

Formulation and Evaluation of Immediate-Release Quetiapine Fumarate Tablets

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ABSTRACT

Antipsychotic medications can help manage the symptoms of schizophrenia. Several demographic and scientific elements have the potential to influence the choice of unusual neuroleptic drugs. Bipolar disorder and schizophrenia can be treated with quetiapine fumarate. When making tablets and hard-shell capsules, disintegrating agents are often utilized ingredients. The primary goal of this study was to develop a dependable immediate-release tablet formulation of the antipsychotic quetiapine. Tablets' enhanced stability and simulated tamper resistance, along with their lower cost, packaging, and delivery, make them popular. Faster-dissolving oral tablets have a higher bioavailability and shorter absorption time. Drugs should dissolve or disintegrate in the stomach shortly after absorption. The most common breakdown agent used in tablet manufacturing is starch. Along with developing a pharmaceutically equivalent instantaneous-release tablet for people with mental illnesses such as bipolar disorder and schizophrenia, this initiative aims to develop a chemically and physically stable generic formulation for the treatment of schizophrenia.

Keywords: In-vitro release, Quetiapine fumarate, Wet granulation, Film-coated, Immediate release

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Introduction

By altering the chemical equilibrium in the brain, antipsychotic drugs can help manage the symptoms of schizophrenia. Medication is merely one component of a comprehensive treatment approach; there is no cure for schizophrenia. The selection of atypical antipsychotic medications is influenced by several clinical and demographic factors. Numerous linear anatomic Magnetic Resonance Imaging (MRI) investigations have revealed growing abnormalities in the brain in individuals with schizophrenia [1, 2]. Bipolar disorder and schizophrenia are treated with quetiapine fumarate. In the brain, it attaches itself to dopamine D1 and D2 sensory receptors as well as serotonin 5HT2 and 5HT1A receptors. Its use is said to result in fewer additional pyramidal symptoms and neuroleptic traits [3].

The preferred and most advised method of administration for therapeutic agents with systemic influence is oral pharmaceutical delivery. Oral drug delivery systems can be classified as Immediate-release, Controlled, and Targeted preparations (IR, CR, and TR) [4].

Disintegrants are chemicals used in tablet production to aid in the dispersion of the dose formulation matrix in dissolving fluids and the diffusion of humidity. Starch has long been the main disintegrant in tablet manufacture and is still used extensively today [5].

Medications must be portable, leave lower residue in the mouth after oral transference, and be able to endure environmental factors such as heat and moisture. They should also disintegrate or dissolve fast in the stomach and begin functioning quickly [6, 7].

According to a study, tablets of immediate-release are more effective than tablets of sustain-release in treating schizophrenia. A 2015 study by Bonafede *et al.* found that patients with acute bipolar mania had a higher chance of being released from the hospital within a few days [8, 9].

Most positive symptoms can be effectively treated with first-generation antipsychotic drugs, which are primarily dopamine D2 receptor antagonists. Quetiapine fumarate is more soluble in 0.1 N HCl, which is concurrent with gastric acid media, so it can be utilized as a dissolution medium [10].

Schlender *et al.* investigated the rising prevalence of drug therapy for psychotic disorders. Based on that, the business might gain from this formulation in the future. He concluded that the need for dig is constantly growing because the demand for the drug was constantly rising [11].

An antipsychotic is quetiapine fumarate. **Figure 1** displays quetiapine fumarate's structure and chemical name. Among other things, it is used to treat bipolar disorder and schizophrenia. Bipolar disorder is associated with substantial depressed episodes as well as manic episodes. The medication functions by blocking dopamine D2 receptors, 5-HT₂, and serotonin (5-hydroxytryptamine) receptors [12].

Schizophrenia is treated with quetiapine fumarate. When taking more medication, helps maintain clinical improvement in individuals who have first responded to treatment. It is also advised for the prevention of recurrence in patients experiencing moderate to severe manic episodes [13].

The risk of developing schizophrenia is highest in boys aged 15–24 years and females aged 25–35 years. In 1910, Swiss psychiatrist Eugen Bleuler (1857–1939) came up with the term schizophrenia. Finding the symptoms and indicators is the first stage [14]. A neuroleptic medication called quetiapine fumarate is being evaluated as a treatment for schizophrenia and bipolar disorder (BD). The medication functions by blocking dopamine D2 receptors and receptors of serotonin (5-hydroxytryptamine) 5-HT₂ [15].

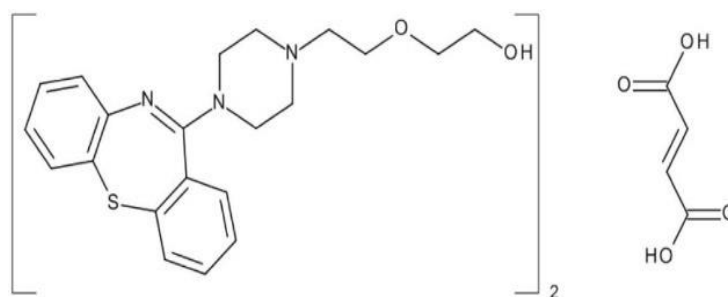


Figure 1. Quetiapine fumarate structure

2-[2-(4-benzo[b][1,4]benzothiazepin-6-yl)piperazin-1-yl]ethoxy]ethanol; but-2-enedioic acid is its IUPAC name.

A type of drug delivery system called immediate release formulation (API) is used to treat mental illnesses like schizophrenia, bipolar disorder, epilepsy, and other conditions where rapid activity onset and drug pharmacological effects are required. It was created with affordability, portability, and precise and convenient patient administration in mind [16-18].

The primary goal of creating a reference product generic version is to supply the market with high-quality, reasonably priced goods. Enhanced patient compliance and an immediate release of medication with fewer adverse effects than other kinds of antidepressants. If enough information about solubility and permeability is supplied, the bio waiver is applicable. In addition to creating a pharmaceutically comparable instantaneous-release tablet for consumption by those suffering from mental illnesses like schizophrenia and bipolar disorder (MND), the study aims to create a stable generic formulation for treating schizophrenia that is both chemically and physically compatible.

Materials and Methods

Nifty Labs Ltd, India presented a gift instance of quetiapine fumarate IP. Microcrystalline cellulose NF (Avicel pH 112) and Microcrystalline cellulose EP (Avicel pH 101) were obtained from FMC Biopolymer (Ireland). Lactose monohydrate EP (Pharmatose 200M) was provided by DFE Pharma (India). Dibasic calcium phosphate dehydrates USP was obtained from Innophos (Chicago). Sodium Starch Glycolate USP (Type A) was provided from DMV-Fonterra Excipient (India). Povidone USP (PVPK-30) was obtained from ISP Private Ltd (India). Talc

USP was provided by Luzenac Pharma (Italy). Magnesium Stearate USP was obtained from Ferro Corporation (Cleveland). Opadry White was obtained from Colorcon Asia Pvt. Ltd. (Goa).

Drug-excipient adaptability study

Blends of drug ingredients and excipients were subjected to a range of humidity and temperature levels. Dry storage was provided for the mixture in sealed clear glass vials. Following an initial examination, the samples were observed weekly for a maximum of 30 days to check for changes in appearance. The spectra for quetiapine fumarate and tablet formulation were obtained using KBr and a Fourier transform infrared spectrometer (FTIR 1615, Perkin Elmer, USA) [19].

Preformulation study

Preformulation is carried out when a recently produced medication exhibits sufficient pharmacological action in animals to be beneficial in humans. These studies focus on the physicochemical characteristics of the substance, which affect how well the medicine works and how it develops into an efficient dosage form. Testing the preformulation removes any possible obstacles to creating efficient dosage forms [20].

DSC studies

The DSC 60, made by Shimadzu in Japan, was used to analyze each sample. In the studies, samples were prepared in aluminum pans. Calibrations of temperature were performed by indium as a reference. Quetiapine fumarate and excipients-containing medications were utilized in this study [21].

XRD studies

The spectra of compressed tablets, granules, quetiapine fumarate, and its constituents were documented. The XRD spectra of different formulations show no discernible variations in peak height. The excipients were found to be compatible with each other and to differ minimally [22].

Preparation of quetiapine fumarate IR tablets

The glatt-powder-coater-granulator (GPCG) wet granulated quetiapine fumarate IR tablets utilizing the following procedures [23]. **Table 1** displays the formula employed in different batches of quetiapine fumarate.

Dispensing

Each component, such as microcrystalline cellulose (Avicel pH 101), sodium starch glycolate (type A), lactose monohydrate, quetiapine fumarate, dibasic calcium phosphate dihydrate, and povidone (PVP K-30), was weighed independently.

Sifting

The above pharmaceutical ingredients and excipients were sifted through a 30# mesh. Binder solution preparation PVPK-30 was solved in filtered water and swirled until a clear dilution was achieved. This mixture was employed as a binder.

Top spraying

The super-dried granules after spraying the binder solution were passed through a 20# mesh through the top spray in a Glatt powder granulator with the following parameters: Fan speed: 45%, spraying speed: 1 g/min, Nozzle diameter: 1 mm, temperature of inlet: 60 °C, temperature of outlet: 50 °C, and temperature of product: 45 °C.

Prelubrication

All of the components— dibasic calcium phosphate dihydrate, sodium starch glycolate (type A), and microcrystalline cellulose (Avicel pH 112)—were weighed based on the amount of dry granules they produced and then sieved through a 40 # mesh screen. For ten minutes, the above-sifted components were combined with dried grains in a Pillar Type Bin mixer.

Lubrication

The materials, Purified Talc and Magnesium Stearate, were measured based on the dried granules yield and then sieved using mesh 60 #. In a Pillar Type Bin blender, lubricated substances were mixed with the previously indicated sifting elements for 3 min. This combination was presently used to compress pills.

Compression

In "B" tooling, 11.0 mm plain round standard concave punches were used to compress the lubricated blend. Stick both punches and turrets, these are the crucial measures for the drug. Using both talc and magnesium stearate during the lubrication steps will solve this issue.

Several factors, including the tablet's weight, hardness, breakdown times, and friability, become increasingly significant during these phases.

Table 1. Quetiapine fumarate IR tablet formulation

Sr. No.	Ingredient (mg/tab)	Batch number of formulation							
		F1	F2	F3	F4	F5	F6	F7	F8
A-Dry Mix									
1	Quetiapine fumarate	200	200	200	200	200	200	200	200
2	Microcrystalline cellulose (Avicel pH 101)	75	100	125	150	75	100	125	150
3	Lactose monohydrate (Pharmatose 200M)	50	50	50	50	50	50	50	50
4	Sodium starch glycolate (type A)	18	18	18	18	18	18	18	18
B-Binder Solution									
5	Povidone K-30	15	15	15	15	20	20	20	20
6	Purified water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
C-Prelubrication									
7	Microcrystalline cellulose (Avicel pH 112)	40	40	40	40	40	40	40	40
8	Sodium starch glycolate (type A)	18	18	18	18	18	18	18	18
9	Dibasic calcium phosphate dihydrate	20	20	20	20	20	20	20	20
D-Lubrication									
10	Magnesium stearate	8	8	8	8	8	8	8	8
11	Purified Talc	6	6	6	6	6	6	6	6
Target weight (mg)		450	475	500	525	455	480	505	530
E-Coating (2% coating)									
12	Opadry white	9	9.5	10	10.5	9.1	9.6	10.1	10.6
Target weight (mg) coated		459	484.5	510	535.5	464.1	489.6	515.1	540.6

Quetiapine fumarate IR tablets evaluation

Pre-compression features

Pre-compression metrics included Hausner's ratio, tapped density, loss on drying, bulk density, compressibility index, and angle of repose. The findings are presented in **Table 2** [24].

Loss on drying (LOD)

The Halogen Moisture Analyser was used to measure the greased granules' humidity. The compound was heated to 105 °C for one gram until the apparatus observed no change in weight [25]. The weight decrease % was disclosed.

$$\text{LOD (\%)} = (\text{Initial weight} - \text{Final weight}) / \text{Initial weight} \times 100 \quad (1)$$

The repose angle is the greatest angle that a pile of powder or grains can form with the horizontal plane [26]. This characteristic is related to particle friction or resistance to particle motion.

$$\theta = \tan^{-1} h/r \quad (2)$$

Where, r = heap circle base radius, h = heap height, and θ = angle of repose.

Density calculation

The volume of powder is measured using a graded cylinder attached to a motorized taping mechanism with a properly cut revolving shaft. The tapings should not result in grain abrasion or a variation in the tested substance's unit size distribution to guarantee repeatability [27].

$$\text{Density of bulk (g/ml)} = \text{Sample weight in gm/Volume engaged by the sample (ml)} \quad (3)$$

The compressibility index has been measured using size, shape, bulk density, material coherence, moisture content, and surface area. Both the density of bulk and the tapped powder density are measured to compute the compressibility index and Hausner's ratio.

$$\text{Index of compressibility} = (\text{Tapped density} - \text{Bulk density})/\text{Tapped density} \times 100 \quad (4)$$

$$\text{Hausner's ratio} = \text{Tapped density/bulk density} \quad (5)$$

Post-compression evaluation parameters

The compressed tablets were investigated for disintegration time, drug content homogeneity, weight variation, friability, thickness, and hardness in vitro dissolution [28, 29].

Hardness

How well a tablet can endure mechanical shocks when handling depends on its hardness. The tablet's hardness was determined by Schleuniger's hardness tester. Ten tablets were selected at random to assess each formulation's hardness, and the mean was calculated for each formulation. **Table 2** displays the findings.

Thickness

The tablets in each batch were measured for thickness and width using digital vernier calipers. The millimeters were measured, and the average was computed. **Table 2** displays the findings.

Friability

The Roche Friabilator assessed it. Percentages (%) are used to measure this. Initially, ten weighted tablets were placed in the friabilator (W_{initial}). After that, it was spun at 25 rpm for 4 minutes. Once more, the tablets were weighed (W_{final}). The percentage of friability was calculated by:

$$F = [(W_{\text{initial}} - W_{\text{final}}) / W_{\text{initial}}] \times 100 \quad (6)$$

It is considered acceptable for tablets to have a friability percentage below 1%. Friability was presented as a mass loss and determined as the initial mass percentage. The findings are provided in **Table 2**.

Weight variation

After randomly weighing twenty tablets, the average weight was determined. Just two of the individual weights perverted from the average weight using more than the percentage. The findings are displayed in **Table 2**.

Determination of drug content

20 tablets were powdered and weighed. 100 milliliters of 6.8 pH phosphate buffer were used to dilute 25 milligrams of quetiapine fumarate powder, which was then thoroughly sieved. A UV-visible spectrophotometer set to 254 nm was then used to measure the drug's concentration after the sample had been diluted with an appropriate solvent [30, 31].

Disintegration time

A tablet disintegration test apparatus was used to measure the decomposition time of each formulation. After the six tablets, the discs were placed into the disintegration test kit's tubes. The water's temperature was maintained at 37 ± 2 °C, and the entire tablet's decomposition time was noted. The outcome is displayed in **Table 2**.

In-vitro solution

The tablets of quetiapine were subjected to these tests for $\frac{3}{4}$ hour in water. The drug release test was conducted using 900 milliliters of dissolving solution. The temperature was maintained at 37 ± 0.5 °C while the speed of the paddle was set at 100 rpm. They were then compared in two different media: pH 4.5 acetate buffer and 0.1 N HCl. Materials were filtered using Whatman filter paper (no. 41), then diluted and examined at 254 nm by a UV-visible double-beam spectrophotometer. The medication release from innovative formulations and batches F1 and F8 is shown as a percentage in **Figure 2**.

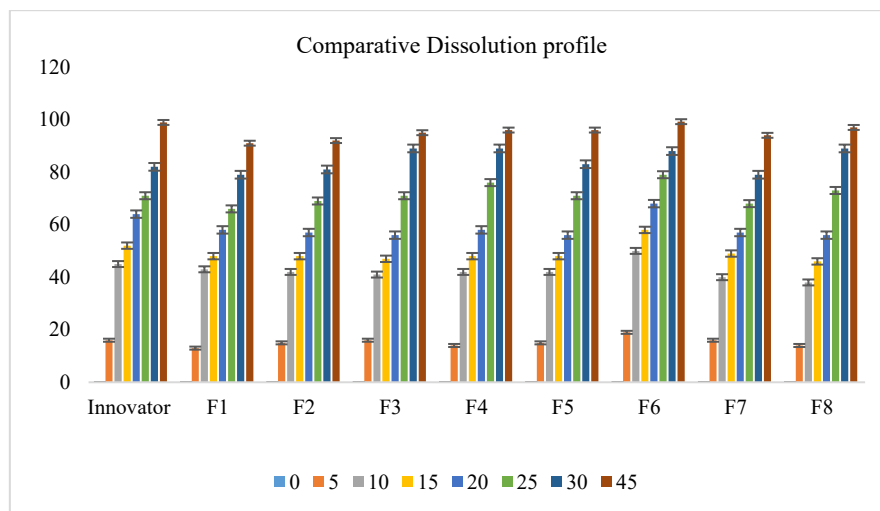


Figure 2. The comparative dissolution profile of batch F1- F8 and innovator product

Calculation of dissimilarity and similarity (f1 and f2) factor

Dissimilarity Factor (f1): To calculate the dissimilarity, contrasted from a pioneer or a locus invention. The factor of dissimilarity (f1) must never be more than 15 (f1 ≤ 15).

$$f_1 = \frac{\sum R_t - T_t}{\sum R_t} \times 100 \quad (7)$$

Factor of similarity (f2)

The reciprocal logarithmic transformation of the square root of one (f2) was used to multiply the mean squared difference in the content % between the reference and test products to determine the similarity factor. To compare the outcomes with reference release profiles, this was calculated [32].

$$f_2 = 50 \times \log_{10} \times \frac{1}{\sqrt{1 + 1/n \times \sum (R_t - T_t)^2}} \times 100 \quad (8)$$

Where, n= number of sampling points.

The method is suitable for comparing dissolution profiles when there are over four dissolution time points; nevertheless, it is limited to T_t and R_t having a mean disparity of ≤ 100 ; if the distinction exceeds 100, the data must be normalized. Having a factor of similarity (f_2) > 50 ($f_2 > 50$) at all times.

Comparison with marketed product

The final product's potential was evaluated using several criteria after the yield was numerically confirmed and examined for tablet characteristics. **Figure 3** displays the results of the following quality control tests conducted on commercially available tablets, specifically the AstraZeneca Seroquel tablet.

Stability studies

The most promising batch F6 tablet formulation was tested for stability following ICH Q1A (R2) guidelines. By giving information on how a drug or product's potential changes over time owing to various factors of environmental including light, warmth, and moisture, stability testing makes it possible to determine the best storage conditions and shelf lives [33].

To perform the current investigation, the produced pills were stored for 3 months at 40 degrees Celsius and 75% relative humidity in dense, airtight polyethylene bottles. The samples were taken on the 15th, 30th, 60th, and 90th days. In vitro dissolving experiments were used to evaluate the tablets' exterior appearance, stiffness, breadth, and percentage of drug content.

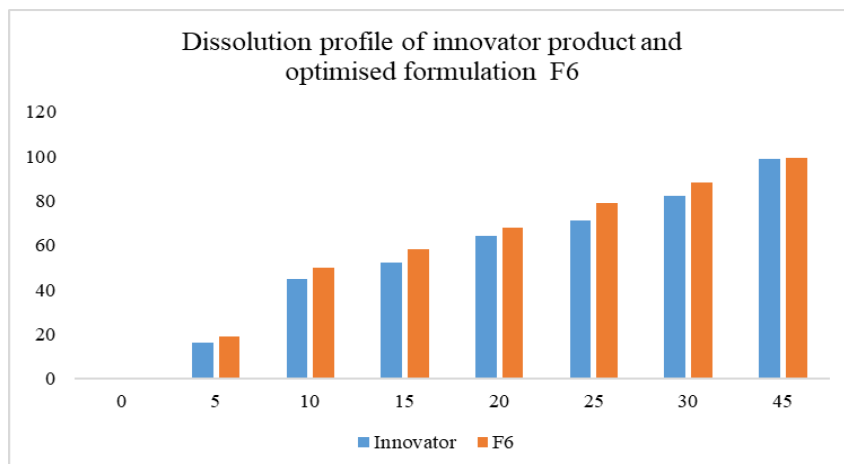
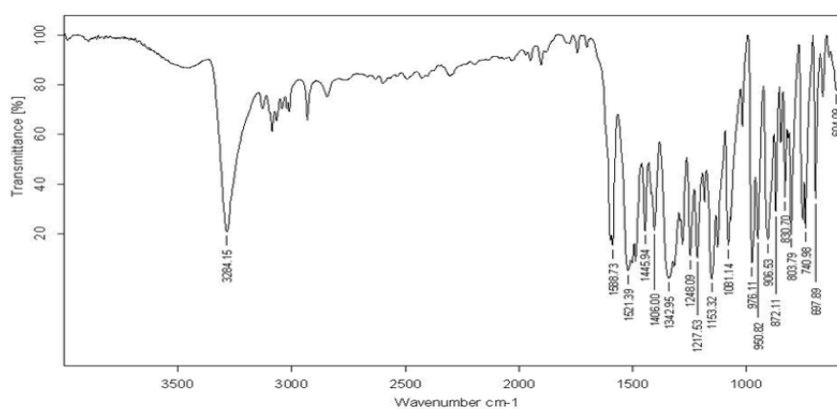


Figure 3. The comparative dissolution profile of optimized formulation and innovator product, F6

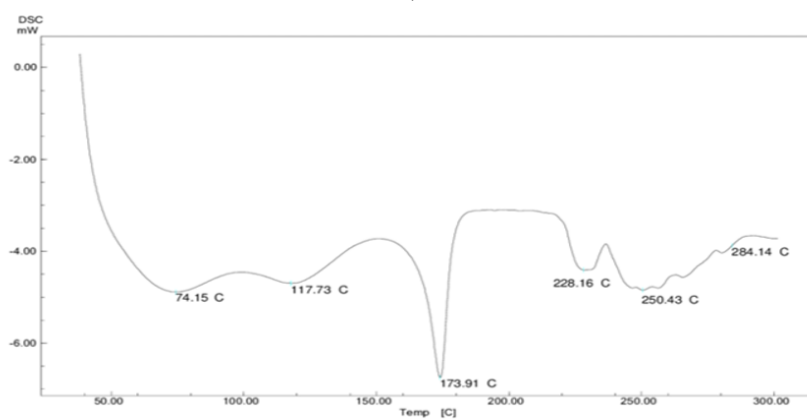
Results and Discussion

Compatibility of drug-excipient

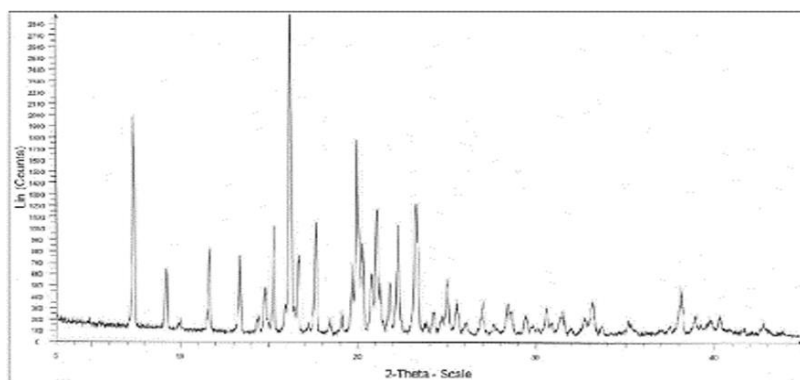
The drug-excipient compatibility of quetiapine was evaluated using a range of excipient groups. The results showed that there was no chemical contact between the parts and the medications. The results of the compatibility of drug-excipient investigations employing X-RD, DSC, and IR analyses are displayed in **Figures 4a-4c**.



a)



b)



c)

Figure 4. a) Quetiapine fumarate IR spectra, b) quetiapine fumarate DSC, and c) X-RD investigation of quetiapine fumarate

Parameters of pre-compression

By drying at 60 °C and using the optimal desiccating time to achieve LOD at a special threshold, the dehydrated grains' LOD was maintained at that level of NMT 1% discrepancy. According to the computations, the drug and its constituents had a theoretical wetness of 2% w/w. The LOD ranged from 1.51%-3.17% w/w. **Table 2** presents the findings.

Features of powder flow

The ideal method for granulating the powder mixture depends critically on the flow properties of the powder that is ready for compression for every given formulation. Therefore, the drug flow was analyzed before selecting a granulation technique. The direct compression method initially has certain flow problems. While the Method of Wet Granulation has suitable granule and final mix flow properties, the powder mix has low flow, which causes weight swing and problems with homogeneity of content. The bulk density range is 0.37-0.49 gm/ml. The tapped density falls between 0.49 and 0.59 gm/ml. Carr's directory has a range of 15.69%-31.58%. The ratio of Hausners is between 1.19-1.46, while the repose angle is between 22.45-28.10. The results show that all of the qualities are suitable for tablet compression due to their good stream features. The results are shown in **Table 2**.

Parameters of post compression

Friability and hardness

Tablets need a certain content of hardness, or stiffness, and a tolerance for friability. The motor shock caused by packing, shipping, and production operations is either essential or substantial. Consumer acceptability requires adequate rigidity, resistance to powdering, and friability. A hardness of the tablet tester was utilized to measure the attributes. Formulations F1 through F8 had friability and hardness ranging from 45-85 (N) and 0.02%-0.1%, respectively. **Table 2** shows the findings. Friability and hardness were found to be within pharmacopeia limitations in the previously described research.

Test of weight variation

Quetiapine levels in F1–F8 were found to range between 455 mg and 530 mg, falling within the Pharmacopoeia limits ($\pm 5\%$ of the actual weight). The findings are presented in **Table 2**.

Drug content uniformity

According to the findings, the quetiapine content in F1 through F8 varied between 97.3% and 100.2%, falling within the Pharmacopoeia standards. The results are shown in **Table 2**.

Disintegration time

The composition of an immediate-release tablet depends on the choice of an appropriate disintegrant and its concentration. The innovative pill took fifteen minutes to dissolve, which was a very lengthy time. It took 3.30 to 9.30 minutes for formulations F1 through F8 to decompose. The results are summarised in **Table 2**.

Table 2. Pre-compression, core- and coated-tablet evaluation of quetiapine fumarate IR tablets

Sr. No.	Parameter	Formulation batch number							
		F1	F2	F3	F4	F5	F6	F7	F8
Pre-compression									
1	Loss on drying (%w/w)	1.92	2.17	2.14	1.97	3.17	1.51	1.88	2.31
2	Density of bulk (gm/ml)	0.41	0.43	0.39	0.47	0.46	0.37	0.44	0.42
3	Density of tapped (gm/ml)	0.53	0.51	0.57	0.59	0.56	0.44	0.57	0.5
4	Index of compressibility (%)	22.64	15.69	31.58	20.34	17.86	15.91	22.81	16.00
5	Ratio of hausner	1.29	1.19	1.46	1.26	1.22	1.19	1.30	1.19
6	Repose angle (°)	24.21	25.47	23.45	22.45	23.76	22.75	28.10	27.58
Core tablets									
7	Weight variation (mg) ± SD	455.5 ±	473.1 ±	496.5 ±	521.4 ±	460.4 ±	475.5 ±	501.1 ±	527.1 ±
		1.1	1.5	1.2	1.4	1.2	1.1	1.5	1.3
8	Hardness (N)	55-60	49-55	47-55	65-70	65-75	60-65	63-68	45-55
10	Thickness (mm)	5.52-5.75	5.56-5.80	5.75-5.85	5.80-5.95	5.50-5.57	5.55-5.70	5.60-5.76	5.66-5.80
11	Time of disintegration (min)	4.00-4.15	5.15-5.30	6.15-6.30	6.30-7.0	9.00-9.30	8.00-8.30	8.00-8.15	7.15-7.45
12	Friability (%)	0.087	0.071	0.19	0.092	0.065	0.060	0.044	0.14
13	Assay	90.15	92.45	97.58	98.45	98.75	99.10	97.75	96.40
Coated tablets									
14	Variation of weight	450.50 ±	475.50 ±	502.15 ±	525.21 ±	456.27 ±	480.75 ±	505.78 ±	532.45 ±
		1.5	1.10	1.15	1.75	1.55	1.00	1.25	1.20
15	Hardness (N)	65-72	56-65	60-70	75-85	70-80	70-72	72-85	70-85
16	Thickness (mm)	5.65-5.80	5.60-5.85	5.80-5.90	5.85-5.98	5.55-5.65	5.60-5.75	5.65-5.80	5.70-5.85
17	Time of disintegration (min)	5.15-6.30	5.30-6.30	6.30-7.00	6.45-7.15	9.00-9.30	8.30-9.00	8.15-8.30	7.30-8.00
18	Weight gain after coating (%)	2%	2%	2%	2%	2%	2%	2%	2%

In-vitro dissolution study

Dissolution rate studies showed that within 45 minutes, 90 to 99.1% of the drug was released from all formulations. Formulation F6 demonstrated complete release, or the release of 99 percent of the medication, in 45 minutes. The results are shown in **Figure 2**. The in-vitro drug releases from all developed formulations were within the range permitted by formal compilations; nevertheless, F8's physical characteristics were determined to be the most comparable to those of commercial preparations. The findings indicate that medication release increases with super disintegrant concentration.

The dissolving profile was compared to the innovator and test product, the Seroquel tablet from AstraZeneca, to calculate the dissimilarity (f1) and similarity (f2) variables. The findings demonstrate that the innovator's and test's release profiles are comparable. In D.M. water as a solution medium, Formulation F6's f2 - value is 87.13; in 0.1 N HCl media and pH 4.5 acetate buffer, it is 68.66 and 59.11, respectively. **Figure 3** compares the innovator product's dissolving profile with the optimized formulation. This score indicates that formulation F6 has a favorable release profile across all media. Consequently, it was selected as the ultimate formulation.

Testing of stability

For three months, the optimized formulation F6's stability tests were conducted in a humidity chamber set at 40 °C and 75% relative humidity).

A table presents the results for 1, 2, 3, and 6 months. Every formulation parameter, including hardness, in-vitro breakdown profile, homogeneity of content, and material properties, was within the parameters of the specification. Consequently, the optimized formulation seems to have been stable. The findings are presented in **Table 3**.

Table 3. Stability studies on formulated quetiapine fumarate IR tablets

Sr. No.	Parameter	RT	40 ± 2 °C/75 ± 5% RH			
		Initial	15 days	30 days	60 days	90 days
1	Description	Round peach color tablet	Round peach color tablet	Round peach color tablet	Round peach color tablet	Round peach color tablet

2	Hardness (N)	70-75	68-75	65-73	65-73	66-75
3	Disintegration time (min)	5.00-5.30	5.15-5.45	5.30-5.45	6.00-6.15	6.00-6.15
4	Assay (%)	99.10	98.78	98.45	98.55	98.50
5	In-vitro dissolution	98.45	98.40	98.50	98.25	98.20

Conclusion

This study aimed to develop a solid oral dose form of quetiapine fumarate that was bioequivalent. The new formulation dissolves exactly like the Innovator Seroquel tablet from AstraZeneca. Significant differences exist in tolerance amongst current neuroleptic medications, despite their improved permissibility outlines compared to earlier antipsychotics. Due to its high patient acceptability profile, quetiapine may improve patients' quality of life and help them take their medications as prescribed. For acute exacerbations of schizophrenia, quetiapine is therefore advised as a first-line antipsychotic.

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Ethics Statement: None

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