RESEARCH PAPER

Formulation and Evaluation of Sildenafil Citrate-Fluoxetine Hydrochloride Capsules with Derivative Spectrophotometric Analysis

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Abstract

Background: Formulation development involves evaluating Preformulation characteristics, powder flow, excipient compatibility, dosage-unit quality, and drug-release behaviour. Reliable analytical methods are essential for the quantitative determination of active pharmaceutical ingredients.

Objective: To prepare and evaluate four capsule formulations containing sildenafil citrate and fluoxetine hydrochloride and summarize the performance of a derivative spectrophotometric method for their analysis.

Methods: Four formulations (F1-F4) were prepared using microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, colloidal silicon dioxide, and magnesium stearate. The recorded evaluations included physicochemical characteristics, powder-flow indices, FTIR, UV and derivative spectrophotometry, capsule quality attributes, in vitro dissolution, moisture uptake, capsule-lock integrity, and stability observations.

Results: The melting points of sildenafil citrate and fluoxetine hydrochloride were 188.2 ± 0.5°C and 159.1 ± 0.4°C, respectively. Carr's index ranged from 13.54% to 13.93%. Formulation F4 showed a disintegration time of 6.25 ± 0.10 min, moisture content of 2.21 ± 0.03%, and moisture uptake of 0.96 ± 0.02%. Sildenafil citrate release from F1-F4 at 30 min was 90.7%, 94.8%, 98.1%, and 100.0%, respectively. Fluoxetine hydrochloride release at 24 h was 90.23%, 92.45%, 91.63%, and 100.00%, respectively. The F4 assay values were 100.2% for sildenafil citrate and 100.0% for fluoxetine hydrochloride.

Conclusion: Formulation F4 demonstrated the most favourable capsule-quality and in vitro release results. However, inconsistencies in the source data, including calibration equations, LOD/LOQ assignments, precision-table labels, and selected statistics, must be resolved using the original laboratory records before definitive analytical validation claims can be made.

Keywords: Sildenafil Citrate; Fluoxetine Hydrochloride; Capsules; Preformulation; Derivative Spectrophotometry; FTIR; Dissolution; Formulation Evaluation.

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1. Introduction

Preformulation studies help characterize active pharmaceutical ingredients and inform the selection of excipients and processing conditions. For oral solid dosage forms, powder flow, dosage-unit uniformity, disintegration, dissolution and moisture-related properties are important quality attributes. Their evaluation helps compare formulation batches and identify candidates for further development [1]. Sildenafil citrate is a phosphodiesterase type 5 inhibitor used in the management of erectile dysfunction, whereas fluoxetine hydrochloride is a selective serotonin reuptake inhibitor primarily used for depressive and other psychiatric disorders. A combination of these agents requires a clear pharmacological rationale and a separate safety and regulatory assessment; in vitro formulation performance does not establish clinical efficacy or safety for erectile dysfunction [2]. UV spectrophotometry is used in pharmaceutical analysis, and derivative

spectrophotometry may help distinguish overlapping spectral responses when the method is suitably developed and validated. Analytical performance should be demonstrated for the intended application using appropriate evidence for specificity, calibration, accuracy, precision, range, detection and quantification limits [3]. This study compares four capsule formulations containing sildenafil citrate and fluoxetine hydrochloride and presents the Preformulation, analytical and in vitro evaluation data recorded in the study presentation. Source-data discrepancies are explicitly identified in a separate author-only verification section at the end of this file.

2. Materials and Methods

2.1 Materials

Sildenafil citrate and fluoxetine hydrochloride were the active ingredients. Microcrystalline cellulose and lactose monohydrate were used as diluents, croscarmellose sodium as a superdisintegrants, and colloidal silicon dioxide as a glident and magnesium stearate as a lubricant. The recorded media included distilled water, methanol, ethanol, 0.1 N hydrochloric acid and phosphate buffer at pH 6.8.

2.2 Preformulation studies

The active ingredients were visually examined for appearance, and the recorded melting points, moisture contents and particle sizes were compiled. Qualitative solubility was assessed in the media listed above. Bulk density and tapped density were calculated from the powder mass and measured volumes [4]. Carr's index was calculated as [(tapped density − bulk density)/tapped density] × 100, and Hausner ratio as tapped density/bulk density. Angle of repose was determined from the cone height and radius using $\theta = \tan^{-1}(h/r)$.

2.3 FTIR and UV spectrophotometry

FTIR spectra were over 400-4000 cm^{-1} for the pure active ingredients and physical mixtures with excipients. UV absorption maxima were recorded at 226 nm for sildenafil citrate and 263 nm for fluoxetine hydrochloride in 0.1 N HCl (pH 1.2). The calibration concentrations and absorbance readings were collated from the source slides [5].

2.4 Derivative spectrophotometry

The presentation described preparation of 100 µg/mL stock solutions in distilled water, preparation of working solutions over 30-90 µg/mL, conversion of zero-order spectra to first-order derivative spectra, and use of zero-crossing points at 226 nm and 263 nm. The presentation's summary table lists the derivative regression equations and validation results. Conflicting values appearing elsewhere in the same presentation are flagged in the author-only verification section [6].

2.5 Capsule preparation

Four powder blends were prepared with constant quantities of the two active ingredients, colloidal silicon dioxide and magnesium stearate, while the amounts of microcrystalline cellulose, lactose monohydrate and croscarmellose sodium were varied. Ingredients were weighed, passed through sieves #40/#60, blended, lubricated and filled into hard-gelatin capsules [7-8]. Capsule closure and visual appearance were inspected.

Table 1. Composition of capsule formulations F1-F4.

Ingredient (mg/capsule)	F1	F2	F3	F4
Sildenafil citrate	70	70	70	70
Fluoxetine hydrochloride	20	20	20	20
Microcrystalline cellulose	180	170	160	150
Lactose monohydrate	80	90	100	110
Croscarmellose sodium	10	15	20	25
Colloidal silicon dioxide	3	3	3	3
Magnesium stearate	2	2	2	2
Total fill weight	365	370	375	380

2.6 Evaluation of capsule formulations

Weight variation was assessed from the individual capsule weight in the source presentation. Drug content was evaluated using the recorded UV-Visible procedure. Disintegration was tested on six capsules per formulation [9]. The sildenafil citrate dissolution conditions were USP Apparatus II (paddle), 900 mL of 0.1 N HCl, 50 rpm and 37 ± 0.5°C, with sampling through 30 min. Fluoxetine hydrochloride release was over 24 h under the same medium, volume, apparatus, speed and temperature. Moisture content, moisture uptake and capsule-lock integrity were also recorded. Stability conditions listed in the presentation were 25 ± 2°C/60 ± 5% RH for long-term storage and 40 ± 2°C/75 ± 5% RH for accelerated storage [10].

3. Results

3.1 Preformulation characteristics

The preformulation results in Table 2 show that both drugs exhibited the crystalline appearance and melting points within their respective reference ranges. Sildenafil citrate and fluoxetine hydrochloride had moisture contents of 0.72 ± 0.03% and 0.58 ± 0.02%, respectively, with mean particle sizes of 85.4 ± 2.1 µm and 78.6 ± 1.8 µm. Their UV absorption maxima were 226 nm and 263 nm (Figure 1 and 2), respectively. The qualitative solubility observations in Table 3 showed differences between the drugs across the tested media, providing preliminary information for formulation and analytical studies.

Table 2. Preformulation characteristics

Parameter	Sildenafil citrate	Fluoxetine hydrochloride
Appearance	White/off-white crystalline powder	White crystalline powder

Melting point (°C)	188.2 ± 0.5	159.1 ± 0.4
Reference range (°C)	187-189	158-160
Moisture content (%)	0.72 ± 0.03	0.58 ± 0.02
Mean particle size (µm)	85.4 ± 2.1	78.6 ± 1.8
UV absorption maximum (nm)	226	263

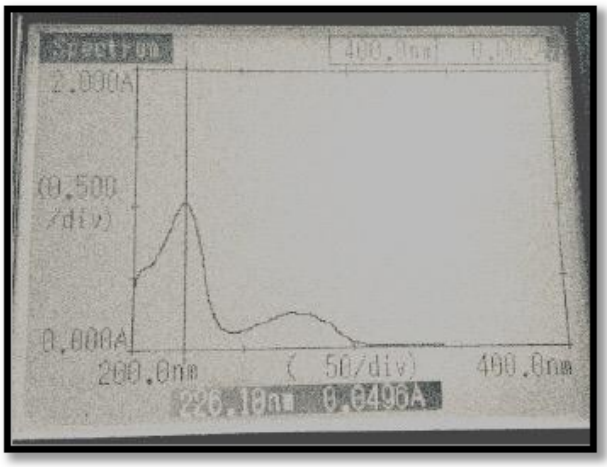


Figure 1. UV absorption spectrum of sildenafil citrate in 0.1 N HCl (pH 1.2).

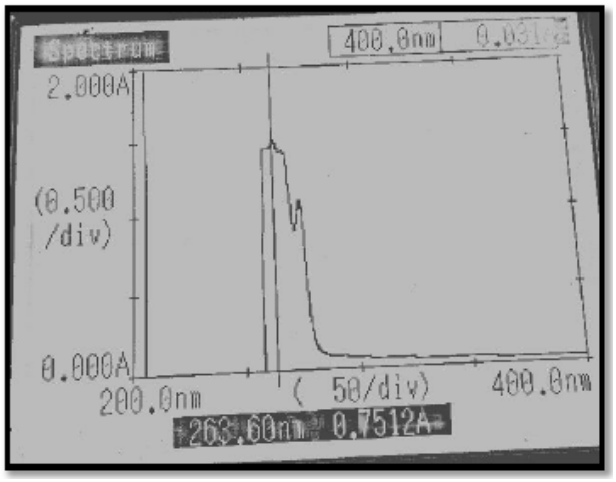


Figure 2. UV absorption spectrum of fluoxetine hydrochloride in 0.1 N HCl (pH 1.2).

Table 3. Qualitative solubility observations.

Medium	Sildenafil citrate	Fluoxetine hydrochloride
Distilled water	Slightly soluble	Freely soluble
Methanol	Soluble	Soluble
Ethanol	Slightly soluble	Soluble
0.1 N HCl	Freely soluble	Freely soluble
Phosphate buffer, pH 6.8	Soluble	Soluble

3.2 Powder-flow properties

As shown in Table 4, the bulk density of formulations F1-F4 ranged from 0.519 to 0.533 g/mL, while the tapped density ranged from 0.602 to 0.617 g/mL. Carr's index ranged from 13.54% to 13.93%, the Hausner ratio was 1.16, and the angle of repose ranged from 24.8° to 25.8°.

Table 4. Powder density and flow indices for F1-F4.

Parameter	F1	F2	F3	F4
Powder weight (g)	25	25	25	25
Bulk volume (mL)	48.2	47.6	47.2	46.9
Bulk density (g/mL)	0.519	0.525	0.530	0.533
Tapped volume (mL)	41.5	41.0	40.8	40.5
Tapped density (g/mL)	0.602	0.610	0.613	0.617
Carr's index (%)	13.79	13.93	13.54	13.61
Hausner ratio	1.16	1.16	1.16	1.16
Angle of repose (°)	25.8	24.8	25.2	24.9

3.3 FTIR analysis

The FTIR spectra of sildenafil citrate and fluoxetine hydrochloride showed characteristic absorption bands corresponding to their respective functional groups, as presented in Table 5. Sildenafil citrate exhibited bands at 1697.23 cm^{-1} (C=O), 2939.30 cm^{-1} (C-H), 3305.50 cm^{-1} (N-H), and 1172.63 cm^{-1} (S=O). Fluoxetine hydrochloride showed characteristic bands at 1612.37 cm^{-1} (N-H bending), 2954.73 cm^{-1} (C-H), 486.03 cm^{-1} (C-F), and 1326.93 cm^{-1} (C-O). The corresponding bands for the physical mixtures are also listed in Table 5. The spectra of the pure drugs and their physical mixtures are shown in Figures 3-6. These spectral observations provide preliminary information for assessing drug-excipient compatibility; however, peak positions alone are insufficient to confirm the absence of chemical interactions.

Table 5. FTIR band positions for the pure drugs and physical mixtures.

Drug / mixture	Functional group assignment	Observed band (cm^{-1})
Sildenafil citrate	C=O stretching	1697.23
Sildenafil citrate	C-H stretching	2939.30
Sildenafil citrate	N-H stretching	3305.50
Sildenafil citrate	S=O stretching	1172.63
Fluoxetine hydrochloride	N-H bending	1612.37
Fluoxetine hydrochloride	C-H stretching	2954.73

Fluoxetine hydrochloride	C-F stretching	486.03
Fluoxetine hydrochloride	C-O stretching	1326.93
Sildenafil citrate physical mixture	C=O stretching	1668.45
Sildenafil citrate physical mixture	C-H stretching	2890.23
Sildenafil citrate physical mixture	N-H stretching	3348.49
Sildenafil citrate physical mixture	S=O stretching	1201.52
Fluoxetine hydrochloride physical mixture	N-H bending	1632.20
Fluoxetine hydrochloride physical mixture	C-H stretching	2912.28
Fluoxetine hydrochloride physical mixture	C-F stretching	587.36
Fluoxetine hydrochloride physical mixture	C-O stretching	1288.23

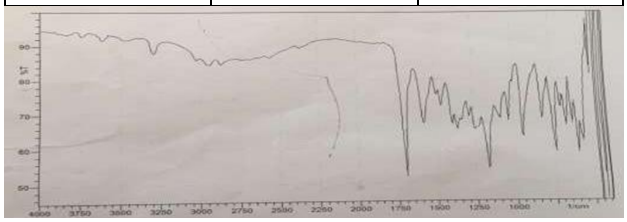


Figure 3. FTIR spectrum of pure standard and experimental sildenafil citrate.

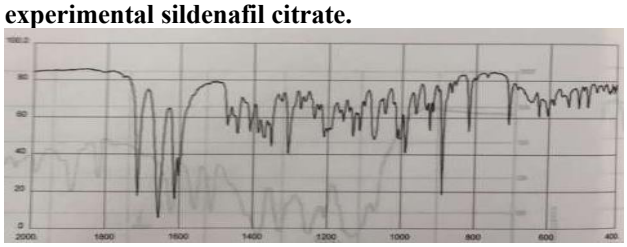


Figure 4. FTIR spectrum of pure standard and experimental fluoxetine hydrochloride.

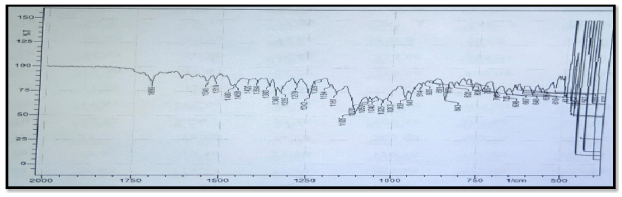


Figure 5. FTIR spectrum of sildenafil citrate with the physical excipient mixture.

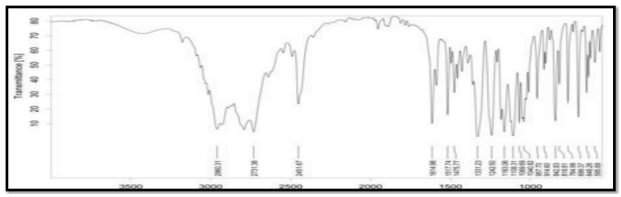


Figure 6. FTIR spectrum of fluoxetine hydrochloride with the physical excipient mixture.

3.4 UV calibration data

The UV calibration observations for sildenafil citrate and fluoxetine hydrochloride at concentrations ranging from 10 to 50 µg/mL are presented in Table 6. Both drugs showed an increase in mean absorbance with increasing concentration, indicating a concentration-dependent response over the tested range. The calibration plots for sildenafil citrate and fluoxetine hydrochloride are shown in Figures 7 and 8, respectively.

Table 6. UV calibration observations transcribed from the source slides (n = 3).

Concentration (µg/mL)	Sildenafil citrate absorbance (mean ± SD)	Fluoxetine hydrochloride absorbance (mean ± SD)
10	0.247 ± 0.002	0.240 ± 0.002
20	0.407 ± 0.003	0.418 ± 0.002
30	0.600 ± 0.002	0.525 ± 0.001
40	0.686 ± 0.011	0.649 ± 0.0015
50	0.819 ± 0.001	0.801 ± 0.0015

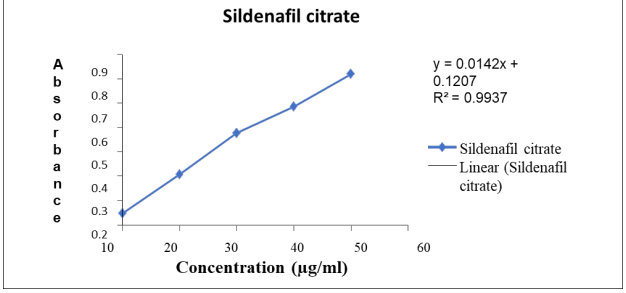


Figure 7. Calibration plot of sildenafil citrate

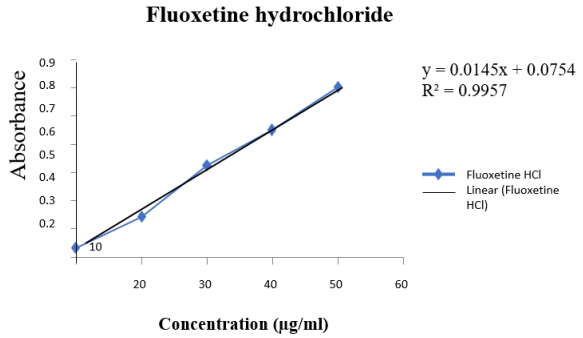


Figure 8. Calibration plot of fluoxetine hydrochloride

3.5 Derivative spectrophotometric method

The derivative spectrophotometric results are presented in Table 7. Both drugs showed a linearity range of 30-90 µg/mL, with correlation coefficients of 0.9976 for

sildenafil citrate and 0.9966 for fluoxetine hydrochloride. The intraday and interday %RSD values indicate the precision of the method, while the LOD and LOQ values represent its detection and quantification limits.

Table 7. Derivative spectrophotometric

Parameter	Sildenafil citrate	Fluoxetine hydrochloride
Linearity range (µg/mL)	30-90	30-90
Regression equation	y = 0.0008x − 0.0116	y = 0.0003x + 0.0008
Correlation coefficient (r)	0.9976	0.9966
Intraday %RSD range	0.73-1.59	0.92-1.78
Interday %RSD range	0.91-1.71	0.89-1.70
LOD (µg/mL)	1.45	2.85
LOQ (µg/mL)	4.39	8.65

3.6 Recovery study

The recovery results are summarized in Table 8. Sildenafil citrate showed recoveries ranging from 99.03% to 100.00%, while fluoxetine hydrochloride showed recoveries ranging from 100.25% to 100.93%. These results indicate recovery values close to 100% at the levels. The total concentration in the final fluoxetine hydrochloride row should be verified because it does not match the sum of the stated amounts taken and added.

Table 8. Recovery study results for sildenafil citrate and fluoxetine hydrochloride.

Drug	Amount taken (µg/mL)	Amount added (µg/mL)	Total concentration (µg/mL)	Amount found (µg/mL)	Recovery, mean ± SD (%)
Sildenafil citrate	40	32	72	72.39	100.00 ± 1.44
Sildenafil citrate	40	40	80	79.70	99.63 ± 0.64
Sildenafil citrate	40	48	88	87.15	99.03 ± 0.24
Fluoxetine hydrochloride	16	12.8	28.8	28.90	100.38 ± 1.00
Fluoxetine hydrochloride	16	16	32	32.29	100.93 ± 0.66
Fluoxetine hydrochloride	16	35.2	35.2	35.37	100.25 ± 1.24

3.7 Capsule quality attributes

The quality attributes of formulations F1-F4 are presented in Table 9. Mean capsule weight increased from 364.9 mg for F1 to 380.0 mg for F4, while disintegration time decreased from 11.97 to 6.25 min. Drug content increased across the formulations, reaching 100.05 ± 0.17% for F4. Moisture content and moisture uptake also decreased progressively, with F4 showing the lowest values. The assay results in Table 10 showed increasing drug content across F1-F4. Formulation F4 exhibited assay values of 100.2% for sildenafil citrate and 100.0% for fluoxetine hydrochloride, representing the highest values among the four batches.

Table 9. Comparative quality attributes of capsule formulations F1-F4.

Parameter	F1	F2	F3	F4
Mean capsule weight (mg), slide 38	364.9 ± 3.3	370.3 ± 2.9	375.1 ± 2.3	380.0 ± 0.7
weight variation	±1.40 %	±1.12 %	±0.82 %	±0.18 %
Drug content (%, mean ± SD)	95.08 ± 0.79	97.27 ± 0.49	98.91 ± 0.30	100.05 ± 0.17
Disintegration time (min, mean ± SD)	11.97 ± 0.22	10.72 ± 0.15	8.90 ± 0.14	6.25 ± 0.10
Moisture content (%, mean ± SD)	3.18 ± 0.07	2.91 ± 0.04	2.71 ± 0.03	2.21 ± 0.03
Moisture uptake (%, mean ± SD)	2.19 ± 0.05	1.83 ± 0.05	1.49 ± 0.03	0.96 ± 0.02

Table 10. Assay results of sildenafil citrate and fluoxetine hydrochloride in capsule formulations F1-F4.

Capsule	Sildenafil citrate assay (%)	Fluoxetine hydrochloride assay (%)
F1	95.8	96.2
F2	97.5	97.8
F3	99.1	99.3
F4	100.2	100.0

3.8 In vitro dissolution

The in vitro dissolution profiles of sildenafil citrate and fluoxetine hydrochloride from formulations F1-F4 are presented in Tables 11 and 12, respectively. As shown in Table 11, sildenafil citrate release increased with time for all formulations. Formulation F4 showed the highest

release, reaching 99.9% at 15 minutes and 100.0% at 20 minutes, whereas F1 reached 90.7% at 30 minutes. Similarly, the fluoxetine hydrochloride release data in Table 12 showed an overall increase in drug release over 24 hours. Formulation F4 exhibited the highest release, reaching 100.0% at 24 hours, compared with 90.23%, 92.45%, and 91.63% for F1, F2, and F3, respectively. The dissolution profiles are given in Figures 9 and 10. F4 demonstrated the highest drug release for both active ingredients among the tested formulations

Table 11. *In-vitro* release of sildenafil citrate from F1-F4.

Time (min)	F1 (%)	F2 (%)	F3 (%)	F4 (%)
5	71.4	75.4	83.6	85.7
10	76.7	80.3	89.1	95.9
15	83.2	87.4	91.3	99.9
20	88.8	91.0	97.4	100.0
30	90.7	94.8	98.1	100.0

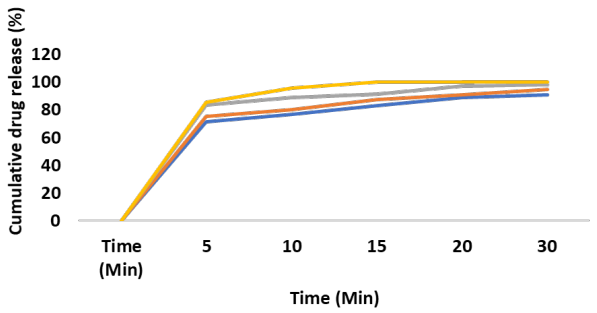


Figure 9. *In-vitro* Dissolution Profiles of Sildenafil Citrate from formulations F1-F4.

Table 12. *In-vitro* release of fluoxetine hydrochloride from F1-F4.

Time (h)	F1 (%)	F2 (%)	F3 (%)	F4 (%)
1	17.58	22.12	28.15	34.25
2	25.55	26.78	28.67	38.18
3	44.54	37.27	42.4	43.25
4	54.77	43.1	45.4	47.33
5	58.15	47.42	50.52	70.12
6	62.22	54.22	55.35	78.54
7	68.45	61.85	60.45	88.45
8	72.78	76.75	67.1	90.12
12	78.61	77.78	79.23	95.12
16	82.12	84.41	82.45	98.12
20	88.32	89.12	84.85	99.99
24	90.23	92.45	91.63	100.0

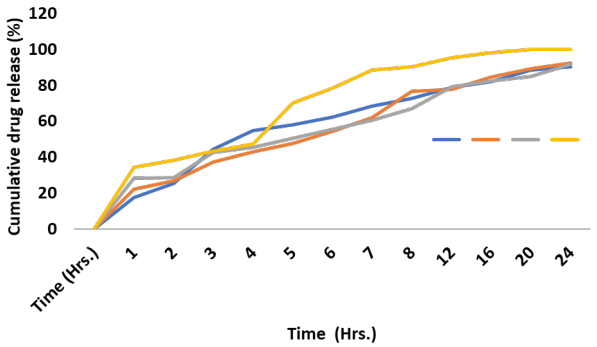


Figure 10. *In-vitro* release profiles of fluoxetine hydrochloride from formulations F1-F4.

3.9 Appearance, capsule lock and stability observations

All four formulations as uniform in colour and oval in shape, with smooth surfaces and no cracks, dents, leakage or powder deposition in its general physical-appearance assessment. A separate capsule-lock assessment records partial locking, minor separation and slight leakage for Batch 1; good locking with occasional leakage for Batch 2; no separation or leakage for Batch 3; and excellent locking without visible separation or leakage for Batch 4.

Table 13. Stability observations result

Batch	Condition	Physical Appearance	Drug-Content Stability	Assessment
F1	Accelerated	Slight discoloration	92-94%	Unstable
F2	Accelerated	Slight change	94-96%	Marginal stability
F3	Long-term	No significant change	97-98% stable	Stable
F4	Long-term + accelerated	No change in appearance	98-100% stable	Highly stable (as labelled in source)

4. Discussion

The preformulation findings indicated that both drugs exhibited the crystalline appearance and melting points within the specified reference ranges. Powder-flow properties were comparable across F1-F4, with Carr's index values of 13.54-13.93%, a Hausner ratio of 1.16, and an angle of repose of 24.8-25.8°. FTIR analysis showed characteristic absorption bands for the pure drugs and their physical mixtures, providing preliminary information for assessing drug-excipient compatibility. The UV calibration data showed an increase in absorbance with increasing concentration. However, discrepancies between the calibration equations and absorbance values, along with inconsistencies in the derivative method's precision and LOD/LOQ assignments, require verification before the analytical method can be considered fully validated.

Among the four formulations, F4 showed the most favourable results, including the shortest disintegration time, lowest moisture content and moisture uptake, and highest drug release for both active ingredients. However, inconsistencies in weight-variation data and incomplete stability results limit definitive conclusions regarding product quality, stability, and shelf life. Further verification of the original experimental records is necessary before making claims of pharmacopeial compliance or clinical effectiveness.

5. Conclusion

Four capsule formulations containing sildenafil citrate and fluoxetine hydrochloride were evaluated using preformulation, analytical, and in vitro quality assessments. Formulation F4 showed the most favourable results, with a disintegration time of 6.25 ± 0.10 min, moisture content of 2.21 ± 0.03%, moisture uptake of 0.96 ± 0.02%, assay values of 100.2% and 100.0%, respectively, and drug release of 100.0% for both drugs at the final sampling points. Nevertheless, the analytical findings and stability conclusions remain provisional until the discrepancies in the source data are resolved. Further experimental verification and stability assessment are required before drawing definitive conclusions about the formulation's suitability.

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