmeyer-Peppas model were used for in-vitro release study. The interpretation was performed and reported which is based on the values of the regression co-efficient were used to determine the best-fit model [23,24].

RESULTS AND DISCUSSION

FTIR Analysis

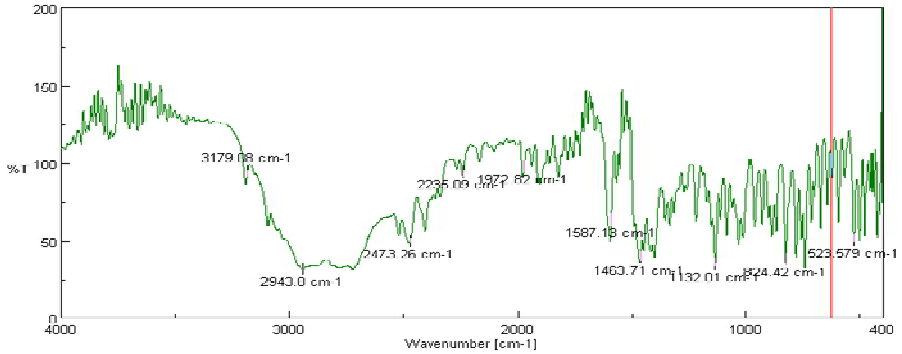


Figure 2: FTIR Studies of Sertraline Hydrochloride (Pure Drug) (A)

Sertraline Hydrochloride show characteristic absorption peaks in spectrum. Below graph shows peaks observed at different wave number and the functional group associated with these peaks. The broad peak observed around 3400-3200 cm^1 was attributed to N-H Stretching vibration (3000-2850) cm^{-1}, C-H Stretching (1600-1500) cm^{-1}, C=C Stretching (1450-1350), C-N Stretching confirming the characteristic structure of Sertraline Hydrochloride.

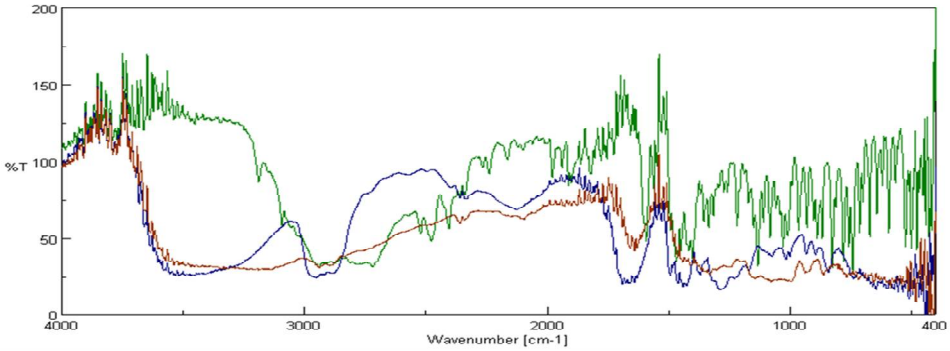


Figure 3: FTIR Spectrum of Sertraline Hydrochloride with Excipients Overlay (B)

FTIR Spectrum of Sertraline Hydrochloride, Crospovidone and Sodium Starch Glycolate showed characteristic functional group peaks without significant shifting or disappearance in the overlay spectrum, In IR spectra show retention of major peaks confirmed the absence of drug-excipients

interaction, No any significant difference, indicating good compatibility of sertraline hydrochloride with selected super-disintegration for fast disintegration tablet formulation.

DSC Analysis

DSC was used to study show Sertraline Hydrochloride and the excipients reacted to changes in temperature. Sertraline was confirmed to be crystal since the thermogram indicated melting and had a peak at 250^{0}C. No new drug-excipients interaction was seen because there were no other peaks in the absorbance. According to these result, Sertraline Hydrochloride can be combined with the selected excipients at high temperatures. As per the thermograms in Figure 4.

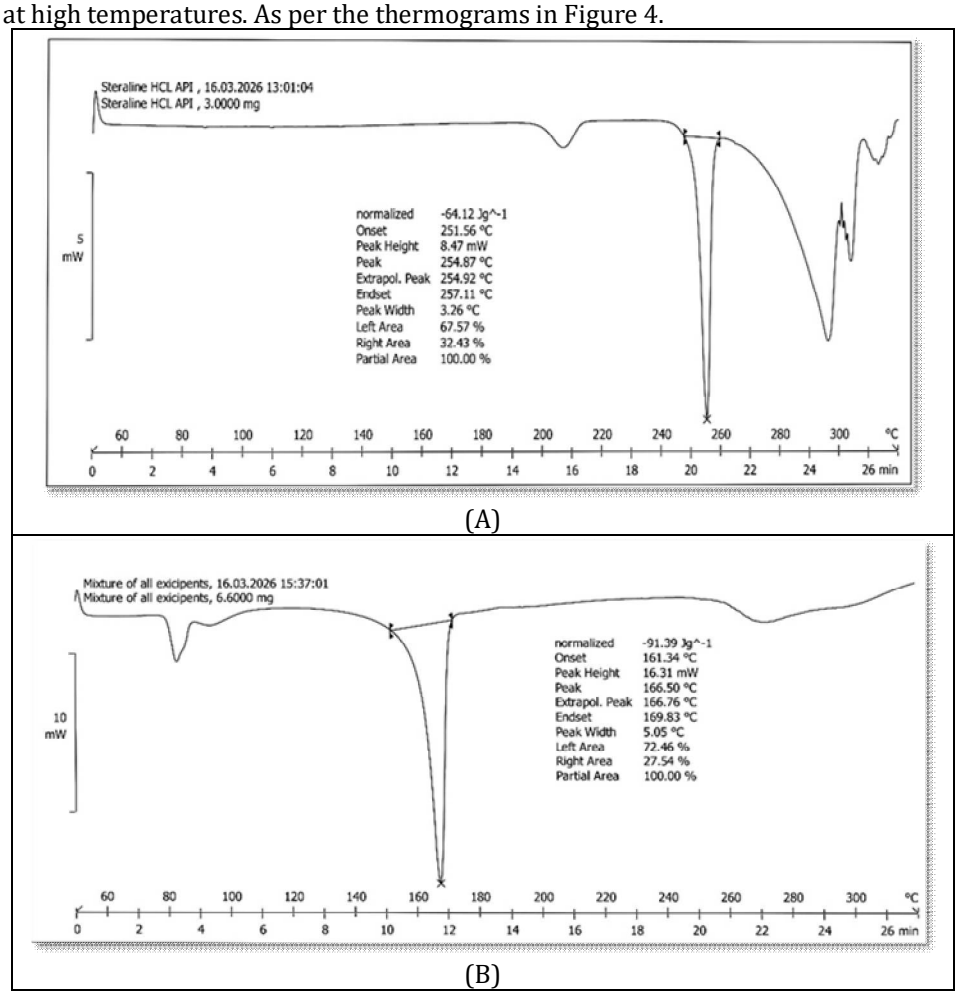


Figure 4: DSC of (A) Pure Drug and (B) Mixture of all excipients

Pre-Compression Parameters

All batches were found to have good floe properties before compression. All results show acceptable compressibility and flow property, ranging from 30.30 to 32.00 for angle of repose, 0.46 g/cm^3 to 0.53 g/cm^3 for bulk density, 0.46 g/cm^3 to 0.59 g/cm^3 for tapped density, 8.48 % to 10.4 % for Carr's index, 1.15 to 1.18 for Hausner ration this result verified the material flowed smoothly in Table 3.

Table 3: Pre-Compression study of FDTs Powder.

Formulation Code	Bulk Density (g/cm^3)	Tapped Density(g/cm^3)	Carr's Index (%)	Hausner's Ratio	Angle of Repose(θ)
RF1	0.46±0.004	0.59±0.055	9.83±0.23	1.18±0.06	32.0±0.81
RF2	0.48±0.004	0.56±0.050	9.13±0.23	1.16±0.03	32.0±0.66
RF3	0.48±0.008	0.49±0.021	9.36±1.03	1.15±0.04	31.4±0.43
RF4	0.53±0.03	0.51±0.028	10.3±0.30	1.16±0.06	31.4±0.41
RF5	0.49±0.008	0.54±0.051	9.47±1.96	1.16±0.06	31.0±0.81
RF6	0.48±0.008	0.52±0.049	9.14±0.91	1.18±0.08	30.6±0.94
RF7	0.47±0.02	0.52±0.026	8.48±0.62	1.16±0.06	30.3±0.44
RF8	0.50±0.005	0.50±0.049	10.4±0.55	1.16±0.06	32.3±0.77
RF9	0.49±0.004	0.58±0.048	9.90±0.77	1.15±0.03	31.3±0.05

Values are expressed as mean± SD: n=3

Post-Compression Parameters

The physical properties of fast disintegration tablets show in table no. Average weight of tablet between 397±4.2 to 400±3.5. The thickness of the prepared tablets ranged from 3.17±0.0 mm to 3.23±0.03 mm. All the formulations were relatively robust in terms of its pharmaco-technical parameters. Small values in friability much less friability during transportation, which is important in terms of fast disintegration tablets. The friability of the developed FDTs tablets fell into the range of 0.42±0.04 to 0.52±0.02 respectively. Hardness of the tablets was in the range 3.1±0.07 to 3.4±0.18 (kg/Cm^2). These results also revealed that the increasing polymer concentration did not alter the hardness and thickness of the tablet significantly. The drug content of the FDTs was found to be in the range of 97.73 ± 0.89 to 99.98±0.02 of the labelled amounts, and have complied with drug content requirement Table 4**.**

Table 4: Post Compression Parameters of FDTs Tablets.

Formulated Batch Code	Average Weight (mg) ± SD	Thickness (mm) ± SD	Diameter (mm) ±SD	Hardness (kg/Cm^2) ± SD	Friability (%) ± SD	Drug Content (%) ± SD
RF1	400±3.5	3.20±0.02	9.00±0.02	3.2±0.10	0.45±0.03	97.73±0.89
RF2	398±0.4	3.18±0.03	9.98±0.03	3.1±0.12	0.50±0.02	98.00±0.8
RF3	402±3.2	3.22±0.01	9.20±0.01	3.3±0.08	0.42±0.04	97.76±0.5
RF4	399±3.8	3.19±0.02	9.10±0.02	3.2±0.9	0.48±0.03	97.87±0.5
RF5	401±3.1	3.21±0.02	9.13±0.02	3.4±0.18	0.40±0.02	98.94±0.4
RF6	403±3.6	3.23±0.03	9.04±0.03	3.3±0.10	0.46±0.03	98.86±0.1
RF7	397±4.2	3.17±0.02	9.98±0.02	3.1±0.09	0.52±0.02	98.65±0.2
RF8	399±3.4	3.20±0.01	9.00±0.02	3.2±0.07	0.44±0.03	99.22±0.5
RF9	400±3.0	3.19±0.02	9.00±0.01	3.3±0.08	0.43±0.02	99.98±0.02

Values are expressed as Mean ± SD: n=3.

Result of Wetting Time, Water absorption ratio, Disintegration Time of Sertraline Hydrochloride Fast Disintegration Tablets

Sertraline Hydrochloride Fast Disintegration Tablets active ingredients are shows the wetting time ranged from 20±0.4 to 33±0.8 Sec which indicate a rapid tablet hydration. This resulted in an efficient moisture uptake of 34.6±3.3 to 38.5±4.6 of water absorption ratio. The findings are consistent with the formulation of rapid wetting time and effective Hydration. Disintegration time show resulted between 39±0.03 to 95±0.04.

Table 5: Result of Wetting Time, Water absorption ratio, Disintegration Time

Formulated Batch Code	Wetting Time (Sec)	Water absorption ratio	Disintegration Time (Sec)
RF1	33±0.8	35.5±4.0	95±0.04
RF2	32±0.9	36.6±1.6	88±0.04
RF3	29±0.8	36.6±1.6	69±0.05
RF4	27±0.8	34.6±3.3	70±0.03
RF5	24±0.4	35.3±4.1	61±0.05
RF6	27±0.8	34.6±4.1	51±0.08
RF7	25±0.8	36.6±4.7	57±0.04
RF8	21±0.8	34.0±4.3	42±0.03
RF9	20±0.4	38.5±4.6	39±0.03

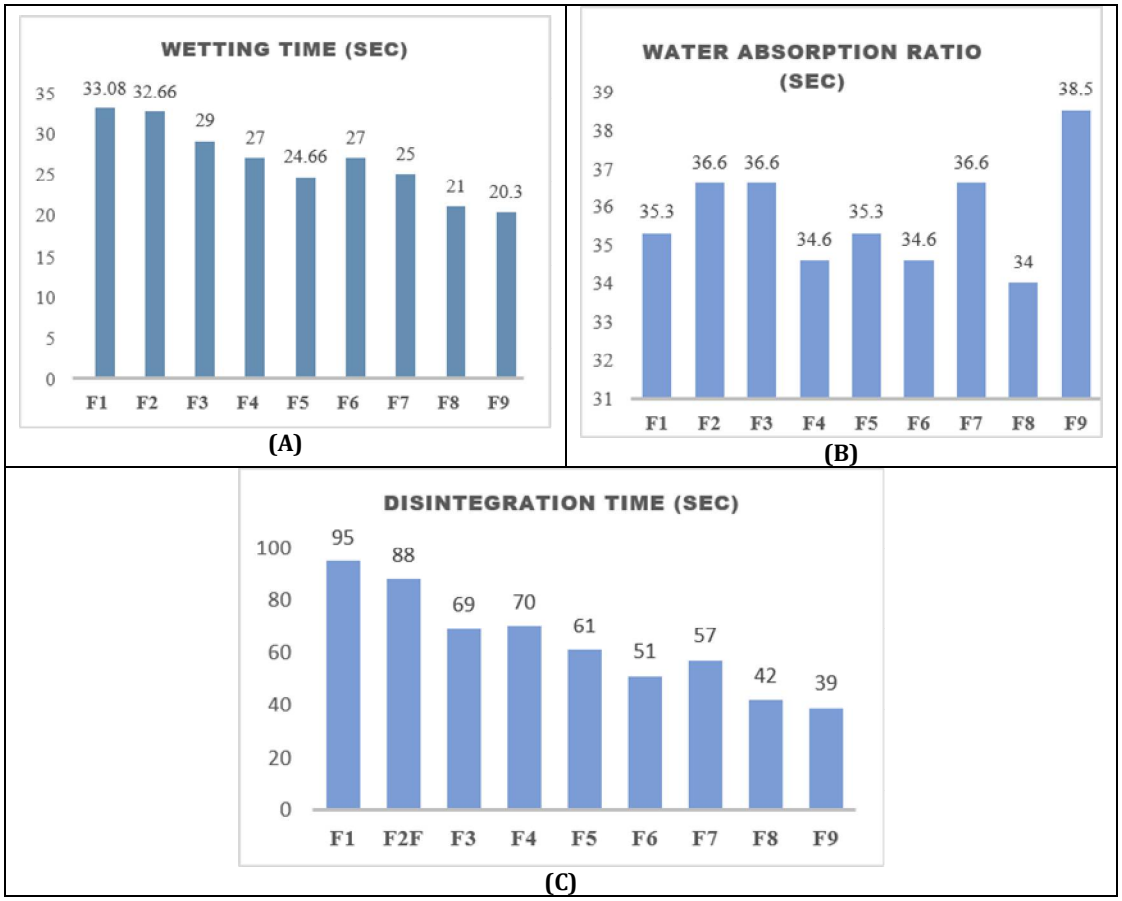


Figure No7: Evaluation of fast dissolving tablets (FDTs) of SRT: (A) Wetting time, (B) Water absorption, and (C) Disintegration time of various formulations.

***In-Vitro* Drug Release**

As shown in figure 8, the in-vitro drug release profile of Sertraline Hydrochloride Fast Disintegration Tablets was fast and highly efficient with all the formulations with the last total amount of drug released varying between 71.0% and 97.1%. The highest release observed in batch RF9 99% was very close to the study prediction. All RF1 -RF9 formulations were found to perform in a similar pattern from the release groups.

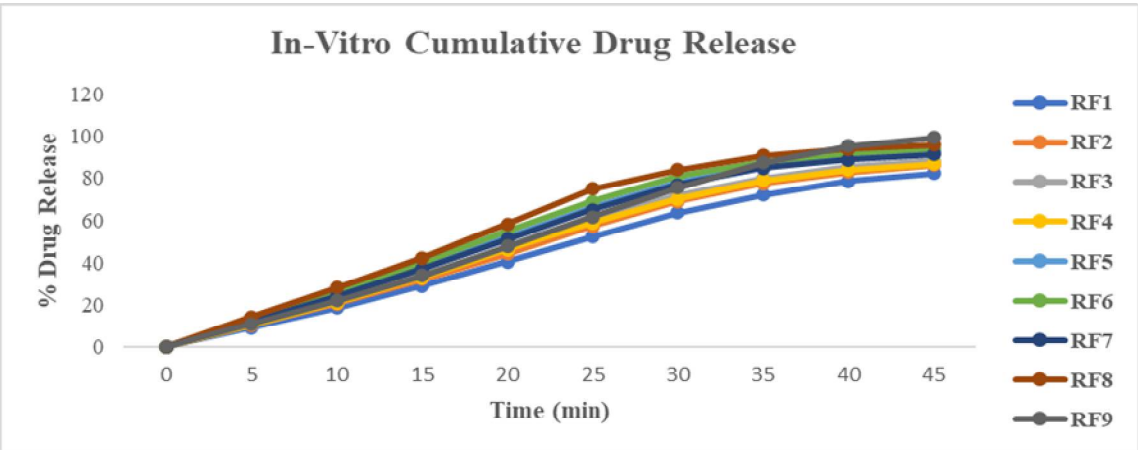


Figure 8: % Cumulative Drug Release Profile of Sertraline Hydrochloride as per Experimental Design.

Optimization of FDTs Tablet

Effect of Disintegration Time

The linear model for disintegration time demonstrated high statistical significance with a p-value < 0.0001, indicating that the model is significant. The model F-value (81.00) suggests that there is only a

0.01% chance that such a large F-value could occur due to noise, confirming the validity of the model. The selected formulation variables significantly contributed to the response. The factor Crospovidone (A) showed a highly significant effect ($F = 124.10$, $p < 0.0001$), whereas Sodium Starch Glycolate (B) also exhibited a significant effect ($F = 37.90$, $p = 0.0008$). Both superdisintegrants played an important role in influencing disintegration time.

Final Regression Equation (in terms of actual factors):

Y1(Disintegrating Time) =125.38889-12.66667A-3.50000B

As observed from the model, an increase in the concentration of Crospovidone (A) and Sodium Starch Glycolate (B) leads to a decrease in disintegration time, as indicated by the negative coefficients. Crospovidone showed a stronger effect in reducing disintegration time compared to Sodium Starch Glycolate, indicating its higher efficiency as a superdisintegrants. The absence of interaction terms indicates a linear relationship within the studied range.

Effect of % Cumulative drug release

The linear model for % cumulative drug release demonstrated high statistical significance with a p-value < 0.0001, indicating that the model is highly significant. The model showed good agreement with experimental data, as reflected by its ANOVA results. The model F-value (148.96) implies that the model is significant and there is only a 0.01% chance that such a large F-value could occur due to noise. This confirms that the selected formulation variables contribute significantly to the response. Among the formulation variables, Crospovidone (A) showed a highly significant effect ($F = 201.67$, $p < 0.0001$), while Sodium Starch Glycolate (B) also exhibited a significant effect ($F = 96.25$, $p < 0.0001$). Both superdisintegrants significantly influenced drug release.

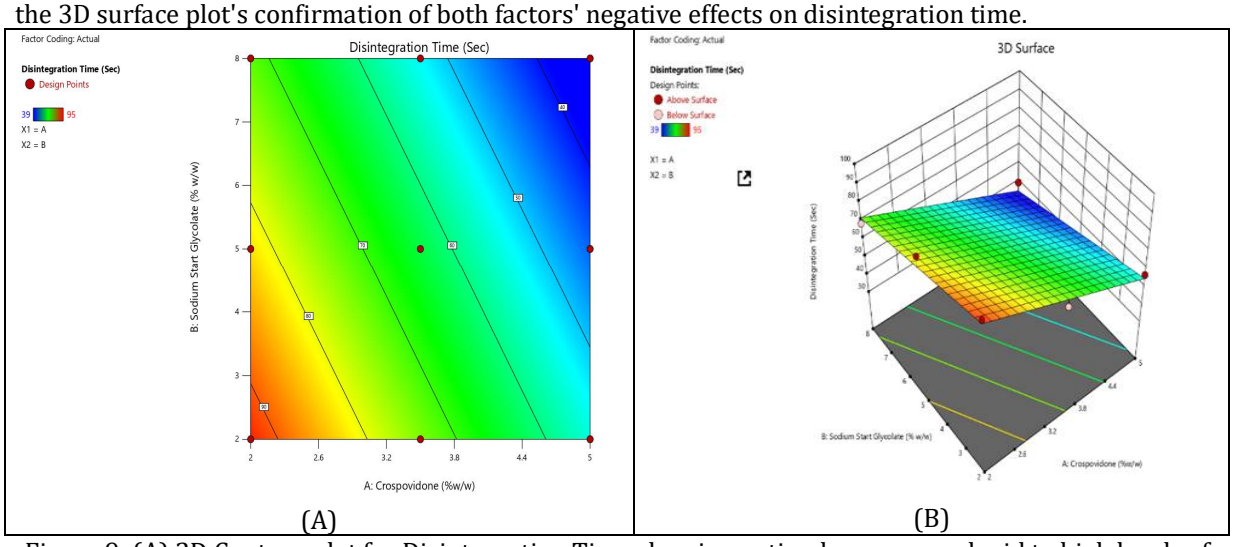
Final Regression Equation:

Y2(% Drug Release) = 73.27778 + 3.35667 A + 1.15944 B

As observed from the model, increase in concentration of Crospovidone (A) and Sodium Starch Glycolate (B) results in an increase in drug release, as indicated by the positive coefficients. Crospovidone showed a more pronounced effect on drug release compared to Sodium Starch Glycolate, indicating its superior efficiency as a superdisintegrant in enhancing drug release. The absence of interaction terms suggests that the model follows a linear relationship within the studied range.

Disintegration Time

The combined effects of crospovidone (A) and sodium starch glycolate (B) on the disintegration time of quickly disintegrating tablets were shown by the contour and three-dimensional surface plots. The response surface showed that when the concentrations of both superdisintegrants increased, the disintegration time reduced. Tablets with higher concentrations of sodium starch glycolate and crospovidone disintegrated more quickly than those with lower quantities. Effective superdisintegrant activity and optimal tablet performance were indicated by the contour plot's linear dropping pattern and the 3D surface plot's confirmation of both factors' negative effects on disintegration time.



(A) (B)

Figure 9: (A) 2D Contour plot for Disintegration Time showing optimal zone around mid to high levels of both excipients (B) 3D response surface plot showing the influence of Crospovidone and sodium starch glycolate concentrations on disintegration time.

% Cumulative Drug Release

The contour and 3D surface plots illustrated the influence of crospovidone (A) and sodium starch glycolate (B) on cumulative drug release of fast disintegrating tablets. The response surface showed that

cumulative drug release increased with increasing concentrations of both superdisintegrants. Higher levels of crospovidone and sodium starch glycolate promoted rapid tablet disintegration and enhanced drug dissolution, resulting in maximum drug release. The contour plot displayed a progressive increase in response values, while the 3D surface plot confirmed a positive and nearly linear relationship between formulation variables and cumulative drug release, indicating improved dissolution performance of the optimized formulation.

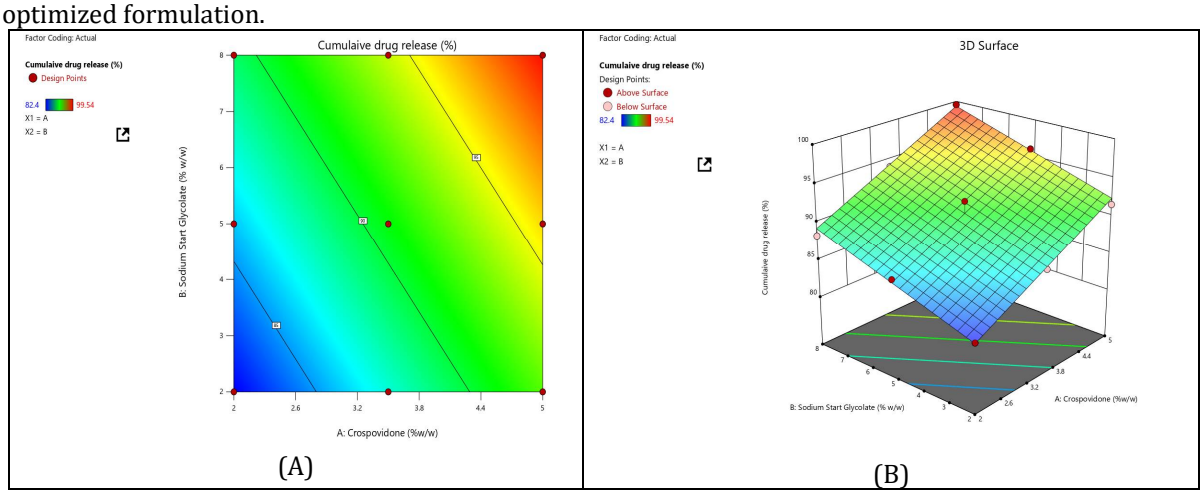
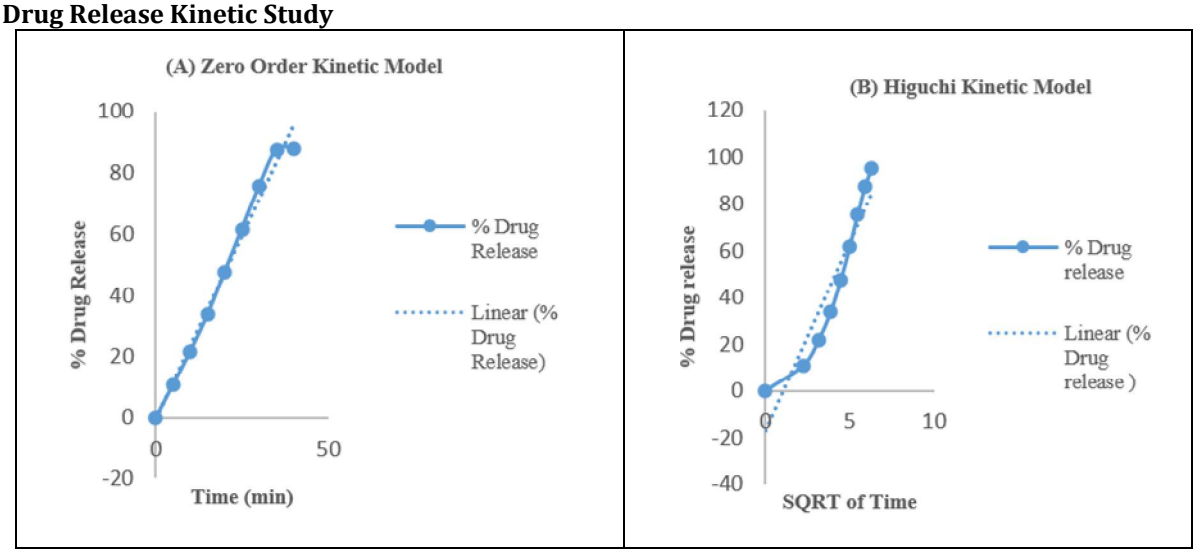


Figure 10: (A) Contour plot for % cumulative drug release (B) 3D Surface plot validating a linear model drug release pattern with indicating high both variables leads to higher drug release.

Drug Release Kinetic Study



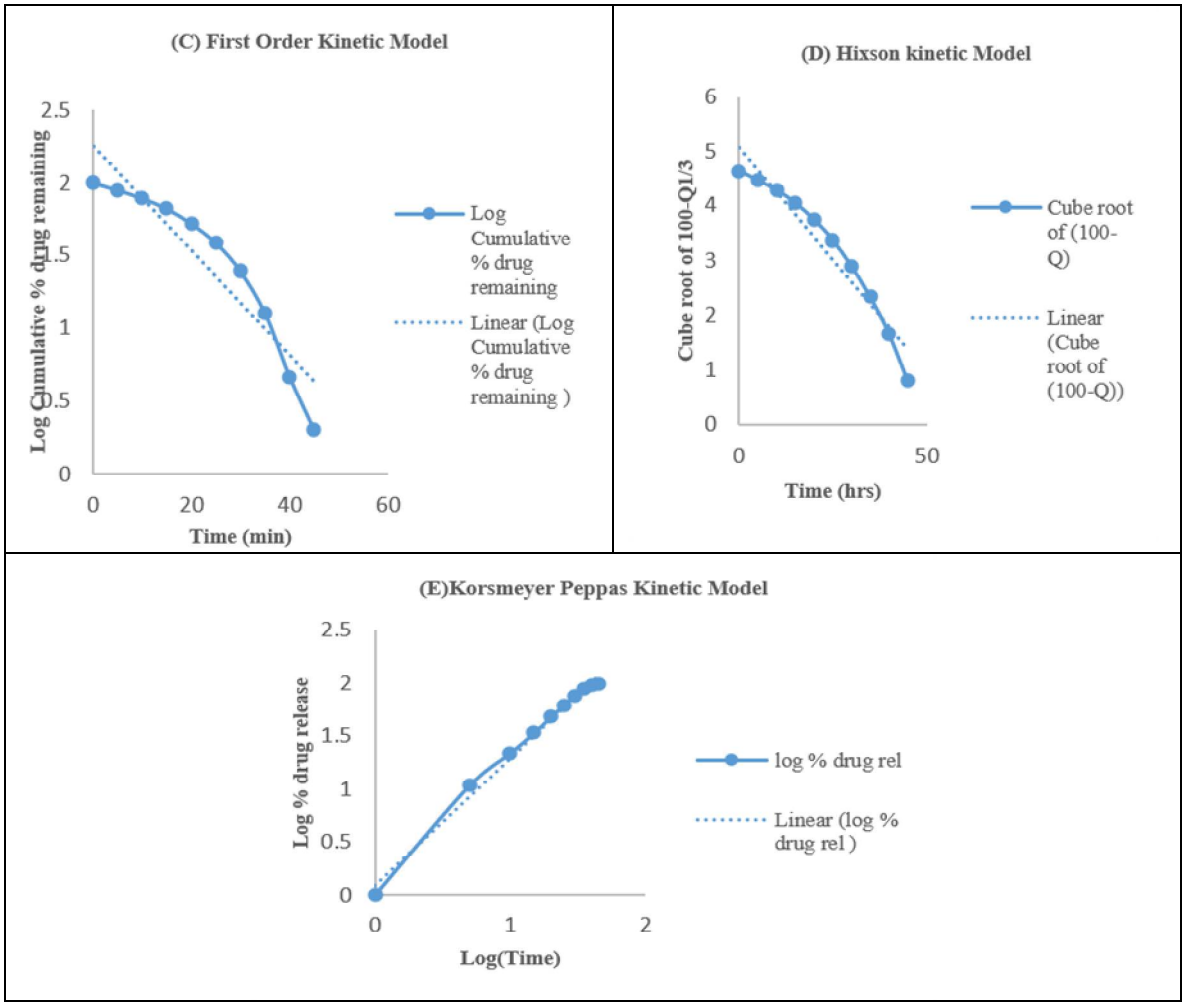


Figure 11: Kinetic Model of Sertraline Hydrochloride of Fast Disintegration Tablets

Cell Cyto-Toxicity Study

MTT assay on SH-SY5Y Cells showed a concentration dependent decrease in cell viability with increasing concentration of the formulation. The IC50 value was found to be 92.81 ug/ml, indicating moderate cytotoxicity and acceptable biocompatibility. Higher cell survival was observed at lower concentration, where as reduced viability was noted at higher concentration.

Table 11: Effect of Test Sample on Cell Viability Assessed by MTT Assay at Various Concentrations

Sr. No.	Concentration (ug/mL)	Average % Cell Survival
1	CTRL	100.00
2	1	87.47
3	5	76.78
4	25	69.98
5	50	65.23
6	100	51.51
7	250	46.11

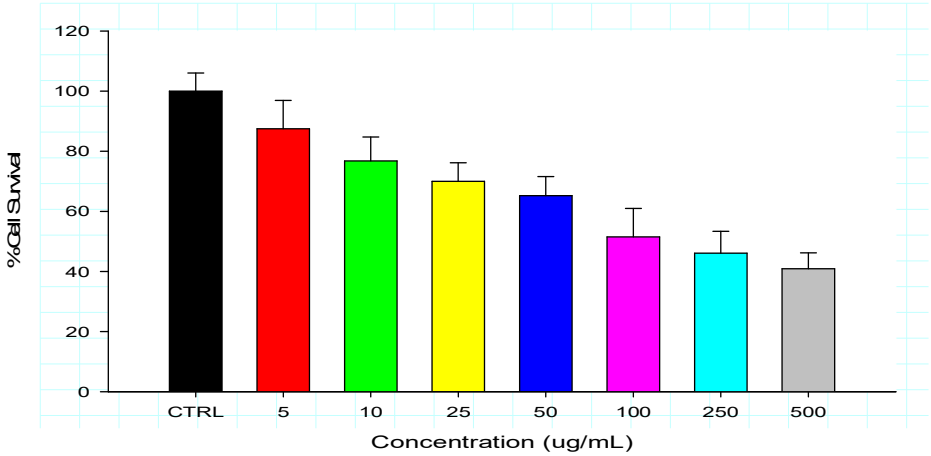


Figure 13: Comparative Cytotoxicity of Sertraline Hydrochloride and STD on SH-SY5Y cells assessed by MTT assay.

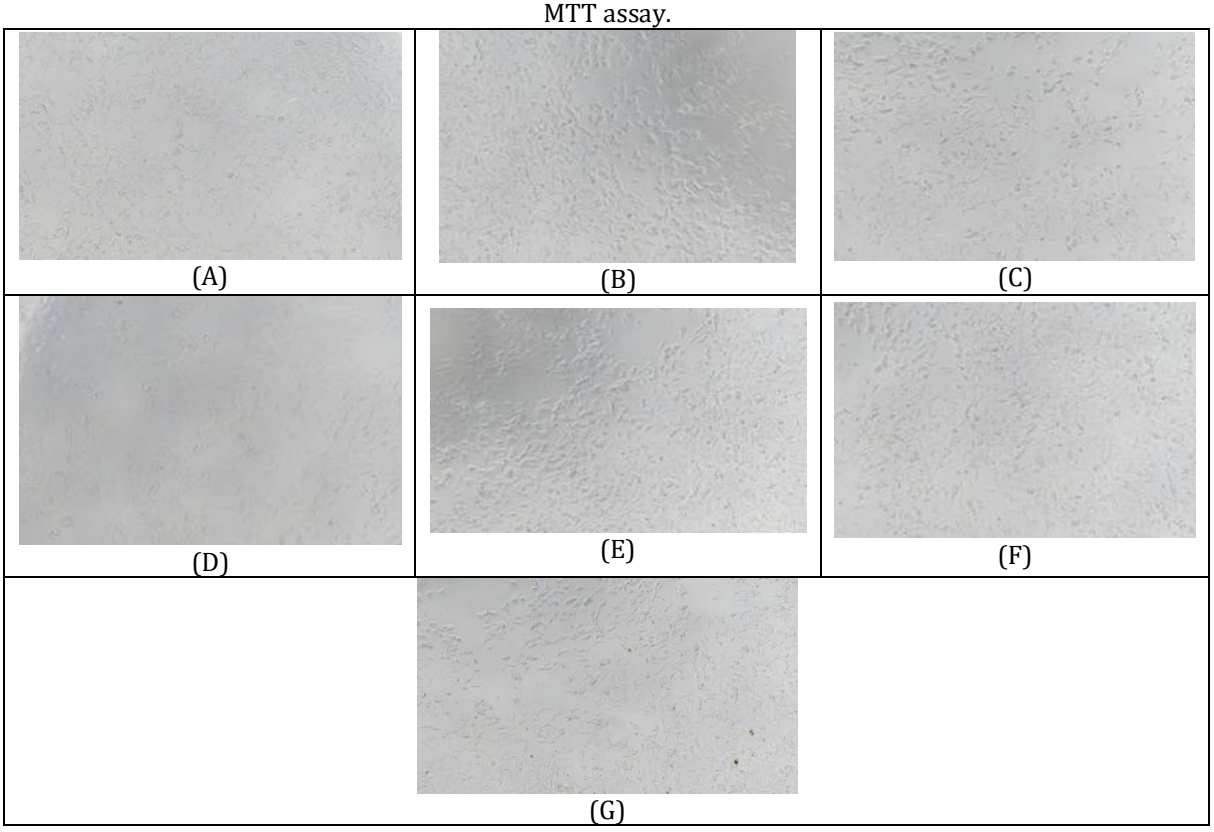


Figure 14: Morphological Observations of SH-SY5Y cells Treated Wells with Sertraline Hydrochloride and STD after 24 hours.

Stability Study

Stability studies were carried out of the Optimized formulation (RF9) at 40ºC ± 2ºC & 75% ± 5% RH for 3 months. At various time intervals (Initial, 1, 2, 3 month). The samples were evaluated for, Drug content (%), Disintegration Time (Sec), In-Vitro drug release in min.

Table 7: Stability studies

Parameters	Initial month	1st month	2nd month	3rd month
Drug Content(%w/w)	99.98±0.20	98.9±0.18	98.02±0.16	97.50±0.15
Disintegration Time (Sec)	39±0.6	37±0.7	39±0.7	38±0.7
% drug release (%)	99.53±0.50	98.80±0.40	99.10±0.35	98.41±0.38

DISCUSSION

The main purpose of this research involved developing an optimized fast disintegration tablet (FDTs) formulation of Sertraline Hydrochloride which should provide swift medication absorption while increasing patient obedience and improved ease of administration. A 3^2 full factorial design was successfully employed to systematically investigate the influence of two independent formulation variables, namely Crospovidone and Sodium Starch Glycolate on critical quality attributes such as disintegration time and % cumulative drug release. The statistical optimization approach enabled a comprehensive understanding of the individual and interactive effects of formulation variables on tablet performance. Both DSC (fig.2,3) and FTIR (fig.4) spectroscopy techniques showed finding that supported the stability of the designed formulation during physicochemical compatibility investigations. The result of the physical characteristics of the pre-compression powder mix were satisfactory as the angle of repose of the formulation (RF1-RF9) ranging from 30.30 to 32.00 for angle of repose, 0.46 g/cm^3 to 0.53 g/cm^3 for bulk density, 0.46 g/cm^3 to 0.59 g/cm^3 for tapped density, 8.48 % to 10.4 % for Carr's index, 1.15 to 1.18 for Hausner ration this result verified the material flow properties. Testing for mechanical strength showed tablets achieved hardness between 3.1±0.07 to 3.4±0.18 (kg/Cm^2) with low friability value below 1% which demonstrates good physical durability when handled and weight variation 397±4.2 to 400±3.5, 9.00±0.01 to 9.98±0.01 diameter, 20±0.4 to 33±0.8 Sec wetting time, water absorption ratio 34.6±3.3 to 38.5±4.6. The disintegration time of the optimize formulation batch is 39±0.03. Drug content analysis found uniform between all batches with result between 97.73 ± 0.89 to 99.98±0.02 for ensuring equivalent dosage distribution. In vitro drug release studies presented fig no:4 revealed quick drug release by using superdisintegrants are Crospovidone and Sodium Starch Glycolate of Sertraline Hydrochloride as Fast Disintegration Tablets. The Korsmeyer-Peppas showed the most fitting pattern to represent drug release kinetic from the optimized formulation with R2 value of because it combines erosion alongside diffusion in a non-fickian transport process. The biological compatibility of RF 9 formulations OF Sertraline Hydrochloride tablets was studied for cell cytotoxicity MTT assay on SH-SY-5Y cells, which showed moderate cytotoxicity at all the concentrations tested, and the cells kept their viability above 40.93% even after being treated with 500 µg/mL of Sertraline Hydrochloride. An IC_{50} value of 92.8171 µg/mL was recorded, showing that the drug is compatible with SH-SY-5Y cells. Examining cells under a microscope proved little variation at lower doses, confirming that it is safe for use in therapies. The results of the accelerated stability study indicate that after three months, the improved formulation did not change significantly in Drug content, Disintegration time, in-vitro drug release. According to the data, the formulation can maintain stability and last for a suitable period, as suggested by the ICH. Overall, each result points to the success of creating a Fast Disintegration Tablets of Sertraline Hydrochloride tablets that is strong enough, Fast releases within seconds, is stable, and helps to improve patient's compliance, therapeutic uses.

CONCLUSION

The present research successfully designed and improved a Sertraline Hydrochloride for Fast Disintegration Tablets formula through a 3^2 factorial design, which led to quick tablet dissolution along with uniform drug content and efficient drug release performance by using superdisintegrants are Crospovidone and sodium starch glycolate. The optimized batch RF9 presented outstanding compatibility along with appropriate mechanical strength and release kinetics order the Koesmeyer-Peppas model that indicated both diffusion and erosion release mechanisms. The evaluated formulation demonstrated moderate toxicity towards SH-SY-5Y cells while maintaining optimal morphology, which supports its safety potential. Additionally, the accelerated stability study found that the formula maintained its physicochemical and release features for three months under ICH conditions. All things considered, Sertraline Hydrochloride tablets development in this study demonstrate good strength, release the medication steadily for a long period, remain stable when exposed to accelerated tasting conditions, and are therefore reliable. This approach improving patient management for Depression and Anxiety Disorder by improves how well patients take their medicines. The formulation was also tested for compatibility and evaluated for safety and quality. The successfully optimized Sertraline Hydrochloride of Fast Disintegration Tablets Formulation Batch RF9, improving patient adherence and therapeutic outcomes in the management of Depression and Anxiety Disorder.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation.

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