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RESEARCH

Formulation and Evaluation of Immediate-Release Quetiapine Fumarate Tablets Via Twin-Screw Melt Granulation

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Abstract

Purpose This study aimed to develop immediate-release Quetiapine Fumarate (QTF) tablets using twin-screw melt granulation (TSMG), a solvent-free and efficient granulation method, and compare their dissolution profiles with the marketed product.

Methods QTF tablets were formulated using TSMG with varying concentrations of Ludiflash® as a diluent and HPMC as a binder. Granules were prepared using a twin-screw extruder at 150 °C, optimized for feed rate and screw design. Granules were characterized for flow properties, thermal stability, and molecular interactions using differential scanning calorimetry (DSC) and Fourier transform infrared (FTIR) spectroscopy. Compressed tablets were evaluated for weight variation, hardness, friability, disintegration, and dissolution. Drug release profiles were compared with a commercial product.

Results TSMG improved granule flow properties, with all formulations exhibiting excellent post-extrusion characteristics. DSC confirmed the retention of QTF crystallinity, and FTIR demonstrated excipient compatibility. The tablets passed pharmacopeial tests for weight variation, hardness, friability, and disintegration. Dissolution studies showed that formulations F4, F5, and F6 released over 85% of the drug within 15 min, comparable to the marketed product.

Conclusion TSMG is a robust and cost-effective technology for manufacturing immediate-release QTF tablets. The solvent-free process ensures compatibility, thermal stability, and rapid drug release, making TSMG a promising alternative for continuous pharmaceutical production.

Keywords Flow properties · Immediate-release · Quetiapine fumarate · Temperature · Twin-Screw melt granulation

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Introduction

The development of oral solid dosage forms can be challenging due to the poor powder flow properties and compressibility of pharmaceutical drugs. These poor properties can be improved through the granulation process [1]. In pharmaceuticals, granulation is typically performed using dry, wet, or melt granulation methods, with the addition of a binder. During dry granulation, the powder is compacted and then milled to form small, desired particles [2]. In wet granulation, a solvent is used to dissolve the polymeric binder or is added directly to the blend, allowing the binder to be uniformly dispersed among the other ingredients. Afterward, the mixture is dried to remove the solvent, leaving polymer bridges that hold the granules together. Melt granulation is similar to wet granulation in that the binder holds the granules together but without the use of a solvent. Instead, as heat is applied above its glass transition temperature, the binder softens and disperses, forming bridges

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between particles and facilitating agglomerate formation. [1, 3].

Melt granulation is typically performed using conventional high-shear granulators, where heat is applied either from jacketed bowls or generated through frictional heating [4]. However, this conventional process is generally limited to low glass transition temperature binders or lipids. The expansion of twin-screw extrusion in pharmaceutical applications, particularly for the formulation of amorphous solid dispersions, has significantly increased interest in continuous granulation, as this equipment can also be used for melt granulation [1].

Twin-screw melt granulation (TSMG) employs rotating screws to mix materials at temperatures above their glass transition temperature (Tg) or melting temperature (Tm). This process enables the molecular-level mixing of active compounds with thermoplastic polymers, ensuring uniform material distribution [5, 6]. In TSMG, the high shearing forces distribute the molten or softened binder throughout the ingredients, forming granules. The process is gaining significant interest in the manufacturing of solid oral dosage forms due to its customizability, robustness, and compatibility with continuous manufacturing processes, making it a scalable and efficient alternative to conventional granulation techniques. Additionally, various process parameters—such as binder concentration, feed rate, residence time, processing temperature, and screw configuration—play a crucial role in determining the final granule properties, further enhancing the adaptability of TSMG in pharmaceutical manufacturing.

During melt granulation, powder blends are heated not only by the heat conducted from the barrel but also by the viscous or frictional heat generated by the rotating screws. This makes it feasible to use thermoplastic materials with a high melting or softening point [7]. The process can convert the components into an amorphous product, potentially enhancing the dissolution profile of poorly water-soluble drugs. However, the amorphous conversion and the uniformity of shape and density of the resulting product depend on the specific process parameters used [8]. Additionally, TSMG has been used for delivering water-soluble drugs, with various applications including taste masking and extended release dosage forms, etc [9]. This technology offers several advantages over conventional pharmaceutical manufacturing processes, such as shorter and more efficient timelines for producing the final product, environmental benefits from eliminating solvent use, and improved efficiency in drug delivery to patients, and reduced production costs, making it a cost-effective approach for pharmaceutical manufacturing [10, 11]. Consequently, hot-melt extrusion (HME) has emerged as an alternative platform technology to other traditional techniques for manufacturing pharmaceutical dosage forms, such as tablets, capsules, films, and implants, for drug delivery via oral, transdermal, and transmucosal routes, etc [12, 13].

In this study, twin-screw melt granulation (TSMG) was utilized to formulate immediate-release tablets as an alternative to conventional wet or dry granulation processes, with the goal of reducing production costs and facilitating seamless integration into a continuous manufacturing process. Quetiapine fumarate was selected as the model drug to develop the formulation using TSMG and compare the resulting tablets with the marketed product. Initial screening studies were conducted to select the appropriate excipients and process parameters. As previously mentioned, various excipient properties and process conditions influence product quality. Given the complexity of studying all formulation and process variables simultaneously, only the concentrations of the diluent and binder were investigated in this study, while other factors were held constant. Screening experiments were conducted to optimize the binder type, screw design, feed rate, and processing temperature. The optimized granules were then characterized and compressed with suitable disintegrating agents and lubricants to achieve the desired tablet hardness and dissolution profile. Finally, the dissolution performance of the formulated tablets was compared with that of the marketed product.

Quetiapine Fumarate is soluble in water and has a log P of 0.45 [14]. It is a psychotropic agent belonging to a chemical class of dibenzo-thiazepine derivatives. It is present in tablets as fumarate salt. Its melting point temperature is 176 °C and it is thermally stable up to 200 °C. The immediate-release formulation of the atypical antipsychotic quetiapine fumarate is approved in the USA and EU for the treatment of schizophrenia and bipolar disorder. Quetiapine fumarate is commercially available as SEROQUEL and it is available in different strengths including 25 mg, 100 mg, 200 mg, 300 mg, and 400 mg tablets [15].

Materials & Methods

Materials

Quetiapine fumarate was purchased from RIA International LLC, Ludiflash® was gifted by BASF, AFFINISOL™ HPMC HME LV15 Hypromellose was gifted by Colorcon, commercially available quetiapine fumarate tablets were procured from Ascend laboratories LLC and other chemicals used such as methanol, deionized water, etc. were purchased from Fisher Scientific.

Table 1 The intragranular composition of formulations

Formulation composition	F1	F2	F3	F4	F5	F6
QTF (%)	28.80	40.32	51.83	28.80	40.32	40.32
Ludiflash® (%)	56.20	49.68	33.17	61.20	54.68	52.18
HPMC (%)	15.00	10.00	15.00	10.00	5.00	7.50
Total weight (%)	100.00	100.00	100.00	100.00	100.00	100.00

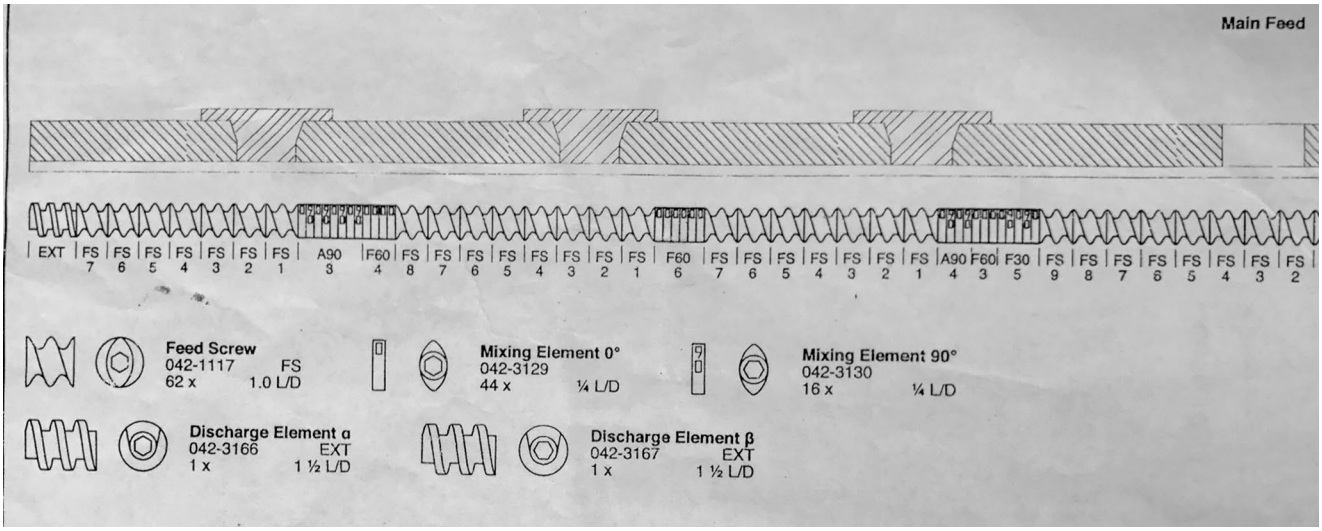

Fig. 1 Screw configuration of TSMG used in the current study

Methods

UV-Visible Spectroscopy Method

The calibration curve of QTF was obtained using UV-Visible spectroscopy (Thermo Scientific Genesys UV-Visible Spectrophotometer, USA) with water as the solvent. A stock solution of 1 mg/mL QTF was prepared, and subsequent dilutions of 5 µg/mL, 10 µg/mL, 15 µg/mL, 25 µg/mL, 35 µg/mL, 40 µg/mL, and 50 µg/mL were made. The calibration curve was generated using the absorbance values measured at the λ_{max} of 290 nm [16].

Twin Screw Melt Granulation (TSMG)

Preparation of Blends A batch size of 50 g was prepared for each of the six formulations, designated as F1 to F6, as shown in Table 1. Each tablet contained 345.56 mg of QTF (Eq. 300 mg base) [17]. The intragranular composition of these formulations included drug loadings of 25%, 35%, and 45% quetiapine base, with different combinations of Ludiflash®and HPMC HME LV15 (HPMC). Ludiflash® and HPMC were used as a diluent and binder, respectively. Ludiflash® is a co-processed excipient, contains mannitol as the major constituent and 4–6% w/w of crospovidone as a disintegrant [18]. The excipients and QTF were sieved through a #35 mesh and blended using a benchtop blender operating at 10 rpm for 10 min before proceeding to further processing.

Granulation Process for Formulated Blends The powder blends were granulated using a 16 mm hot melt twin-screw extruder (ThermoFisher Scientific, 16 mm twin-screw extruder). The screw design, illustrated in Fig. 1, was strategically configured to ensure the solid feed underwent thorough and consistent mixing throughout the extrusion process. The design included an extended mixing zone to maximize uniformity, a material conveying zone to maintain smooth material flow, and a terminal mixing zone to ensure final homogenization before ejecting the processed granules.

The twin-screw extruder was operated at a screw speed of 50 rpm, with the temperature set to 150 °C, ensuring controlled thermal conditions. The torque was consistently maintained below 50%, signifying efficient mixing and minimal mechanical resistance during extrusion. The feed rate was maintained at 2–3 g/min, enabling a consistent and uniform material throughput. Following extrusion, the granules were milled using a benchtop blender and then sieved through a #35 mesh to achieve uniform particle size.

Flow Properties

The flow properties of all granules were assessed by calculating Carr's Index and Hausner's ratio with the help of bulk density (BD) and tapped density (TD). A 250 mL measuring cylinder was weighed, and its empty weight was recorded. Granules were carefully weighed and transferred into the cylinder. The combined mass of the cylinder and granules, along with the volume of the untapped granules, was documented. To measure tapped density, the cylinder was tapped using a tapping device for 10, 500, and 1250 taps, or until the volume change between consecutive measurements was less than 2 mL. If the volume difference exceeded 2 mL, additional sets of 1250 taps were performed until two consecutive readings showed a difference of less than 2 mL. The final tapped volume of the granules was recorded to ensure consistency and accuracy. The bulk density, tapped density, and Hausner Ratio of the granules were calculated using the following Eqs. 1, 2 and 3 [19].

$$Bulk\ Density = \frac{Mass\ of\ the\ granules}{Untapped\ volume} \quad (1)$$

$$Tapped\ Density = \frac{Mass\ of\ the\ granules}{Tapped\ volume} \quad (2)$$

$$\text{Hausner's Ratio} = \frac{Tapped\ density}{Bulk\ density} \quad (3)$$

Differential Scanning Calorimetry

DSC measurements of QTF, HPMC, Ludiflash®, physical mixtures, and extrudates were conducted using a Discovery DSC 25 instrument (TA Instruments, Newcastle, DE, USA) equipped with a Refrigerated Cooling System (RCS90). Approximately 5 mg of each sample was placed in standard aluminium pans, which were then crimped and sealed with aluminium lids. The samples were scanned at a consistent rate of 20 °C per minute across a temperature range of 25–200 °C, with a nitrogen purge flow of 50 mL/min. An empty pan was used as a reference [20].

Attenuated Total Reflection (ATR)

IR spectroscopy was conducted to identify molecular interactions of pure QTF, both in isolation and in the presence of Ludiflash® and HPMC HME LV15 Hypromellose within the formulations, before and after exposure to high shear forces and elevated temperatures. The IR spectra of QTF, HPMC, Ludiflash®, physical mixtures, and extrudates were obtained using an Agilent Cary 660 FTIR spectrometer (Agilent Technologies, Santa Clara, CA, USA). A small sample was placed on the diamond crystal and compressed using a Miracle high-pressure clamp. The samples were analyzed over a scanning range of 4000–650 cm^{-1} with a resolution of 4 cm^{-1}. The FTIR spectrometer was equipped with an attenuated total reflection (ATR) accessory (Pike Technologies, Madison, WI, USA), featuring a single bounce and a diamond-coated ZnSe internal reflection element [21].

Compression

Compression of Granules Before tablet compression, 5% of the super-disintegrant croscarmellose sodium was added to the granular mixture and blended in a benchtop V-blender at 10 rpm for 5 min. Following this, 1% of the lubricant magnesium stearate was added, and blended using bench-top V-blender at 10 rpm for an additional 5 min. The blended material was then compressed using a Natoli manual single station compression machine (Natoli NP-RD10A) under a compression force of 4000 to 5500 kPa, using an oval die with dimensions of 11 mm x 18.8 mm. The weight of tablets prepared from six formulations was given in Table 2. Though the final weight of each formulation varied, the dose remained constant at 345.56 mg of QTF (Eq. 300 mg base) per tablet.

Assay of Compressed & Commercially Available Quetiapine Fumarate Tablets The strength of the commercial quetiapine fumarate tablet was 345.56 mg of QTF (Eq. 300 mg base). An assay was performed for each of the compressed formulations (F1, F2, F3, F4, F5, F6) as well as the commercially available quetiapine fumarate tablets. The 10 tablets of each formulation were crushed in a motor and pestle, and the powder equivalent to one tablet weight was dissolved in a methanol and water mixture at a ratio of 30:70 [22]. The mixture was sonicated for one hour, and the absorbance of

Table 2 Final composition and final weight of the tablets

Formulation	F1	F2	F3	F4	F5	F6
Intragranular composition weight to obtain 300 mg of quetiapine base	1200.0	857.1	666.7	1200.0	857.1	857.1
Croscarmellose sodium	60.0	42.9	33.3	60.0	42.9	42.9
Magnesium stearate	12.0	8.6	6.7	12.0	8.6	8.6
Final tablet weight	1272.0	908.6	706.7	1272.0	908.6	908.6

each solution was recorded using UV-visible spectroscopy at a λmax of 290 nm.

Evaluation of Tablets The evaluation of the tablets included tests for weight variation, hardness, thickness, friability, and disintegration time. For the weight variation test, the individual weights of 20 tablets from each formulation were recorded using an balance. The weight variation test was performed because the percentage of QTF in the formulation is ≥25 mg and constitutes≥25% of the total weight of the tablet. The acceptance value for the weight variation was then calculated using Eq. 4 [23].

$$AV = |M - X| + k * s \tag{4}$$

If 98.5% ≤X≤101.5%, then M=X.

If X<98.5%, then M=98.5%, (AV=98.5 – X+ks)

If X>101.5%, then M=101.5%, (AV=X – 101.5+ks)

$$X = \frac{\sum_{i=1}^{n} x_i}{n}$$

$$x_i = {w_i * A}\Big/{W}$$

X: Mean content of the dosage units (expressed as a percentage of label claim).

χ_i: Individual content of each unit (expressed as a percentage of label claim).

n: Number of units tested.

w_i: individual weight.

A: Assay.

W: Average weight.

The hardness test was conducted on 10 tablets from each formulation batch using a tablet hardness tester (VK 200, Optimal) to determine the average tablet hardness or crushing strength. Tablet thickness was measured individually for 10 tablets using a digital vernier callipers.

For the friability test, 10 tablets were tested, as the weight of each tablet exceeded 650 mg. The tablets were weighed and placed into a friability tester (FT2, Sotax), then subjected to 100 revolutions (4 min at 25 rpm). The initial weight (I W) and final weight (FW) of the tablets were recorded, and the percentage friability was calculated using Eq. 5 [24].

$$\%\,\text{Friability} = \frac{\text{FW} - \text{IW}}{\text{IW}} * 100 \tag{5}$$

For the disintegration time test, one dosage unit was placed in each of the six tubes of the disintegration test basket, and a disk was inserted in each tube. The apparatus (Dr.Schleuniger Pharmatron DT2-IS) was operated using water as the immersion fluid, maintained at 37±2℃ The disintegration time for each formulation was recorded.

Dissolution Studies of Compressed & Commercially Available Quetiapine Fumarate Tablets

The drug release studies were conducted for each batch of compressed QTF tablets as well as for the commercially available tablets using the dissolution method outlined in FDA. A USP Type-II paddle apparatus was used at 37 °C with 900 mL of water as the dissolution medium, operating at 50 rpm. Samples of 2 mL were drawn at intervals of 10, 15, 20, 30, 45, and 60 min, following FDA criteria. The samples from each of the six batches were then diluted by a dilution factor of 10, and the diluted samples were analysed using UV-visible spectroscopy at 290 nm. The absorbance of each sample was recorded, and the cumulative percentage release of the compressed tablets was calculated [25]. The drug release profiles of the compressed formulations were compared with the commercially available tablets by calculating the dissimilarity factor (f1) and similarity factor (f2) as defined in the USP. The formulation that most closely matched the drug release profile of the commercial product was selected as the lead formulation.

Results & Discussion

Twin-Screw Melt Granulation

Initially, preliminary studies were conducted to establish the optimal upper and lower concentration limits for both the diluent and the polymer. These studies revealed critical concentration-dependent effects on granulation and drug release. When the polymer concentration was below 5% w/w, granulation was poor, as insufficient polymer presence failed to provide the necessary binding to form the granules. This resulted in a significant portion of fine or ungranulated material in the extrudates, which could negatively affect the uniformity and processability of the final product [26]. Conversely, when the concentration of HPMC exceeded 15% w/w, it caused a slower drug release profile. Specifically, less than 75% of the drug was released by the end of 60 min, likely due to the formation of a highly viscous gel layer that hindered the tablet's disintegration, subsequently the drug diffusion [27]. For Ludiflash®, it was observed that by increasing its concentration above 65% w/w, the tablet weight increased significantly, surpassing 1200 mg, which

caused issues during compression due to the excessive tablet size and weight.

The granules produced through TSMG are depicted in Fig. 2. The concentration of HPMC was found to significantly influence both granulation and dissolution. Higher concentrations of HPMC resulted in slower drug release due to the formation of a viscous gel matrix, whereas lower concentrations led to inadequate granulation with an increased presence of fines. Ludiflash®, which contains 3.0 to 6.5 w/w% of Kollidon® CL-SF (a super-disintegrating agent), effectively modulated tablet disintegration and subsequently dissolution [28].

The formulation process temperature was set at 150 °C, a temperature carefully selected to be above the glass transition temperature (Tg) of HPMC. This temperature does not affect Ludiflash® or QTF, as it remains below their respective melting points. This elevated temperature is critical for softening the HPMC and thereby enabling the desired granulation and drug release profiles. Additionally, the feed rate and screw speeds were meticulously optimized to maintain torque at less than 50% on the machine, ensuring efficient processing.

Flow Properties

Granulation is a critical process in pharmaceutical manufacturing, performed for several reasons, one of which is to enhance the flow properties of the powder blend. Improved flowability is essential for ensuring uniformity and efficiency during the compression stage of tablet manufacturing, particularly in large-scale production. Poor flow properties can lead to issues such as inconsistent tablet weights, segregation of components, or operational inefficiencies during high-speed compression [29].

The flow property assessment results for all formulations are summarized in Table 3, highlighting a significant improvement in blend flow properties following extrusion compared to the physical mixture. After extrusion, all formulations exhibited excellent flow characteristics. This enhancement is attributed to the granulation process, which optimizes particle size, shape, and surface characteristics, thereby reducing inter-particle friction and enhancing cohesiveness. Consequently, the final blend achieves superior flowability, facilitating smoother processing and reducing potential challenges during compression.

Differential Scanning Calorimetry

The thermograms of QTF, individual excipients, the physical mixture, and the F4 formulation are depicted in Fig. 3. The thermogram of QTF exhibited an endothermic peak corresponding to its melting point at 177 °C, indicating its crystalline nature [30]. For the polymer HPMC HME 15LV, no distinct Tg was observed; instead, a broad endothermic region was detected, with minima around 50–60 °C and 105 °C, likely due to moisture content or inherent polymer transitions [31]. The thermogram of Ludiflash® revealed an endothermic peak at 167 °C, corresponding to the melting

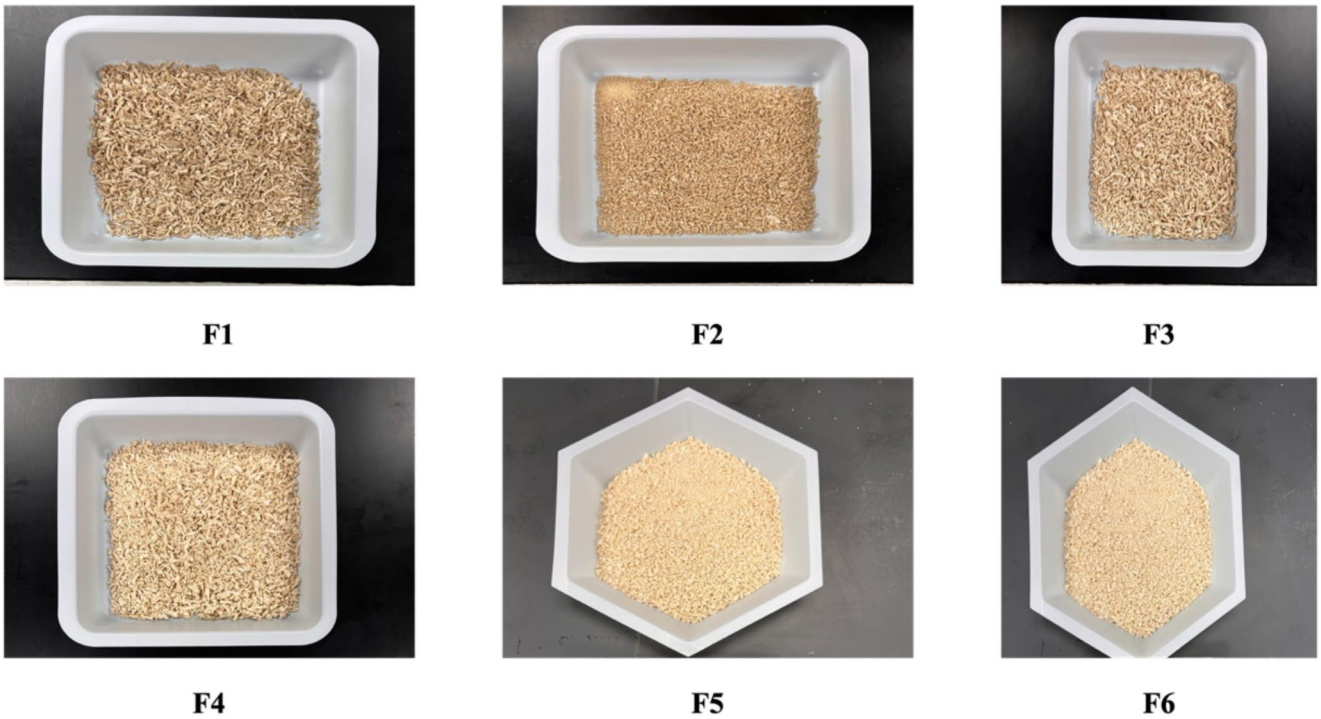

Fig. 2 Granules from formulations F1 to F6 following the granulation process

Table 3 Flow properties of pre-granular blends and granules after extrusion

Formulation		Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner Ratio	Flow Character
Physical Mixture	**F1**	0.50	0.80	37.50	1.60	Poor
	F2	0.52	0.78	33.33	1.50	Fair
	F3	0.54	0.76	28.95	1.41	Good
	F4	0.50	0.80	37.50	1.60	Poor
	F5	0.51	0.77	33.77	1.51	Fair
	F6	0.53	0.77	31.17	1.45	Good
After Extrusion	**F1**	0.71	0.76	6.58	1.07	Excellent
	F2	0.72	0.77	6.49	1.07	Excellent
	F3	0.73	0.77	5.19	1.05	Excellent
	F4	0.71	0.77	7.15	1.08	Excellent
	F5	0.76	0.77	6.91	1.08	Excellent
	F6	0.72	0.77	6.49	1.07	Excellent

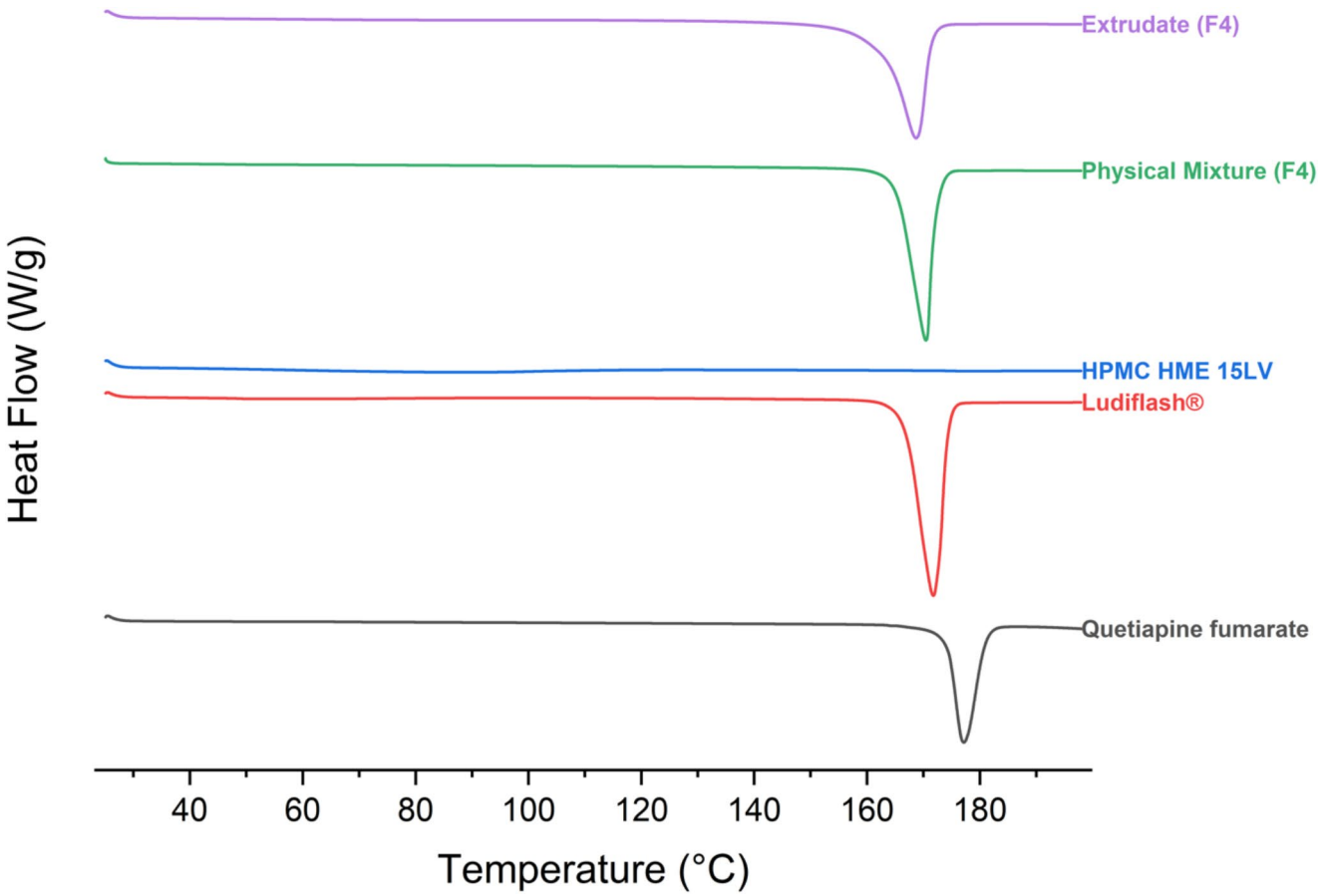

Fig. 3 DSC overlay of QTF, Ludiflash®, HPMC HME 15LV Hypromellose, physical mixture before granulation and extrudate

point of mannitol, which is the primary constituent of Ludiflash® [32].

Importantly, none of the formulation components exhibited signs of degradation below the processing temperature of 150 °C, and stability was maintained even up to 200 °C, confirming the thermal robustness of the materials. The physical mixture displayed an endothermic peak at 169.6 °C, attributed to combined endothermic peaks of Ludiflash® and QTF validating their thermal stability. The final extruded granules of the F4 formulation demonstrated a similar thermogram to the physical mixture, with an endothermic peak at 165 °C. This result indicates that the processing temperature of 150 °C did not affect the crystalline nature of QTF during granulation, preserving its structural/crystalline integrity.

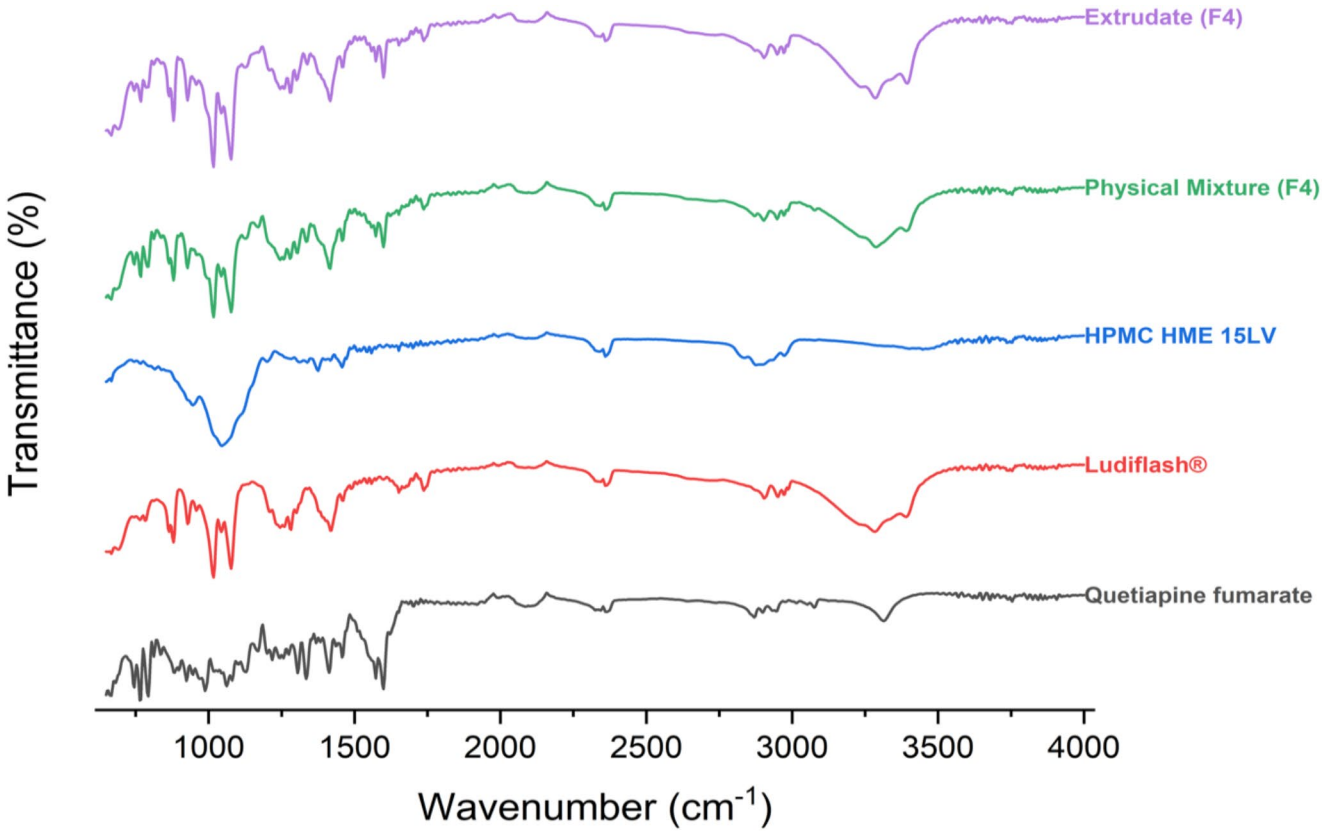

Fig. 4 FTIR of QTF, HPMC HME 15LV(Hypromellose), Ludiflash®, Physical mixture before granulation and Extrudates

Table 4 Assay of compressed quetiapine fumarate tablets

Formulations	Assay (%w/w)
F1	94.33
F2	96.06
F3	94.21
F4	98.60
F5	94.14
F6	96.15

Fourier Transform Infrared Spectroscopy

The FTIR spectra of QTF, the excipients, the physical mixture of F4, and the extrudates of the F4 formulation are shown in Fig. 4. The IR spectrum of QTF displayed characteristic peaks at 3310 cm^{-1} (O-H vibration), 2941 cm^{-1} (C-H stretching), 1741 cm^{-1} (C=O stretching), 1597 cm^{-1} (N-H bending), 1371 cm^{-1} (C-H stretching), and 1070 cm^{-1} (C-C stretching) [33]. The spectrum of the physical mixture reflects a superimposition of the spectra of its individual components. In the extruded granules of the F4 formulation, no new bonds were formed, no existing bonds were missing, and no significant shifts or broadening of IR bands were observed. This confirms that there are no strong chemical interactions among the formulation components [32].

Assay of Compressed Quetiapine Fumarate Tablets

The assay results for all formulations are presented in Table 4, with values ranging from 90 to 100%. This range is well within the acceptable limits i.e., NLT 90% to NMT 110% for QTF tablets, ensuring consistency and compliance with regulatory standards of USP [25]. The consistency in assay values might be attributed to the high percentage of QTF in the formulations, contributing to uniform API distribution.

Evaluation of Tablets

The results of the weight variation test are summarized in Table 5. The acceptance values for weight variation were consistently below the standard threshold of 15 for all batches, demonstrating compliance with pharmacopeial standards, and indicating that all batches successfully passed the weight variation test.

The hardness, thickness, friability, and disintegration time of all the tablet batches are presented in Table 6. The hardness of all batches was within the targeted range of 8–10 kPa. The thickness of the tablets varied proportionally with their weight, with deviations within each formulation remaining below 5% [34]. The friability of all batches was

Table 5 Weight variation results of compressed quetiapine fumarate tablets

Formulation	Mean Assay (%w/w)	Standard Deviation	Acceptance Value (AV)
F1	94.66	0.51	4.06
F2	96.00	0.47	3.63
F3	94.32	0.28	4.85
F4	98.79	0.35	2.84
F5	94.14	0.27	5.01
F6	96.14	0.22	2.89

Table 6 Hardness, thickness, friability and disintegration time of compressed QTF tablets

Formulation	Hardness (kPa)	Thickness (mm)	Friability (%)	Disintegration time (min)
F1	8.5±0.61	9.1±0.44	0.75	5:42
F2	9.1±0.82	7.3±0.28	0.80	6:05
F3	8.9±0.61	6.11±0.2	0.50	6:37
F4	9.6±0.56	9.41±0.42	0.50	5:50
F5	9.1±0.77	6.92±0.29	0.75	7:05
F6	9.2±0.72	7.11±0.26	0.80	6:15

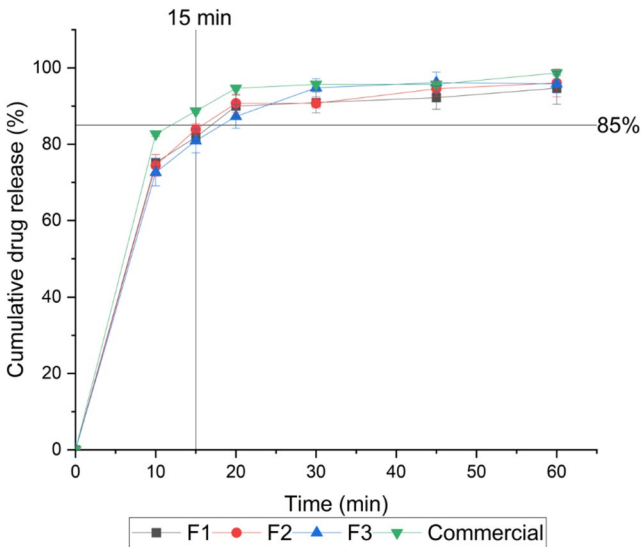

Fig. 5 Dissolution profile of F1, F2, F3 and commercial formulations

below 1%, meeting the standard requirement for tablet durability. Additionally, the disintegration time for all batches was under 10 min, reflecting rapid disintegration attributed to the inclusion of disintegrating agents in the formulations.

Dissolution Studies

The dissolution profiles of all the formulations, along with the commercial tablet, are presented in Figs. 5 and 6. All formulations demonstrated ≥85% of the drug release by

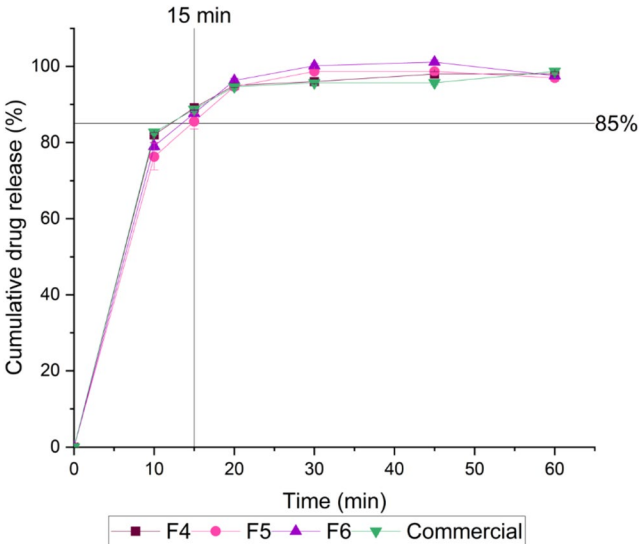

Fig. 6 Dissolution profile of F4, F5, F6 and commercial formulations

the end of the dissolution study. Notably, formulations F4, F5, F6 containing less than 10% w/w of binder (HPMC), and the commercial product achieved ≥85% drug release within the first 15 min, indicating very rapid drug release [35]. In contrast, the other formulations released less than 85% within the same time frame (within 15 min) but exhibited rapid release by achieving more than 85% drug release within 30 min [36].

The very rapid dissolution observed in formulations F4, F5, F6, and the commercial product can be attributed to a synergistic effect of multiple factors, including the high solubility of QTF, the presence of low quantities of HPMC, and the use of high quantities of Ludiflash®, which is known for enhancing disintegration and drug release.

The formulations F4, F5, F6, and the commercial product released ≥85% of the drug within 15 min, calculating similarity (f2) and dissimilarity (f1) factors was deemed unnecessary as per the USP. The high release rate of ≥85% within 15 min, itself demonstrates that the developed formulations are comparable to the commercial product in terms of dissolution efficiency and performance [37].

Conclusion

Twin-screw melt granulation is gaining interest in manufacturing solid oral dosage forms due to its customizability, robustness, and compatibility with continuous manufacturing processes. This solvent-free technology eliminates the need for solvent and a drying step, making it a cost-effective and efficient alternative to traditional granulation methods. The current study successfully demonstrated the application of TSMG in developing immediate-release QTF tablets with

drug release profiles comparable to the marketed product. The influence of drug loading, diluent, and binder concentrations on flowability, tableting, and dissolution properties was systematically evaluated. Notably, higher concentrations of HPMC were observed to retard dissolution, while optimized levels ensured rapid drug release. Thermal studies confirmed the retention of QTF crystallinity post-granulation, and infrared spectroscopy verified no strong chemical interactions between formulation components. This study highlights TSMG as a reliable and economical approach for producing immediate-release tablets, offering a promising alternative for integrating advanced manufacturing technology into continuous production workflows.

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Declarations

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