

DEVELOPMENT AND CHARACTERIZATION OF SOLID DISPERSIONS OF
SERTRALINE HYDROCHLORIDE FOR IMPROVED DISSOLUTION PERFORMANCEMohammad Taleb Hossain¹, Md. Mufakkarul Islam¹, Mohammad Sofi¹, Ruminoman Dipu¹, Md. Harun Ar
Rashid¹, Mohammad Anisur Rahman Uzzal², Md. Sahab Uddin*¹¹Department of Pharmacy, Faculty of Health Science, Northern University Bangladesh, Dhaka, Bangladesh.²Popular Pharmaceuticals PLC, Dhaka, Bangladesh.***Corresponding Author: Md. Sahab Uddin**

Department of Pharmacy, Faculty of Health Science, Northern University Bangladesh, Dhaka, Bangladesh.

Email id: <https://doi.org/10.5281/zenodo.23032415>**How to cite this Article:** Mohammad Taleb Hossain¹, Md. Mufakkarul Islam¹, Mohammad Sofi¹, Ruminoman Dipu¹, Md. Harun Ar Rashid¹, Mohammad Anisur Rahman Uzzal², Md. Sahab Uddin*¹. (2026). Development and Characterization of Solid Dispersions Of Sertraline Hydrochloride For Improved Dissolution Performance. European Journal of Pharmaceutical and Medical Research, 13(10), 238–250.

This work is licensed under Creative Commons Attribution 4.0 International license.



Article Received on 29/08/2026

Article Revised on 19/09/2026

Article Published on 01/10/2026

ABSTRACT

Sertraline hydrochloride (HCl) is a widely prescribed selective serotonin reuptake inhibitor (SSRI) characterized by poor aqueous solubility, that severely limits its oral bioavailability. This study is designed to increase the dissolution rate of sertraline HCl through solid dispersion formulations using hydrophilic polymeric carriers. Using a design of experiments (DOE) approach, nine solid dispersions were made using the solvent evaporation method at a 1:3 drug-to-carrier ratio. Formulations combined sertraline HCl (100 mg) with varying proportions of hydroxypropyl cellulose (HPC), polyethylene glycol 6000 (PEG 6000), polyvinylpyrrolidone K90 (PVP K90), and sodium lauryl sulfate (SLS). In vitro dissolution profiles were assessed in standard phosphate buffer (pH 6.8) using a USP Type II apparatus. All solid dispersions demonstrated significantly improved dissolution efficiency compared to pure sertraline HCl ($60.92 \pm 1.13\%$ at 60 min). Formulation F7 (containing 65% HPC, 30% PEG 6000, and 5% PVP K90) emerged as optimal, achieving $95.38 \pm 0.70\%$ drug release at 60 minutes—representing a 56.56% relative improvement. F7 exhibited superior dissolution efficiency ($61.96 \pm 0.81\%$), remarkable reproducibility (RSD = 1.51%), and rapid initial kinetics. One-way ANOVA confirmed highly significant variations in drug release across formulations during early time intervals ($p < 0.001$), with profiles converging toward the 60-minute endpoint ($p = 0.626$). Pearson correlation analysis verified HPC as the primary performance-determining carrier ($r = +0.695$, $p = 0.038$). These findings demonstrate that solid dispersion strategies using optimized polymeric balances offer a robust and highly reproducible methodology for accelerating the dissolution profiles of BCS Class II antidepressants.

KEYWORDS: Sertraline hydrochloride, solid dispersions, dissolution enhancement, hydrophilic carriers, design of experiments.**1. INTRODUCTION**

Depression and related psychiatric disorders, including anxiety, obsessive-compulsive disorder, and post-traumatic stress disorder, affect millions worldwide and pose significant public health challenges. Sertraline hydrochloride, a selective serotonin reuptake inhibitor (SSRI), is widely used for treating these conditions; however, its poor aqueous solubility and low oral bioavailability limit its therapeutic effectiveness (Abdkarimi et al., n.d.; Hirave et al., 2024; Ratnaraju et al., 2015).

As a BCS Class II drug, sertraline HCl exhibits low solubility but high permeability, making its absorption dissolution-rate limited. Solid dispersion technology has emerged as an effective strategy to enhance the solubility and dissolution of poorly water-soluble drugs by dispersing them within hydrophilic carriers such as PVP, PEG, and surfactants (Sharma et al., n.d.; Tran et al., n.d.; Mohammed et al., 2024). Previous studies have reported significant improvements in the dissolution rate of sertraline HCl using solid dispersions prepared with

carriers such as PEG 6000 and PVP (Hirave et al., 2024; Nikghalb et al., 2012; Ratnaraju et al., 2015).

Furthermore, formulations incorporating solid dispersions have demonstrated faster and more complete drug release than conventional dosage forms (Al-Nimry

& Jaber, 2017; Kukde & Bharkatiya, n.d.-a; A. Nair et al., n.d.; Nikghalb et al., 2012). Therefore, this experiment aims to enhance the solubility of sertraline hydrochloride through solid dispersion technology by optimizing formulation variables to improve drug performance and therapeutic outcomes.

2. MATERIALS AND METHODS

2.1 Materials

Category	Material	Source	Grade
API	Sertraline Hydrochloride ($C_{17}H_{17}Cl_2N \cdot HCl$)	Renata Pharmaceuticals PLC, Gazipur, Bangladesh	USP
Carrier	PVP K90 (Kollidon® 90)	Renata Pharmaceuticals PLC	USP
Carrier	Hydroxypropyl Cellulose (HPC)	Renata Pharmaceuticals PLC	USP
Carrier	Polyethylene Glycol 6000 (PEG 6000)	Pharmaceutical Technology Lab, Dept. of Pharmacy, NUB	Analytical
Carrier	Sodium Lauryl Sulfate (SLS)	Pharmaceutical Technology Lab, Dept. of Pharmacy, NUB	Analytical
Solvent	Ethanol (C_2H_5OH)	Inorganic Pharmacy Lab, Dept. of Pharmacy, NUB	Analytical Reagent
Solvent	Distilled Water	Microbiology Lab, Dept. of Pharmacy, NUB	—
Medium	Phosphate Buffer (pH 6.8)	Prepared Fresh	—

2.2 Equipment and Instruments

Equipment/Instrument	Location	Purpose
UV-Visible Spectrophotometer	NUB, Pharmacy Department Lab	Drug assay, dissolution analysis
Dissolution Apparatus (USP Type II)	NUB, Pharmacy Department Lab	<i>In vitro</i> dissolution testing
Analytical Balance	NUB, Pharmacy Department Lab	Precision weighing (0.1 mg readability)
pH Meter	NUB, Pharmacy Department Lab	pH measurement of buffers and media
Desiccator	NUB, Pharmacy Department Lab	Storage of hygroscopic materials
Mortar and pestle	NUB, Pharmacy Department Lab	Grinding and mixing
Sieve Set	NUB, Pharmacy Department Lab	Particle size control
Sonicator	NUB, Pharmacy Department Lab	Sonicator
Membrane Filter Under Vacuum	NUB, Pharmacy Department Lab	Filtration of the drug substance

Standard Calibration Curve of Sertraline HCl

A linear calibration curve is essential for the quantitative determination of drug concentration in various analytical procedures.

2.3.1 Preparation of Phosphate Buffer pH 6.8 (USP)

The pH meter was calibrated using standard buffer solutions (pH 4.00 and 6.75). KH_2PO_4 (4.87 g) and K_2HPO_4 (2.48 g) were dissolved in approximately 700 mL of distilled water. The solution was transferred to a 1 L volumetric flask and diluted to volume with distilled water. The pH was measured and adjusted to 6.8 ± 0.02 using 0.1 M HCl or 0.1 M NaOH, if necessary. The prepared buffer was labeled and stored at room temperature.

2.3.2 Preparation of Working Standard Solutions

A total of 10 mg of sertraline HCl was dissolved in 100 mL of phosphate buffer and sonicated to ensure complete dissolution, yielding a stock solution with a concentration of **100 µg/mL**.

2.3.3 Preparation of Samples

- Six test tubes were prepared by transferring 0–5 mL of the 100 µg/mL sertraline HCl stock solution and diluting each to 20 mL with phosphate buffer. This produced standard solutions with concentrations of **0, 5, 10, 15, 20, and 25 µg/mL**.

Stock solution (ml) + phosphate buffer (ml)	Concentration (mcg/ml)
0+20	0
1+19	5
2+18	10
3+17	15
4+16	20
5+15	25

2.3.4 UV Spectrophotometric Analysis

- The samples of different concentrations are ready to be analyzed further. The UV spectrophotometer was set at the photometric method at a wavelength of 273 nm.
- Absorbance of each sample was taken thrice, and the average value of absorbance was calculated for further analysis.

Concentration (mcg/ml)	Absorbance
0	0.0000
5	0.0273
10	0.0561
15	0.0864
20	0.1135
25	0.1387

- With the absorbance value, using Microsoft Excel 2021, the calibration curve and relevant equation were determined.

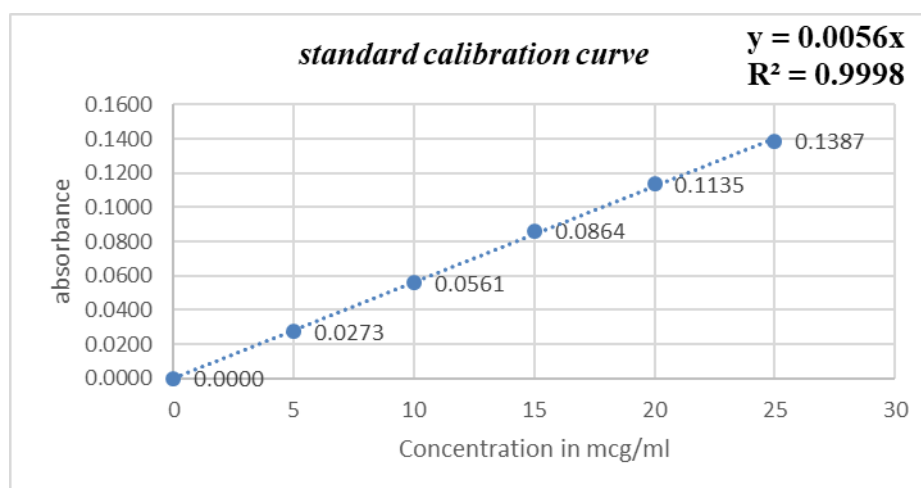


Figure 1: Standard calibration curve.

From the calibration curve, we got the calibration equation,

$$Y = 0.0056x, \text{ where } R^2 = 0.998$$

2.4 Formula and Statistical Parameters

2.4.1 Drug Release Amount

It is the amount of drug that has been released in an in vitro dissolution study at a certain time point.

Usually, the sample of each time point gives a specific absorbance reading in a UV spectrophotometer. That absorbance is compared to the Calibration curve equation to determine the drug release amount.

Beer-Lambert Law

The Beer-Lambert Law states:

$$A = \epsilon lc$$

Where A is absorbance, ϵ is molar absorptivity ($L \cdot mol^{-1} \cdot cm^{-1}$), l is path length (typically 1 cm), and c is concentration. The law establishes that absorbance is directly proportional to concentration and path length.

Derivation of Calibration Curve

Under constant path length and molar absorptivity, the Beer-Lambert equation simplifies to:

$$A = k \cdot c$$

Where $k = \epsilon l$ is constant, representing a linear relationship. In practice, background absorbance from

solvents and instrumental variations introduce a non-zero intercept, resulting in the practical equation:

$$y = mx + c$$

Where m = slope (ϵl adjusted for system variations) and c = y-intercept (corrects for background absorbance).

Practical Application

Standard solutions of known concentrations are measured at the analytical wavelength (λ_{max}), and linear regression determines slope and intercept. Unknown concentrations are calculated using:

$$x = \frac{y - c}{m}$$

So, x concentration per ml (without adjusting diluting factor)

$$\text{Amount released} = \frac{\text{Concentration (x)} \times \text{volume of media} \times \text{Dilution Factor}}{1000}$$

2.4.2 Cumulative drug release

During the sample withdrawal and later replacement with fresh media diluents, a gap occurs in the calculation that is later compensated for by a calculation named cumulative amount determination.

Cumulative drug release = Drug concentration at t time interval + correction factor of all previous 5 ml samples.

- If the drug release amount in 30 minutes is 48 mg, 20 minutes is 35 mg, and 10 minutes is 22 mg. Here, sample withdrawn = 5 ml, Media volume = 900 ml, then,

✓ Cumulative drug amount at **10 minutes**: 22mg

✓ Cumulative drug amount at **20 minutes**:

$$35 \text{ mg} + \frac{5 \times 22}{900} \text{ mg} = 35.12 \text{ mg}$$

✓ Cumulative drug amount at **30 minutes**:

$$48 \text{ mg} + \frac{5 \times 35.12}{900} \text{ mg} + \frac{5 \times 22}{900} \text{ mg} = 48.32 \text{ mg}$$

2.4.3 Percentage Drug Release

$$\text{Percentage of drug release} = \frac{\text{Amount of drug release}}{\text{label claim of drug}} \times 100$$

In case of our experiment, as a single formulation is made thrice to compare reproducibility and efficiency, the percentage release of three times was determined individually, then the average was calculated for each time interval of a formulation.

And, with percentage drug release, the standard deviation data were also added, which basically shows the typical distance of each data point from the mean.

➤ Consistency vs. variability

Low SD → data points are tightly clustered (high consistency).

High SD → data points are widely spread (less consistent, more variability).

In simple terms, Standard deviation tells you how spread out your data is around the mean. A small standard deviation means most values are close to the average, while a large standard deviation means the values are more scattered.

What Standard Deviation Represents

- **Measure of variability:** It shows the *typical distance* of each data point from the mean.

- **Consistency vs. variability:**

Low SD → data points are tightly clustered (high consistency).

High SD → data points are widely spread (less consistent, more variability).

$$s = \sqrt{\frac{\sum (x_i - \bar{x})^2}{n - 1}}$$

Where:

- x_i = each data point
- $\bar{x}$ = sample mean
- n = sample size

Dissolution Efficiency

Dissolution Efficiency (DE%) quantifies the overall extent and rate of dissolution as the area under the dissolution curve relative to the total possible area.

Instead of comparing only single time points, DE% integrates the entire dissolution curve.

$$DE\% = \frac{\int_0^t y dt}{y_{100} \cdot t} \times 100$$

Where:

- y = % drug dissolved at time t
- y_{100} = 100% dissolution (theoretical maximum)
- Numerator = area under the dissolution curve (AUC) up to time t
- Denominator = rectangle representing 100% dissolution over the same time

Interpretation: Higher DE% = faster and more complete dissolution. Useful for BCS Class II drugs, where dissolution is the rate-limiting step.

f2 Similarity Factor

f2 (Similarity Factor) is a logarithmic measure of closeness between two profiles; values between 50–100 indicate similarity.

It is recommended by the FDA/EMA to compare dissolution profiles.

$$f_2 = 50 \cdot \log \left\{ \left[1 + \frac{1}{n} \sum_{t=1}^n (R_t - T_t)^2 \right]^{-0.5} \cdot 100 \right\}$$

Where:

- R_t = % dissolved of reference at time t
- T_t = % dissolved of test at time t
- n = number of time points
- **Acceptance:**
- 50–100 → profiles are similar
- <50 → not similar

f1 Difference Factor

f1 (Difference Factor) measures the *percent difference* between two dissolution profiles at each time point.

$$f_1 = \frac{\sum_{t=1}^n |R_t - T_t|}{\sum_{t=1}^n R_t} \times 100$$

Where:

- R_t = % dissolved of reference at time t
- T_t = % dissolved of test at time t

The 9 different formulas are

Serial	Solid Dispersion Formulations (1: 3)			
	Sertraline HCl (1) =100 gm	Carriers (3) =300 gm		
	Sertraline HCl (mg)	K90	PEG 6000	HPC
1	100	240	45	15
2	100	195	75	30
3	100	150	120	30
4	100	105	150	45
5	100	60	180	60
6	100	45	150	120
7	100	15	90	195
8	100	90	30	180
9	100	135	15	150

2.6 Solid Dispersion making

- Although there are many techniques of solid dispersions available, this research followed the solvent evaporation method. Ethanol is the solvent in this case.
- All the carriers and pure Sertraline HCl were brought, and those that have a crystal structure were made into powder using a mortar and pestle.
- After all the carriers and Pure HCL were weighed accurately, 9 different petri dishes were taken and labeled respectively 1 to 9.
- In each petri dish, the corresponding DOE formulation's carriers and sertraline were placed.

- n = number of time points

Acceptance

- 50–100 → profiles are similar
- <50 → not similar

Statistical Significance Testing (ANOVA & P Value)

In addition to model-independent factors, statistical tests such as **ANOVA (Analysis of Variance)** may be applied to compare mean dissolution values across multiple formulations. ANOVA generates an **F-statistic**, from which a **p-value** is derived. The p-value indicates the probability of observing the data if the null hypothesis (no difference between groups) is true. A p-value ≤ 0.05 is generally considered statistically significant.

Microsoft Excel & Python Programming Language

For our calculation & Data analysis of all the calculations' accuracy, robustness, we used **Microsoft Excel 2021, Python programming language** integrated with Perplexity AI Pro version (research).

2.5 Design of Experiment

With sertraline HCl, carriers are mixed to maintain the ratio 1:3. The amount of sertraline in each formula is 100 mg, and the mix of carriers (PVP k-90, PEG 6000, HPC, and SLS) is 300 mg. Thus, 9 different formulas were made based on varying amounts of the mix of carriers.

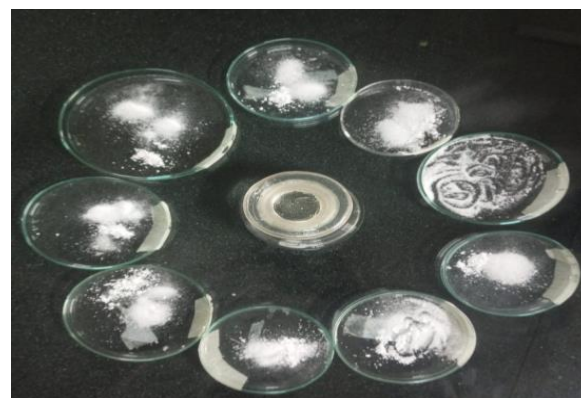


Figure 2: Prepared solid dispersions.

- In each petri dish, initially 20 ml of ethanol is added and stirred vigorously for 20-30 minutes to ensure homogeneous uniform mixing.
- Following the mixing, all 9 formulations were kept for further evaporation at room temperature for 24 hours.
- Consequently, the Petri dishes containing formulations were dried using a dry heat sterilizer at 60 degrees Celsius for 90 minutes.



Figure 3: Prepared solid dispersions after drying.

- The solid dispersion formulations were then extracted from the petri dishes and milled with 40-60 mesh sieves and stored in air-tight bags.



Figure 4: Prepared solid dispersions after sieving.

- For most of the solid dispersion formulations, the yield amount was 80-90% equivalent to 320 to 360 mg.

Dissolution Sample Preparation

The yield samples are milled and mixed homogeneously. And, 200 mg of the sample, which is equivalent to 50 mg pure sertraline, was taken for dissolution studies.

Firstly, a dissolution test of pure Sertraline HCl was conducted three times, and later a dissolution test of 9 new formulations took place; each test was conducted three times to get better replicates and an efficient result from a statistical aspect.

Dissolution Condition

For the dissolution test, the following criteria were strictly maintained-

- **Media:** Phosphate buffer,
- $P^H = 6.8$, strength 0.05 M,
- **Volume:** as per sample, diluents & testing requirement
- **RPM= 75**
- **Time: 60 Minutes**
- **Temperature= 37°C**
- **Time intervals:** 10,20,30,45,60 minutes.

Filtration, diluting, and making ready for UV analysis
After samples are collected at each interval of 5ml, they are all filtered using a membrane filter having a pore size

of 0.45 μm under vacuum. And followed by the filtration process, the samples were diluted three times (10 ml diluent phosphate buffer was added to each sample).

Taking a reading of the UV spectrophotometer

After filtration and dilution, the samples were analyzed using a UV spectrophotometer. The instrument was operated in photometric mode at a wavelength of 273 nm (λ_{max}) for sertraline HCl. A phosphate buffer blank was used for calibration and auto-zeroing. Following calibration, the absorbance of the prepared samples was measured for quantitative analysis.

RESULTS AND DISCUSSION

3.1 UV Absorbance Result

The recorded absorbance values were converted to concentrations using the calibration curve equation. The concentrations were then adjusted for the dilution factor and dissolution medium volume (900 mL). Dissolution tests for each formulation were performed in triplicate, and the final percentage drug release was expressed as the mean $\pm$ standard deviation (SD) of the three measurements.

Pure Sertraline HCl		
Time interval (minutes)	Average Percentage Drug Release of three replicate tests	Standard deviation
10	18.71	1.01
20	29.39	0.84
30	40.80	0.84
45	52.95	0.59
60	60.92	1.13

DOE FORMULATION 01		
Time interval (minutes)	Average Percentage Drug Release of three replicate tests	Standard deviation
10	27.45	1.15
20	43.42	1.32
30	78.30	2.30
45	87.77	1.41
60	93.87	1.31

DOE FORMULATION 02		
Time interval (minutes)	Average Percentage Drug Release of three replicate tests	Standard deviation
10	28.06	0.26
20	45.32	0.94
30	73.40	2.27
45	86.85	1.20
60	93.25	1.35

DOE FORMULATION 03		
Time interval (minutes)	Average Percentage Drug Release of three replicate tests	Standard deviation
10	29.64	0.46
20	46.38	0.93
30	75.38	1.98
45	86.33	0.90
60	93.98	1.80

DOE FORMULATION 04		
Time interval (minutes)	Average Percentage Drug Release of three replicate tests	Standard deviation
10	30.31	1.34
20	47.67	0.76
30	74.68	1.60
45	82.03	1.38
60	92.67	2.14

DOE FORMULATION 05		
Time interval (minutes)	Average Percentage Drug Release of three replicate tests	Standard deviation
10	30.73	0.97
20	49.80	1.17
30	67.43	1.54

45	79.98	1.95
60	93.38	1.55

DOE FORMULATION 06		
Time interval (minutes)	Average Percentage Drug Release of three replicate tests	Standard deviation
10	28.70	1.02
20	43.13	0.50
30	74.81	1.75
45	82.48	1.16
60	93.54	0.92

DOE FORMULATION 07		
Time interval (minutes)	Average Percentage Drug Release of three replicate tests	Standard deviation
10	33.62	0.82
20	50.30	0.68
30	79.89	1.50
45	88.84	1.03
60	95.38	0.70

DOE FORMULATION 08		
Time interval (minutes)	Average Percentage Drug Release of three replicate tests	Standard deviation
10	29.44	0.90
20	47.64	1.36
30	78.31	0.96
45	85.65	1.20
60	94.25	1.71

DOE FORMULATION 09		
Time interval (minutes)	Average Percentage Drug Release of three replicate tests	Standard deviation
10	27.26	0.55
20	42.48	1.59
30	77.85	1.22
45	85.51	1.93
60	94.05	1.40

3.2 Dissolution at Key Time Points

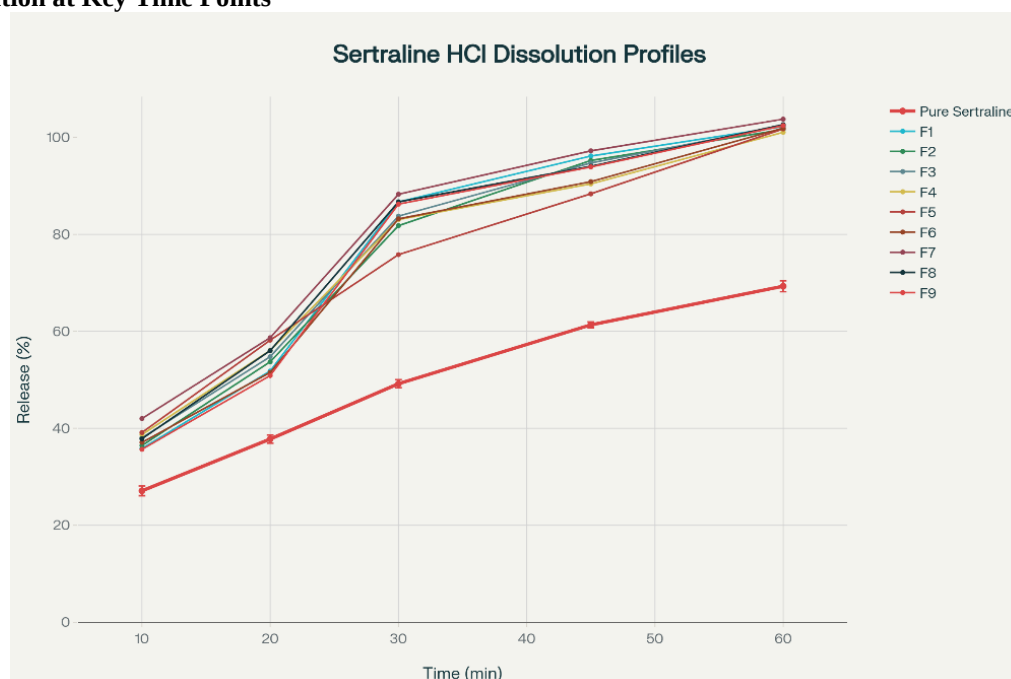


Figure 5: Dissolution profiles of Sertraline HCL.

1. **Pure Sertraline Performance:** Only 60.92% drug release at 60 minutes
2. **Solid Dispersion Performance:** All formulations achieved >92% drug release at 60 minutes

3. Best Formulation (F7)

- 95.38% $\pm$ 0.70% at 60 minutes
- 34.46 percentage point improvement over the pure drug
- 56.56% relative improvement
- 1.57-fold increase in dissolution

1. **Minimum Enhancement:** Even the lowest-performing formulation (F4) showed 31.75 percentage point improvement (51% relative increase)

2. **Statistical Significance:** All solid dispersions showed dramatically superior dissolution profiles compared to pure sertraline

Final Dissolution at 60 Minutes (Ranking)

1. F7: 95.38% $\pm$ 0.70% (Best performer)
2. F8: 94.25% $\pm$ 1.71%
3. F9: 94.05% $\pm$ 1.40%
4. F3: 93.98% $\pm$ 1.80%
5. F1: 93.87% $\pm$ 1.31%
6. F6: 93.54% $\pm$ 0.92%
7. F5: 93.38% $\pm$ 1.55%
8. F2: 93.25% $\pm$ 1.35%
9. F4: 92.67% $\pm$ 2.14% (Lowest performer)

It is worth noticing that formulation 7,8,9 has a carrier HPC amount higher than other formulations. So, it is an indication that further formulation with a higher HPC ratio can make the formulations even better optimized.

3.3 Dissolution Efficiency

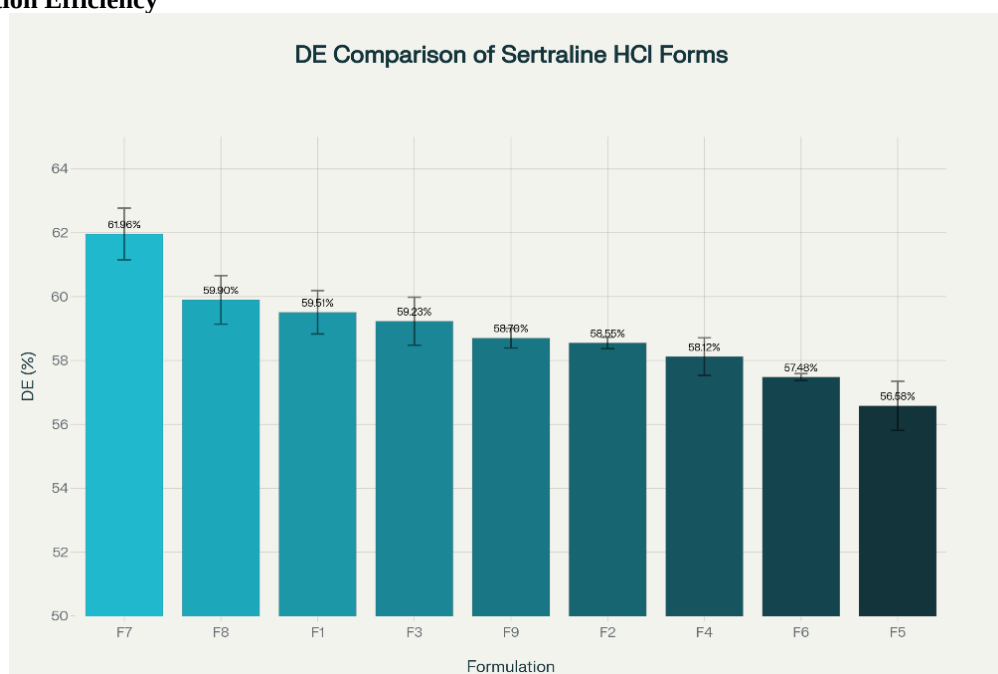


Figure 6: Comparison of dissolution efficiency of sertraline HCL formulas.

Dissolution Efficiency (DE) comparison shows F7 as the best performing formulation with the highest area under the dissolution curve.

Dissolution efficiency represents the area under the dissolution curve as a percentage of the total possible dissolution. This parameter provides insight into the overall dissolution performance:

Rankings by DE

1. F7: 61.96% $\pm$ 0.81% (Superior overall dissolution)
2. F8: 59.90% $\pm$ 0.76%
3. F1: 59.51% $\pm$ 0.68%
4. F3: 59.23% $\pm$ 0.75%
5. F9: 58.70% $\pm$ 0.31%
6. F2: 58.55% $\pm$ 0.18%

7. F4: 58.12% $\pm$ 0.59%

8. F6: 57.48% $\pm$ 0.11%

9. F5: 56.48% $\pm$ 0.77%

F7's superior DE indicates consistent high-rate dissolution throughout the test period, not just at the endpoint. The 5.38 percentage difference between F7 and F5 represents a clinically significant improvement in dissolution performance.

3.4 Similarity factor

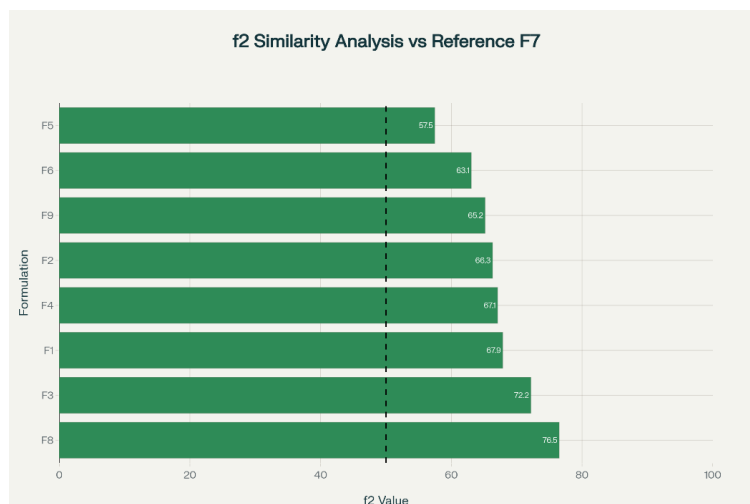


Figure 7: Comparison of similarity factor (f_2) with reference F7.

Similarity factor (f_2) comparison showing all formulations meet FDA criteria ($f_2 \geq 50$) for similarity to reference formulation F7, with F8 showing highest similarity

Similarity factor (f_2) analysis compared all formulations against F7 (reference). All formulations demonstrated similar similarity to F7 ($f_2 \geq 50$), meeting FDA guidelines for bioequivalence:

f_2 Rankings (vs F7):

- F8: 76.51 (Highly similar)
- F3: 72.18 (Highly similar)
- F1: 67.88 (Similar)
- F4: 67.09 (Similar)
- F2: 66.31 (Similar)
- F9: 65.17 (Similar)
- F6: 63.06 (Similar)
- F5: 57.47 (Similar, but lowest)

The high f_2 values indicate that all formulations follow similar dissolution patterns, suggesting consistent solid dispersion formation across different compositions.

F8 showed the highest similarity to F7, making it a potential alternative formulation.

3.5 One-Way ANOVA Results (p values)

Statistical analysis revealed significant differences between formulations at early to mid-time points:

- **10 minutes:** F-statistic = 14.71, $p < 0.001$ (Highly significant)
- **20 minutes:** F-statistic = 21.17, $p < 0.001$ (Highly significant)
- **30 minutes:** F-statistic = 13.90, $p < 0.001$ (Highly significant)
- **45 minutes:** F-statistic = 13.20, $p < 0.001$ (Highly significant)
- **60 minutes:** F-statistic = 0.78, $p = 0.626$ (Not significant)

The convergence of dissolution values at 60 minutes indicates that while formulations differ in dissolution rates, they achieve similar final release levels.

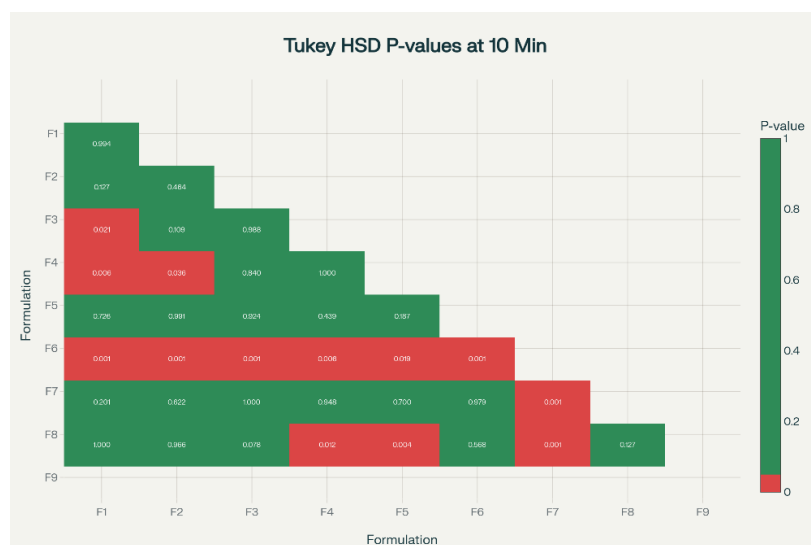


Figure 8: Tukey HSD P-values at 10 minutes.

Tukey HSD post-hoc test results at 10 minutes showing pairwise comparisons, with F7 significantly different from all other formulations ($p < 0.05$)

Tukey HSD testing at 10 minutes revealed that F7 was significantly different from all other formulations ($p < 0.05$), confirming its superior early dissolution performance. This statistical validation supports F7's selection as the optimal formulation.

3.6 Reproducibility Analysis

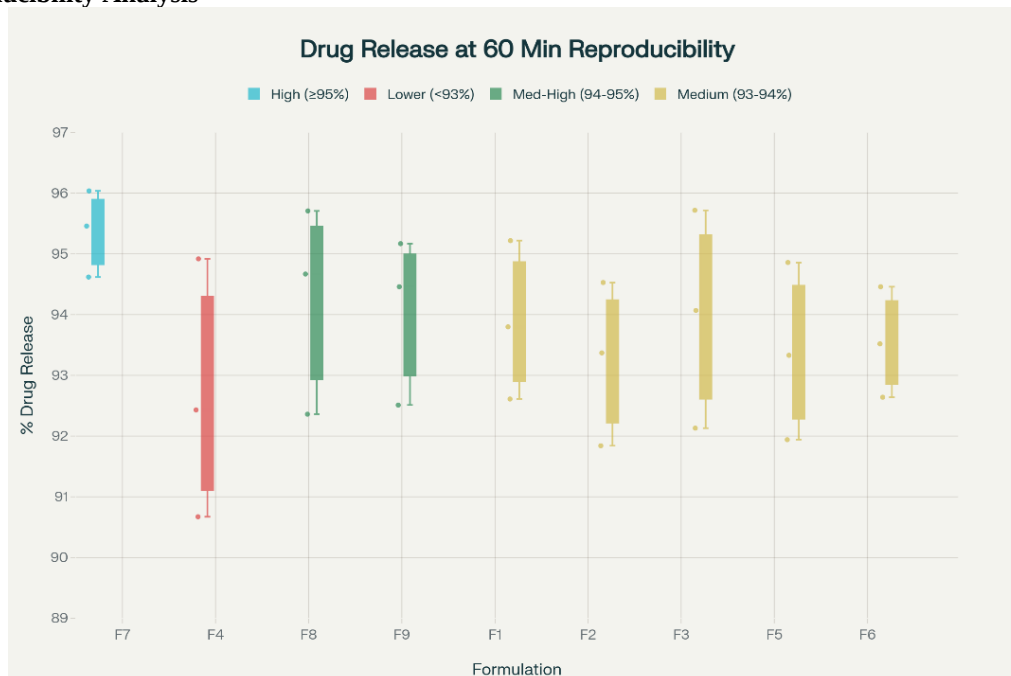


Figure 9: Reproducibility analysis- drug release in 60 minutes.

Box plot showing distribution and reproducibility of final drug release at 60 minutes, with F7 showing tight clustering and high median release.

3.7. Relative Standard Deviation (RSD)

All formulations demonstrated excellent reproducibility with RSD values well below the 10% acceptance criteria:

Best Reproducibility (Lowest Average RSD)

1. F7: 1.51% (Excellent)
2. F2: 1.78% (Excellent)
3. F3: 1.82% (Excellent)
4. F6: 1.89% (Excellent)
5. F8: 2.07% (Very good)

F7 not only showed the best dissolution performance but also the highest reproducibility, indicating robust formulation consistency crucial for pharmaceutical manufacturing.

CONCLUSIONS

The data confirms that the solid dispersion method successfully enhanced sertraline HCl solubility across every blend evaluated. Formulation F7 stands out as the top performer, exhibiting superior performance in dissolution rate, extent, efficiency, and reproducibility.

Statistical validation confirms significant performance differences between formulations, while similarity factor analysis ensures all formulations meet regulatory

acceptance criteria. The absence of data anomalies and excellent reproducibility support the reliability of these findings for pharmaceutical development decisions.

Moving forward, F7 should be selected for advanced pharmaceutical development, with F8 maintained as a backup formulation due to its high similarity and good performance characteristics.

REFERENCES

1. Ratnaraju, k., jyothirmayi, p., & saibabu, s. (2015). Solubility enhancement of sertraline hydrochloride-formulation & comparative evaluation of liquid solid compacts with solid dispersions.
2. Abdkarimi, F., & Haghtalab, A. Solubility measurement and thermodynamic modeling of sertraline hydrochloride and clopidogrel bisulfate in deep eutectic solvent of choline chloride and malonic acid. *Journal of Molecular Liquids*, 2021; 344: 117940.
3. Shaikh, S. N., Khan, J., Fakir, H. S., Shaikh, M. F., Shaikh, S. I., & Shaoor, A. S. Drug-drug solid dispersion a unique approach in solubility enhancement. *International journal of Pharma research and review*, 2016; 5(1): 19-27.
4. Hirave, P., Kakade, S., Khade, P., & Bhosale, A. Formulation & evaluation of fast disintegrating tablet of solid dispersion of Sertraline HCl. *Journal of Emerging Technologies and Innovative Research*

- (JETIR), 2024; 11(10). Retrieved from <https://www.jetir.org/papers/JETIR2410139.pdf>
5. Tran, P., Pyo, Y. C., Kim, D. H., Lee, S. E., Kim, J. K., & Park, J. S. Overview of the manufacturing methods of solid dispersion technology for improving the solubility of poorly water-soluble drugs and application to anticancer drugs. *Pharmaceutics*, 2019; 11(3): 132.
 6. Sharma, D., Kumar, D., Sehwat, S., Kumar, D., & Kumar, S. Various Aspects of Solid Dispersion Technology: A Review. *Research Journal of Pharmacy and Technology*, 2025; 18(4): 1872-1878.
 7. Mohammed, E. A., Alfahad, M., & Qazzaz, M. E. Solid dispersion: Application and limitations. *Journal of Drug Delivery & Therapeutics*, 2024; 14(2): 222–232. <https://doi.org/10.22270/jddt.v14i2.6410>
 8. Nair, A. B., Singh, B., Shah, J., Jacob, S., Aldhubiab, B., Sreeharsha, N., ... & Shinu, P. Formulation and evaluation of self-nanoemulsifying drug delivery system derived tablet containing sertraline. *Pharmaceutics*, 2022; 14(2): 336.
 9. Kukde, D., & Bharkatiya, M. Formulation And Evaluation Of Sertraline Hydrochloride Tablet By Self Micro-Emulsifying Drug Delivery System For Solubility Enhancement.
 10. Al-Nimry, S. S., & Jaber, M. A. Preparation and optimization of sertraline hydrochloride tablets with improved dissolution through crystal modification. *AAPS PharmSciTech.*, 2017; 18(4): 1190-1202.
 11. Cipriani, A., Furukawa, T. A., Salanti, G., Chaimani, A., Atkinson, L. Z., Ogawa, Y., ... & Geddes, J. R. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. *The Lancet*, 2018; 391(10128): 1357-1366.
 12. Wikipedia contributors. (n.d.). *Sertraline*. In Wikipedia. Retrieved October 31, 2025, from <https://en.wikipedia.org/wiki/Sertraline>
 13. Farah, N., Bambarkar, S., Jannin, V., Kapadia, C., Nagarsenker, M., & Marwah, M. (2016, January 14). *Pharmaceutical composition comprising solid dispersion of BCS class II drugs with Gelucires* (Patent No. WO 2016005994 A2). World Intellectual Property Organization. <https://patents.google.com/patent/WO2016005994A2/en>
 14. Pawar, A. R., Choudhari, P. D., & Nidhane, A. B. Oral bioavailability enhancement of sertraline hydrochloride by nanoprecipitation and solvent diffusion techniques for stable nanosuspension. *Asian Journal of Pharmaceutics*, 2016; 10(3): S250-S257. <https://doi.org/10.22377/ajp.v10i03.762>
 15. Ammar, H. O., Ghorab, M. M., Mostafa, D. M., & Ghoneim, A. M. Spray dried self-nanoemulsifying drug delivery systems for sertraline HCl: Pharmacokinetic study in healthy volunteers. *Int J Pharm Sci Dev Res.*, 2018; 4(1): 009-19.
 16. Sarimova, B., & Cardello, L. M. *Antidepressant Drugs*, 2022; 308–324. Elsevier eBooks. <https://doi.org/10.1016/b978-0-12-820472-6.00044-x>
 17. Anusha, M., Banerjee, J., Padmalatha, H., & Chanda, R. Formulation and In-vitro Evaluation of Sertraline Liquid-Solid Compacts. *Pharmacological and Pharmaceutical Reports*, 2018; 1(2): 1-8.
 18. *How Do Antidepressants Work?* (n.d.). <https://my.clevelandclinic.org/health/treatments/9301-antidepressants-depression-medication>
 19. Sheffler, Z. M., Patel, P., & Abdijadid, S. (2023). Antidepressants. In *StatPearls [internet]*. StatPearls Publishing.
 20. Boyce, R. D., Hanlon, J. T., Karp, J. F., Kloke, J., Saleh, A., & Handler, S. M. A review of the effectiveness of antidepressant medications for depressed nursing home residents. *Journal of the American Medical Directors Association*, 2011; 13(4): 326-331.
 21. Chen, T., Cheng, L., Ma, J., Yuan, J., Pi, C., Xiong, L., ... & Zhao, L. Molecular mechanisms of rapid-acting antidepressants: New perspectives for developing antidepressants. *Pharmacological research*, 2023; 194: 106837.
 22. Zelek-Molik, A., & Litwa, E. Trends in research on novel antidepressant treatments. *Frontiers in Pharmacology*, 2025; 16: 1544795.
 23. Racagni, G., & Popoli, M. The pharmacological properties of antidepressants. *International Clinical Psychopharmacology*, 2010; 25(3): 117–131. <https://doi.org/10.1097/YIC.0B013E3283311ACD>
 24. Moraczewski, J., Awosika, A. O., & Aedma, K. K. (2023). Tricyclic antidepressants. In *StatPearls [Internet]*. StatPearls Publishing.
 25. Fasipe, O. J. Neuropharmacological classification of antidepressant agents based on their mechanisms of action. *Archives of Medicine and Health Sciences*, 2018; 6(1): 81–94. https://doi.org/10.4103/AMHS.AMHS_7_18
 26. Sheffler, Z. M., Patel, P., & Abdijadid, S. (2025). Antidepressants. *StatPearls Publishing*. <https://www.ncbi.nlm.nih.gov/books/NBK538182/>
 27. Stahl, S. M. Basic psychopharmacology of antidepressants, part 1: Antidepressants have seven distinct mechanisms of action. *The Journal of Clinical Psychiatry*, 1998; 59(4): 5–14. <https://www.psychiatrist.com/read-pdf/1759>
 28. Edinoff, A. N., Raveendran, K., Colon, M. A., Thomas, B. H., Trettin, K. A., Hunt, G., Kaye, A. M., Cornett, E. M., & Kaye, A. D. Selective Serotonin Reuptake Inhibitors and Associated Bleeding Risks: A Narrative and Clinical Review. *Health Psychology Research*, 2022; 10(4): 39580. <https://doi.org/10.52965/001c.39580>
 29. Lorman, W. J. Pharmacology Update: The Selective Serotonin Reuptake Inhibitors. *Journal of Addictions Nursing*, 2018; 29(4): 260–261. <https://doi.org/10.1097/JAN.0000000000000250>

30. Chu, A., & Wadhwa, R. (2023). *Selective serotonin reuptake inhibitors*. In **StatPearls [Internet]**. StatPearls Publishing. Retrieved November 1, 2025, from <https://www.ncbi.nlm.nih.gov/books/NBK555912/>
31. Elsevier Health. (n.d.). *Selective serotonin reuptake inhibitors (SSRIs)*. Retrieved November 1, 2025, from <https://elsevier.health/en-US/preview/selective-serotonin-reuptake-inhibitors-ssris>.
32. Marken, P. A., & Munro, J. S. Selecting a selective serotonin reuptake inhibitor: clinically important distinguishing features. *Primary care companion to the Journal of clinical psychiatry*, 2000; 2(6): 205.
33. Gartlehner, G., Hansen, R. A., Morgan, L. C., Thaler, K., Lux, L. J., Van Noord, M., Mager, U., Gaynes, B. N., Thieda, P., Strobelberger, M., Lloyd, S., Reichenpfader, U., & Lohr, K. N. (2011).
34. *Second-Generation Antidepressants in the Pharmacologic Treatment of Adult Depression: An Update of the 2007 Comparative Effectiveness Review*. Agency for Healthcare Research and Quality (US). <http://www.diva-portal.org/smash/get/diva2:810275/FULLTEXT01>
35. WebMD. (2024, June 7). *Types of antidepressants: SSRIs, SNRIs and more*. Retrieved November 1, 2025, from <https://www.webmd.com/depression/drugs-treat-depression>
36. Mayo Clinic Staff. (n.d.). *Selective serotonin reuptake inhibitors (SSRIs)*. In Mayo Clinic. Retrieved November 1, 2025, from <https://www.mayoclinic.org/diseases-conditions/depression/in-depth/ssris/art-20044825>
37. Tarivtla, L. P., & Reddy, M. S. An Overview of the Biopharmaceutics Classification System (BCS). *GSC Biological and Pharmaceutical Sciences*, 2021; 14(2): 217–221. <https://doi.org/10.30574/gscbps.2021.14.2.0012>
38. Samineni, R., Chimakurthy, J., & Konidala, S. Emerging role of biopharmaceutical classification and biopharmaceutical drug disposition system in dosage form development: A systematic review. *Turkish journal of pharmaceutical sciences*, 2022; 19(6): 706.
39. Seema, R., Ankur, R., Marwaha, R. K., Arun, N., & Rohilla, S. (2011). *Biopharmaceutics classification system: a strategic tool for classifying drug substances*.
40. Ku, M. S. Use of the biopharmaceutical classification system in early drug development. *The AAPS journal*, 2008; 10(1): 208-212.
41. Wu, C. Y., & Benet, L. Z. Predicting drug disposition via application of BCS: transport/absorption/elimination interplay and development of a biopharmaceutics drug disposition classification system. *Pharmaceutical research*, 2005; 22(1): 11-23.
42. U.S. Food and Drug Administration. (2021, May). *M9 Biopharmaceutics Classification System-Based Biowaivers: Guidance for Industry* (Guidance Document No. FDA-2018-D-3614). U.S. Department of Health and Human Services. Retrieved from <https://www.fda.gov/media/148472/download>
43. Polli, J. E., Yu, L. X., Mehta, M. U., Amidon, G. L., Zhao, H., Lesko, L. J., ... & Hussain, A. S. (2002). Biopharmaceutics classification system: the scientific basis for biowaiver extensions.
44. National Center for Biotechnology Information (2025). PubChem Compound Summary for CID 63009, Sertraline Hydrochloride. Retrieved October 28, 2025 from <https://pubchem.ncbi.nlm.nih.gov/compound/Sertraline-Hydrochloride>.
45. DrugBank. (n.d.). *Sertraline – DB01104*. Retrieved November 1, 2025, from <https://go.drugbank.com/drugs/DB01104>
46. ChemicalBook. (n.d.). *Sertraline hydrochloride (CAS 79559-97-0) — Chemical & physical properties* [Web page]. Retrieved November 1, 2025, from https://www.chemicalbook.com/ProductChemicalPropertiesCB8157645_EN.htm#chemi
47. National Center for Biotechnology Information (2025). PubChem Compound Summary for CID 68617, Sertraline. Retrieved November 1, 2025 from <https://pubchem.ncbi.nlm.nih.gov/compound/Sertraline>.
48. DrugBank. (n.d.). *Sertraline hydrochloride (Salts) — DBSALT000808*. Retrieved November 1, 2025, from <https://go.drugbank.com/salts/DBSALT000808>
49. Echemi. (n.d.). *Sertraline (CAS 79617-96-2) — Product PD1805103344*. Retrieved November 1, 2025, from <https://www.echemi.com/products/pd1805103344-sertraline.html>
50. De Vane, C. L., Liston, H. L., & Markowitz, J. S. Clinical pharmacokinetics of sertraline. *Clinical pharmacokinetics*, 2002; 41(15): 1247-1266.