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FORMULATION, DEVELOPMENT, AND EVALUATION OF QUETIAPINE FUMARATE IMMEDIATE RELEASE TABLETS

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ABSTRACT

Antipsychotic medications can help control the symptoms of schizophrenia. A variety of scientific and demographic factors show the capability to sway the selection of odd neuroleptic medications. Quetiapine Fumarate is indicated for the treatment of schizophrenia and bipolar disorder. Disintegrating agents are materials that are commonly used in the formulation of tablets and hard-shell capsules. Within a short period after administration, drugs should dissolve or disintegrate in the stomach. The most preferred decomposition agent in the making of tablets is starch. The primary purpose of this research was to create a reliable immediate-release tablet formulation of the antipsychotic Quetiapine. Tablets are popular due to their low cost, packaging, and shipping, as well as their greater stability and virtual tamper resistance. Orally administered tablets with a faster disintegration time have a shorter absorption time and higher bioavailability. The goal of the study is to create a stable and physically and chemically compatible generic formulation for treating schizophrenia, as well as a pharmaceutically equivalent instant release tablet for individuals with mental illnesses like schizophrenia and bipolar disorder.

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Introduction

Antipsychotic medications can help control the symptoms of schizophrenia by changing the balance of chemicals in the brain. There is no complete treatment for schizophrenia, but medications are only part of a comprehensive treatment plan. Various demographic and clinical characteristics influence the choice of atypical antipsychotic drugs. Increasing brain abnormalities have been identified in several linear anatomic Magnetic Resonance Imaging (MRI) analyses in people with schizophrenia [1, 2].

The drug quetiapine fumarate is used to treat schizophrenia and bipolar disorder. It binds to serotonin 5HT2 and 5HT1A receptors in the brain, as well as dopamine D1 and D2 sensory receptors. Lesser added pyramidical symptoms and neuroleptic characteristics are alleged to be the result of its use [3].

For therapeutic agents with systemic effects, oral medication delivery is the most desirable and recommended form of administration. Three types of oral drug delivery systems are Targeted, Controlled, and Immediate-release preparations, (TR), (CR), and (IR) respectively [4].

Disintegrants are the substances employed in tablet manufacture to help in the diffusion of humidity and spreading the formulation matrix of the dose in dissolution solutions. In tablet manufacturing, starch has long been the primary disintegrant, and it is still widely employed today [5].

Drugs should dissolve or disintegrate fast in the stomach after administration and have a rapid onset of action. They should be easily transportable, leave minimal residue in the mouth after oral delivery, and be resistant to surrounding circumstances like dampness and warmth [6, 7].

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A study has shown that immediate-release tablets are better than sustain-release tablets for the treatment of schizophrenia. Bonafede *et al*., 2015, studied patients with acute bipolar mania and found that they were more likely to be discharged from the hospital after a few days [8, 9].

Quetiapine Fumarate has more soluble in 0.1 N HCl, which is simultaneous to gastric acid media, so can be used for the dissolution as a medium. The majority of positive symptoms are effectively treated with antipsychotic medications of the first generation, which are predominantly antagonists of dopamine D2 receptors [10].

Schlander *et al*., 2011, Studied the increasing use of medication for the treatment of a psychotic disorder. Based on that this formulation may give benefit to the company in the future. The demand for the drug was continually increasing based on this he concluded that the need for dug is continually increasing [11].

Quetiapine Fumarate is an antipsychotic agent. The structure and chemical name of Quetiapine Fumarate are given in **Figure 1**. It is used to treat schizophrenia and bipolar illness, among other things. Manic episodes are connected with bipolar disorder, as are significant depressive episodes in bipolar disorder. The drug works by antagonizing serotonin (5-hydroxytryptamine) 5-HT2 and dopamine D2 receptors [12].

The drug quetiapine fumarate is used to treat schizophrenia. In patients who have shown initial treatment responses, it is useful in maintaining the clinical improvement during continued medication. In patients with a moderate to a severe manic episode, it is also recommended for the prevention of recurrence [13].

For males around 15-24 and females in the 25-35 age bracket, there is the highest risk of Schizophrenia striking. The name Schizophrenia was coined by Eugen Bleuler (1857-1939), a Swiss psychiatrist in 1910. The first step is to identify the signs and symptoms [14]. Quetiapine Fumarate is a neuroleptic drug that is considered for the remedy of bipolar disorder (BD) and schizophrenia. The drug works by antagonizing serotonin (5-hydroxytryptamine) 5-HT2 and dopamine D2 receptors [15].

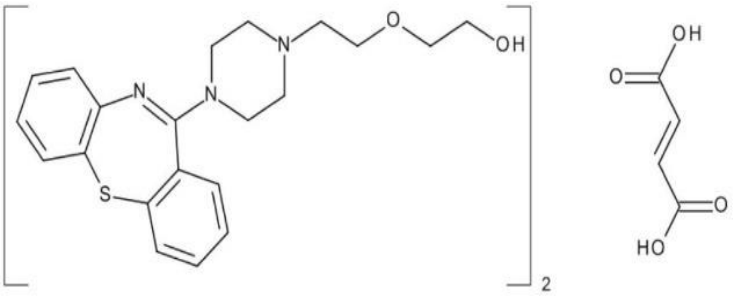


Figure 1. Structure of Quetiapine Fumarate

IUPAC Name: 2-[2-(4-benzo[b][1,4]benzothiazepin-6-ylpiperazin-1-yl)ethoxy]ethanol;but-2-enedioic acid

Immediate release formulation (API) is a form of drug delivery system used for the management of mental disorders such as schizophrenia, bipolar disorder, epilepsy, and other environments that need a quick activity commencement and drug pharmacological effects. It has been developed to be cost-effective, easy to carry, and administered to patients accurately and conveniently [16-18].

The main objective to formulate a generic version of the reference product is to provide cost-effective quality products to the market. Immediate release of drug with very few side effects than other classes of anti-depressant drugs and improved patient compliance. The Bio waiver is applicable if sufficient solubility & permeability data are provided. The purpose of the study is to develop a stable and physically and chemically compatible and stable generic formulation for treating schizophrenia, as well as formulate a pharmaceutically equivalent immediate release tablet for use in patients with mental health conditions such as schizophrenia and bipolar disorder (MND).

Materials and Methods

Nifty Labs Ltd, India provided with a gift sample of Quetiapine Fumarate IP. Microcrystalline cellulose EP (Avicel pH 101) and Microcrystalline cellulose NF (Avicel pH 112) were procured from FMC Biopolymer, Ireland. Lactose monohydrate EP (Pharmatose 200M) was obtained from DFE Pharma, India. Dibasic calcium phosphate dehydrates USP was acquired from Innophos, Chicago. Sodium Starch Glycolate USP (Type A) was obtained from DMV-Fonterra Excipient, India. Povidone USP (PVPK-30) was procured from ISP Private Ltd, India. Talc USP was obtained from Luzenac Pharma, Italy. Magnesium Stearate USP was procured from Ferro Corporation, Cleveland. Opadry White was procured from Colorcon Asia Pvt. Ltd., Goa.

Drug-Excipient Compatibility Study: Drug substance and excipient blends were exposed to a variety of temperature and humidity conditions. In sealed clear glass vials, the mixture was kept dry. The samples were first inspected and then monitored for changes in appearance every week for up to 30 days. A Fourier transform infrared spectrophotometer (FTIR 1615, Perkin Elmer, USA.) and KBr were used to obtain spectra for Quetiapine Fumarate and tablet formulation [19].

Preformulation Study: When a newly manufactured drug displays enough pharmacological action in animals to be helpful in people, preformulation is done. These investigations concentrate on the compound's physicochemical properties that influence the drug's performance and development into an effective dosage form. Preformulation testing eliminates any potential barriers to the production of effective dosage forms [20].

DSC Studies: All of the samples were analyzed using DSC 60, Shimadzu, Japan. Samples were prepared in aluminum pans in the studies. Indium was used as a reference for temperature calibrations. For this investigation, quetiapine fumarate and medication containing excipients were used [21].

XRD Studies: The spectra of quetiapine fumarate and its components, as well as granules and compressed tablets, were recorded. There are no notable changes in peak height in the XRD spectra of various formulations. It was determined that the excipients are compatible with one another and do not differ considerably [22].

Preparation of Quetiapine Fumarate IR Tablets: Following steps were used in the preparation of Quetiapine Fumarate IR tablets using wet granulation by Glatt-Powder-Coater-Granulator (GPCG) [23]. The formula used in various batches of Quetiapine Fumarate is shown in **Table 1**.

Dispensing: All the ingredients including Quetiapine Fumarate, Dibasic Calcium Phosphate Dihydrate, Microcrystalline cellulose (Avicel pH 101), Lactose monohydrate, Sodium Starch Glycolate (Type A), Povidone (PVP K-30) were weighed separately.

Sifting: Drug Substance and above excipients were sifted through mesh 30 #.

Binder Solution Preparation: Dissolved the PVPK-30 in purified water, stirred till a clear solution was obtained. This solution was used as a binder solution.

Top Spraying: Binder solution was sprayed through the top spray in Glatt Powder Coater Granulator with the following parameter, above dried granules were passed through mesh 20 #.
Inlet Temperature: 60ºC, Exhaust Temperature: 50ºC, Product Temperature: 45ºC, Fan Speed: 45%, Spray Rate: 1gm/min and Nozzle diameter: 1mm.

Prelubrication: All the ingredients named Microcrystalline cellulose (Avicel pH 112), Sodium Starch Glycolate (Type A), Dibasic Calcium Phosphate Dihydrate were weighed according to the yield of dried granules, and sifted through mesh 40 #. Above sifted materials mixed with dried granules in Pillar Type Bin blender for 10 minutes.

Lubrication: Ingredients named Magnesium Stearate, Purified Talc were weighed according to the yield of dried granules, and sifted through mesh 60 #. The above-sifted materials were mixed with Lubricated materials in a Pillar Type Bin blender for 3 minutes. Now, this blend was used for tablet compression.

Compression: Lubricated blend was compressed using 11.0 mm plain circular standard concave punches in 'B' tooling. These are the critical steps for the drug, who sticks both the punches along with the turrets. This problem can be overcome by using the magnesium stearate as well as the talc during the lubrication stages.
During these stages, various parameters become more important like the weight of the tablet, Hardness and periods of decomposition of the tablets as well as Friability, etc.

Table 1. Formulation of Quetiapine Fumarate IR Tablets

Sr. No.	Ingredient (mg/tab)	Formulation Batch Number							
		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

Evaluation of Quetiapine Fumarate IR tablets

Pre-compression Characteristics: Loss on drying, angle of repose, bulk density, tapped density, compressibility index, and Hausner's ratio were all considered as pre-compression parameters. **Table 2** displays the results [24].

Loss on Drying (LOD): The humidity of the greased granules was determined using the Halogen Moisture Analyzer. A gramme of the compound was warmed to 105°C till the equipment detected no variation in weight [25]. The percentage loss of weight was reported.

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

The Angle of Repose: The maximum angle a pile of powder or granules can make with the horizontal plane is called the angle of repose [26]. This property is linked to the friction between particles, or opposition to particle locomotion.

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

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

Density Determination: A graded cylinder fitted on a motorized taping mechanism with a correctly chopped rotating shaft is used to measure powder's volume. To ensure reproducibility, the tapings ought not to cause grain abrasion or a unit size distribution variance of the tested substance [27].

$$\text{Bulk density (g/ml)} = \text{Weight of sample in gm/ Volume occupied by the sample in ml} \quad (3)$$

Size, bulk density, form, surface area, moisture content, and material coherence have all been proposed as measures for the compressibility index. Both the bulk density and the tapped powder's denseness are measured to determine the compressibility index and Hausner's ratio.

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

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

Post-compression Assessment Parameters: Hardness, thickness, friability, weight fluctuation, drug content homogeneity, disintegration time, and in vitro dissolution were all assessed in the compressed tablets [28, 29].

Hardness: The ability of a tablet to tolerate mechanical shocks during handling is determined by its hardness. Schleuniger's hardness tester was used to evaluate the tablet's hardness. Each formulation's hardness was tested by selecting ten tablets at random as of every formulation in addition, the mean was computed. **Table 2** shows the conclusions.

Thickness: Digital Vernier calipers were used to measure the thickness and width of each batch's tablets. The average was calculated after millimeters were measured. The results are shown in **Table 2**.

Friability: It was evaluated by The Roche Friabilator. This is measured in percentages (%). Ten weighted tablets were positioned in the friabilator at first ($W_{initial}$). It was then spun for 4 minutes at 25 rpm. The tablets were weighed again (W_{final}). The calculation of % friability was done by:

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

Tablets having a friability percentage of less than 1% are thought to be acceptable. Friability was determined as a percentage of the initial mass and reported as a mass loss. **Table 2** indicates the outcomes.

Weight Variation: The average weight was derived after weighing twenty tablets at random. Only two of the individual weights differed by more than the % from the average weight. **Table 2** shows the results.
Drug Content Determination: 20 tablets were weighed and powdered. An equivalent of 25 mg Quetiapine Fumarate powder was diluted in 100 ml 6.8 pH phosphate buffer and sieved adequately. The amount of the drug was then evaluated by a UV-Visible spectrophotometer set to 254 nm after the sample was diluted using a suitable solvent [30, 31].

Disintegration Time: The decomposition time of all formulations was determined by a tablet disintegration test device. The discs were inserted in the tubes of the disintegration test kit following the six tablets. The temperature of the water was kept constant at 37±2°C, with the total decomposition time of the whole tablet being recorded. **Table 2** shows the result.

In-vitro Dissolution: These tests were performed on the Quetiapine Tablets in water for ¾ hour. 900 mL of dissolving media was used in the drug release test. The temperature was held at 37°C±0.5°C and with a 100rpm paddle velocity. After that, they were matched in two mediums: 0.1 N HCl and pH 4.5 acetate buffer. A UV-Visible double beam spectrophotometer was used to filter samples using Whatman filter paper (no. 41), dilute them, and analyze them at 254 nm. **Figure 3** depicts the drug release as a percentage from innovators formulations and batch F1 and F8.

Calculation of Dissimilarity (f1) & Similarity (f2) Factor
Dissimilarity Factor (f1): To determine the dissimilarity, contrasted from a locus or a pioneer invention. The dissimilarity factor (f1) must never exceed 15 (f115).

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

Similarity Factor (f2): The similarity factor was calculated by multiplying the mean squared difference in the liquefied percentage between the test and reference products by the logarithmic reciprocal square root transformation of one (f2). This was computed to compare the results to reference release profiles [32].

$$f_2 = 50 \times log10 \times \frac{1}{\sqrt{1 + 1/n \times \Sigma}(R_t - T_t)^2} \times 100 \quad (8)$$

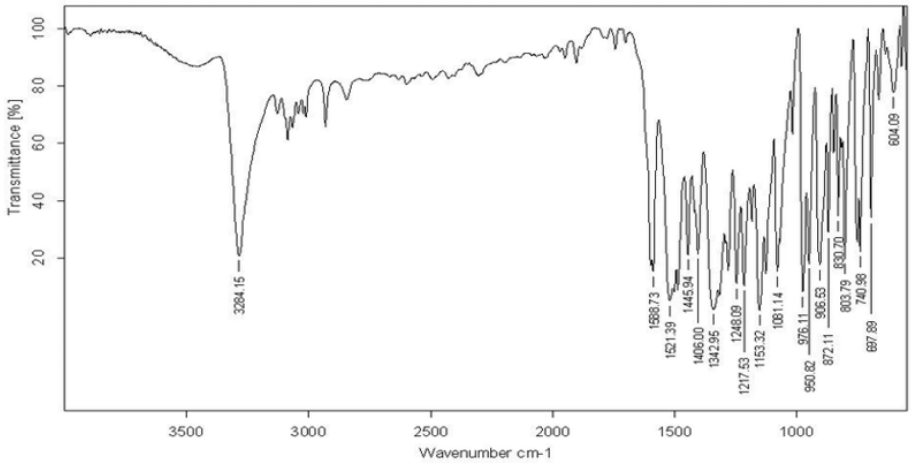
Where, n= sampling point number.
Having a similarity factor (f2) greater than 50 (f2>50) at all times. When more than four dissolution time points are present, the approach is appropriate for comparing dissolution profiles; however, it is restricted to Rt and Tt is having a mean disparity of 100 or less. The data must be normalized if the difference is more than 100.

Comparison with Marketed Product: The product yielded was numerically verified and analyzed for tablet qualities with the end product's potential being assessed using a variety of parameters. The following quality control tests were done on commercially available tablets, specifically the AstraZeneca Seroquel tablet, and the findings are presented in **Figure 4**.

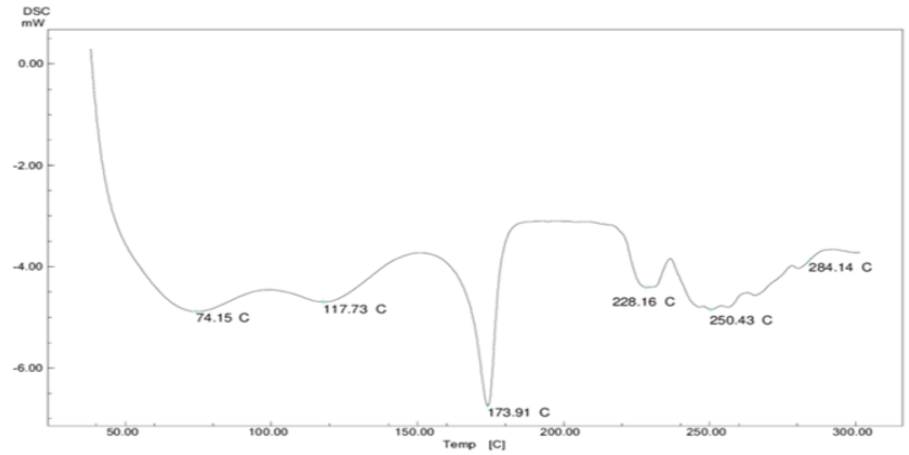
Stability Studies: The tests for stability were undertaken as per ICH Q1A(R2) recommendations for batch F6 tablet formulation, which was the most promising. Stability testing enables optimal storage settings and shelf lives to be determined by providing information on the fluctuation of drug or product potential over time due to several surrounding elements such as light, warmth, and dampness [33].
The current study was carried out by storing the produced tablets in dense airtight polyethylene bottles for three months at 40°C and relative humidity of 75%. The samples were taken on the 15th, 30th, 60th, and 90th days. *In vitro* dissolution tests, tablets were evaluated for exterior manifestation, breadth, stiffness, and drug content percentage.

Results and Discussion

Drug-excipient Compatibility: Quetiapine was tested for drug–excipient compatibility with a variety of excipient groups. According to the findings, the parts did not have chemical contact with the drugs. **Figures 2a, 2b, 2c** show the outcomes of drug-excipient compatibility studies using IR, DSC, and X-RD studies.



a)



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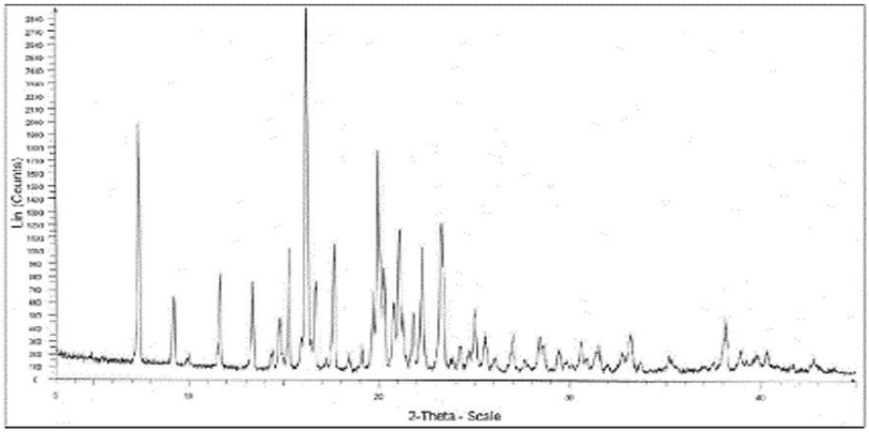

c)

Figure 2. a) IR Specta of Quetiapine Fumarate. b) DSC of Quetiapine Fumarate. c) X-RD study of Quetiapine Fumarate

Pre-Compression Parameters

Loss on drying: According to the calculations, the theoretical dampness of the drug and components was 2% w/w, and the LOD of dehydrated grains was kept at that level NMT 1% disparity through desiccating at 60°C and the optimum desiccating duration to obtain LOD in a specific threshold. The LOD ranged between 1.51 and 3.17% w/w. **Table 2** displays the results.

Powder Flow Characteristics

The flow characteristics of powder ready for compression for any formulation are critical in determining the best procedure for granulating the powder mixture. As a result, before deciding on a granulation process, the drug flow was examined. In the beginning, the direct compression approach has some flow issues. Powder Blend has weak flow, resulting in weight fluctuation and content homogeneity issues; however, the Wet Granulation Method has good granule and final blend flow qualities. The bulk density ranges from 0.37 to 0.49 gm/ml. Tapped density spans from 0.49 to 0.59 gm/ml. Carr's directory ranges from

15.69 to 31.58%. Hausner's ratio is between 1.19 and 1.46, while the angle of repose is between 22.45 and 28.10. According to the findings, all qualities have good stream properties making them viable for tablet compression. **Table 2** displays the findings.

Post Compression Parameters

Hardness and Friability: Tablets necessitated a specific level of stiffness, or hardness, as well as forbearance to friability. The motor shock from manufacturing management, packing, and transportation are required or important. For consumer approval, satisfactory stiffness, endurance against friability, and powdering are required. A tablet hardness tester was used to quantify the properties. Formulations F1 to F8 had hardness and friability in the range of 45 to 85 (N) and 0.02 to 0.1 percent, respectively. **Table 2** displays the results. Hardness and friability were found to be within pharmacopeia limitations in the investigations mentioned above.

Weight Variation Test: The amount of Quetiapine in F1 to F8 was determined, ranging from 455 to 530 mg, which is in the Pharmacopeia limitations (±5% of the actual weight). **Table 2** displays the results.

Drug Content Uniformity: The findings showed that the Quetiapine content in F1 to F8 ranged from 97.3 percent to 100.2 percent, within the norms of Pharmacopeia. **Table 2** displays the results.

Disintegration Time: The selection of a suitable disintegrant and its concentration is critical for the development of an immediate-release tablet's formulation. The innovator pill had a disintegration duration of 15 minutes, which was extremely long. Formulations F1 to F8 took 3.30 to 9.30 minutes to disintegrate. **Table 2** summarizes the findings.

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	Bulk Density (gm/ml)	0.41	0.43	0.39	0.47	0.46	0.37	0.44	0.42
3	Tapped Density (gm/ml)	0.53	0.51	0.57	0.59	0.56	0.44	0.57	0.5
4	Compressibility index (%)	22.64	15.69	31.58	20.34	17.86	15.91	22.81	16.00
5	Hausner Ratio	1.29	1.19	1.46	1.26	1.22	1.19	1.30	1.19
6	Angle of repose (^{0})	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 ±1.1	473.1 ±1.5	496.5 ±1.2	521.4 ±1.4	460.4 ±1.2	475.5 ±1.1	501.1 ±1.5	527.1 ±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	Disintegration Time (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	Weight variation	450.50 ±1.5	475.50 ±1.10	502.15 ±1.15	525.21 ±1.75	456.27 ±1.55	480.75 ±1.00	505.78 ± 1.25	532.45 ±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	Disintegration Time (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: All formulations released 90 to 99.1% of the medication after 45 minutes, according to dissolution rate experiments. In 45 minutes, Formulation F6 showed full release, i.e., 99 percent of the drug was released. **Figure 3** depicts the results. All of the created formulations' in-vitro drug releases were in the permitted range specified in formal compilations,

however, the physical attributes of F8 were found to be the most equivalent to commercial preparations. The results show that when the concentration of super disintegrant rises, so does drug release.

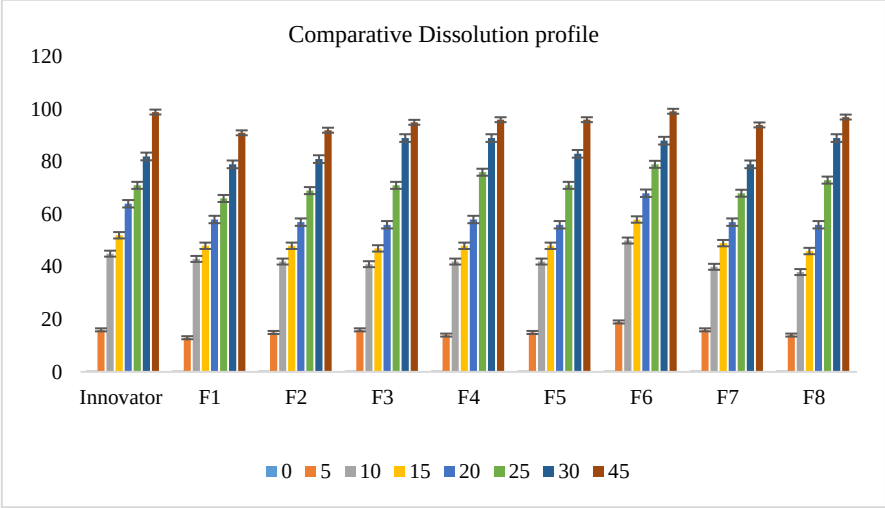

Figure 3. Comparative Dissolution Profile of Innovator Product and Batch F1- F8

The dissimilarity (f1) and similarity (f 2) variables were determined using the dissolution profile in comparison to the test and innovator product, AstraZeneca's Seroquel tablet. The results show that the release profiles of the test and innovator are similar. Formulation F6 has an f2 – value of 87.13 in D.M. water as a dissolution medium, and f2 – values of 68.66 and 59.11 in pH 4.5 acetate buffer and 0.1 N HCl media, respectively. A comparison of dissolution profile of innovator product and optimized formulation is shown in **Figure 4**. Formulation F6 has a favorable release profile in all media, according to this value. As a result, it was chosen as the final formulation.

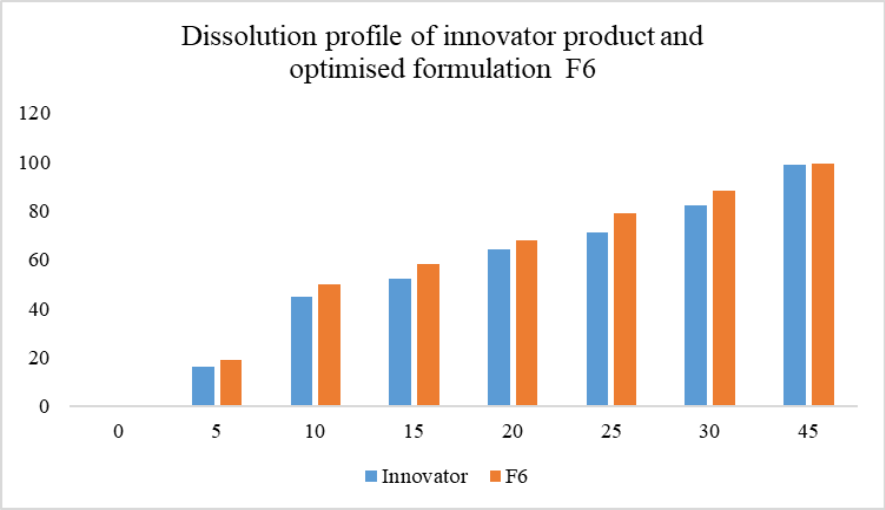

Figure 4. Comparative Dissolution profile of innovator product and optimized formulation, F6

Stability Testing: The stability tests of the optimized formulation F6 were carried out for three months in a humidity chamber (40°C/75% RH).

For 1, 2, 3, and 6 months, the findings are shown in a table. All formulation parameters were within specification limits, comprising material characteristics, content uniformity, hardness, and in-vitro decomposition profile. As a result, it appears that the optimized formulation was stable. **Table 3** displays the results.

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

The goal of this study was to create a bioequivalent solid oral dosage form of Quetiapine Fumarate. In terms of dissolving, the current formulation is identical to AstraZeneca's Innovator Seroquel tablet. Although recent neuroleptic drugs have better permissibility outlines than previous antipsychotics, there are significant variances in tolerance amongst them. Quetiapine has a strong patient acceptance profile, which may help patients stick to their meds and have a higher quality of life. As a result, quetiapine is recommended as a first-line antipsychotic for acute schizophrenia exacerbations.

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References

1. Stroup TS, Gray N. Management of common adverse effects of antipsychotic medications. World Psychiatry. 2018;17(3):341-56.
2. Raeisi M, Navidian A, Rezaee N. Comparison of the effect of nurses' education on stress, anxiety and depression of family caregivers of patients hospitalized with schizophrenia disorder. Arch Pharm Pract. 2020;11(1):82-7.
3. Hanawi SA, Saat NZ, Zulkafly M, Hazlenah H, Taibukahn NH, Yoganathan D, et al. Impact of a Healthy Lifestyle on the Psychological Well-being of University Students. Int J Pharma Res Allied Sci. 2020;9(2):1-7.
4. Vinarov Z, Abrahamsson B, Artursson P, Batchelor H, Berben P, Bernkop-Schnürch A, et al. Current challenges and future perspectives in oral absorption research: An opinion of the UNGAP network. Adv Drug Deliv Rev. 2021;171:289-331.
5. Markl D, Zeitler JA. A review of disintegration mechanisms and measurement techniques. Pharm Res. 2017;34(5):890.
6. Hua S. Physiological and pharmaceutical considerations for rectal drug formulations. Front Pharmacol. 2019;10:1196.
7. Patel D, Patel U, Shukla M, Bhimani B, Patel G. Formulation and Evaluation of Immediate Release Tablet of Simvastatin. Res J Pharm Technol. 2020;13(1):421-4.
8. Bonafede M, Locklear JC, Wahlqvist P, Fajutrao L, Szamosi J, Pan K, et al. Impact of once-daily extended-release quetiapine fumarate on hospitalization length in patients with acute bipolar mania. J Comp Eff Res. 2015;4(1):51-9.
9. Ahmed M, Kumar R, Narayanaswamy VB, Haque I, Hoque M. Formulation and Evaluation of Fast Dissolving Tablets of Doxazosin Mesylate. Asian J Pharm Res. 2016;6(3):131-46.
10. Kalyankar P, Panzade P, Lahoti S. Formulation design and optimization of orodispersible tablets of quetiapine fumarate by sublimation method. Indian J Pharm Sci. 2015;77(3):267.
11. Schlander M, Schwarz O, Trott GE, Banaschewski T, Scheller W, Viapiano M, et al. PMH73 Increasing Use of Medication for Treatment of Attention-Deficcit/Hyperactivity Disorder (ADHD) in Germany between 2003 and 2009. Value Health. 2011;14(7):A300.
12. Ribolsi M, Magni V, Rubino IA. Quetiapine fumarate for schizophrenia and bipolar disorder in young patients. Drugs Today (Barc). 2010;46(8):581-7.
13. Muneer A. Pharmacotherapy of bipolar disorder with quetiapine: a recent literature review and an update. Clin Psychopharmacol Neurosci. 2015;13(1):25.
14. Kishi T, Ikuta T, Sakuma K, Matsuda Y, Iwata N. Comparison of quetiapine immediate-and extended-release formulations for bipolar depression: A systematic review and network meta-analysis of double-blind, randomized placebo-controlled trials. J Psychiatr Res. 2019;115:121-8.
15. Endomba FT, Tankeu AT, Nkeck JR, Tochie JN. Leptin and psychiatric illnesses: does leptin play a role in antipsychotic-induced weight gain?. Lipids Health Dis. 2020;19(1):1-12.
16. Zorkina Y, Abramova O, Ushakova V, Morozova A, Zubkov E, Valikhov M, et al. Nano carrier drug delivery systems for the treatment of neuropsychiatric disorders: Advantages and limitations. Molecules. 2020;25(22):5294.
17. Potu AR, Pujari N, Burra S, Veerareddy PR. Formulation and evaluation of buccoadhesive quetiapine fumarate tablets. Braz J Pharm Sci. 2012;48(2):335-45.

18. Gormez V, Avery B, Mann H. Switching from immediate release to sustained release methylphenidate in the treatment of children and adolescents with attention deficit/hyperactivity disorder. Eur Rev Med Pharmacol Sci. 2013;17(17):2345-9.
19. Patel MA, Pingale PL. Comparative effect of different high functionality excipients on various characteristics of vardenafil HCl tablets (BCS II drug). Int J Pharm Sci Res. 2014;5(12):5447.
20. Alexander A, Agrawal P, Banjare T, Bhatt A, Gupta S, Bhandarkar A, et al. Formulation and Evaluation of immediate release tablet of Risperidone. Res J Pharm Technol. 2018;11(6):2301-5.
21. Shaik F, Karnatham P, Dugganpalli R, Panga S, Akepati LP. Development and pharmaceutical evaluation of sacubitril sodium loaded oral fast dissolving films. Res J Pharm Technol. 2020;13(8):3553-8.
22. Komati S, Swain S, Rao ME, Jena BR, Unnam S, Dasi V. QbD-based design and characterization of mucoadhesive microspheres of quetiapine fumarate with improved oral bioavailability and brain biodistribution potential. Bull Fac Pharm, Cairo Univ. 2018;56(2):129-45.
23. Mohan A, Sangeetha G. Formulation and Evaluation of Immediate Release Film Coated Tablets of an Anticancer Drug (Dasatinib). Res J Pharm Technol. 2019;12(2):729-34.
24. Narala A, Veerabrahma K. Preparation, characterization and evaluation of quetiapine fumarate solid lipid nanoparticles to improve the oral bioavailability. J Pharm. 2013;2013.
25. Pingale PL, Amrutkar SV, Telange DR. Formulation, Characterization and In-Vitro Dissolution Studies of Metadoxine Tablets Prepared by Various Granulation Methods. J Med Pharm Allied Sci. 2021:2712-9.
26. Sahoo BK, Pattajoshi SP, Pattajoshi S. Formulation and Evaluation of Bimolar Release of Ciprofloxacin HCl from Bilayer Gastro-Retentive Floating System. Asian J Pharm Clin Res. 2018;8(2):61-70.
27. Selvamuthukumar R, Murali R, Srinivasan N, Mohankumar A, Panicker N. Formulation development and evaluation of immediate release tablet of terbinafine hydrochloride. Res J Pharm Technol. 2020;13(10):4648-54.
28. Patil MB, Maru AD, Bhadane JS. Formulation and Evaluation of Sustained Release Bilayer Matrix Tablet of Glimepiride and Metformin Hydrochloride. Asian J Res Pharm Sci. 2021;11(4):273-9.
29. Pingale Prashant L, Nikhilitha P. Effect of Natural Polymer on Release Retarding Rate of Glimepiride Sustained Release Tablet. J Adv Sci Res. 2021;12(1 Suppl 1):145-50.
30. Moravkar KK, Korde SD, Bhairav BA, Shinde SB, Kakulade SV, Chalikwar SS. Traditional and Advanced Flow Characterization Techniques: A Platform Review for Development of Solid Dosage Form. Indian J Pharm Sci. 2020;82(6):945-57.
31. Mandake GR, Patil IS, Patil OA, Nitalikar MM, Mohite SK. UV Spectroscopy Analysis and Degradation Study of Rivaroxaban. Asian J Res Pharm Sci. 2018;8(2):57-60.
32. Sri KV, Reddy R, Mahesh R. Diphendramine Hydrochloride Oral Dispersible Tablets: Preparation and Evaluation. Asian J Pharm Res. 2014;4(3):123-8.
33. Akiladevi D, Nappinnai M, Sudha T. A Study on the Effect of disintegrants and Processing Methods on the Physicochemical and In Vitro Release Characteristics of Immediate Release Tablets of Bosentan Monohydrate. Asian J Res Pharm Sci. 2017;7(4):222-6.