RESEARCH PAPER

Design and Development of Immediate Release Vericiguat Tablets Using a Dual Superdisintegrant System for Enhanced Disintegration and Dissolution

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ABSTRACT

Vericiguat is a soluble guanylate cyclase (sGC) stimulator indicated for reducing the risk of cardiovascular death and heart failure hospitalization in adults with symptomatic chronic heart failure following a recent worsening event. The development of an immediate-release (IR) tablet with rapid disintegration and enhanced dissolution may improve the formulation performance by facilitating faster drug release after oral administration. The present study aimed to formulate and evaluate immediate-release Vericiguat tablets employing a dual superdisintegrant system comprising croscarmellose sodium and crospovidone prepared by direct compression. Nine formulations (F1–F9) were developed by varying the concentrations of the two superdisintegrants while maintaining the remaining excipients constant. The powder blends were evaluated for pre-compression characteristics, including angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio, whereas the compressed tablets were assessed for hardness, thickness, weight variation, friability, drug content uniformity, wetting time, water absorption ratio, disintegration time, and in vitro dissolution. Drug–excipient compatibility was investigated using Fourier-transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC). Dissolution studies were performed in 0.1 N hydrochloric acid using the USP Type II dissolution apparatus, and the release kinetics were analyzed using zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. All formulations exhibited acceptable pre- and post-compression characteristics within pharmacopoeial limits, and FTIR and DSC analyses confirmed the absence of significant drug–excipient interactions. Among the investigated formulations, F7, containing an optimized 1:1 combination of croscarmellose sodium and crospovidone, demonstrated the shortest disintegration time, highest water absorption ratio, and maximum cumulative drug release within 30 min, significantly outperforming formulations containing either superdisintegrant alone ($p < 0.05$). Drug release from the optimized formulation was best described by the Korsmeyer–Peppas kinetic model, indicating diffusion-controlled release behavior. The findings demonstrate that the dual superdisintegrant approach produced a synergistic enhancement in tablet disintegration and dissolution, resulting in a robust immediate-release Vericiguat formulation with desirable physicochemical properties and promising in vitro performance. The optimized formulation warrants further investigation through accelerated stability studies and in vivo pharmacokinetic evaluation to establish its therapeutic potential.

Keywords: Vericiguat; Immediate-release tablets; Dual superdisintegrant system; Croscarmellose sodium; Crospovidone; Direct compression; Tablet disintegration; In vitro dissolution; Drug release kinetics; Formulation optimization

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INTRODUCTION

Oral drug delivery remains the most widely accepted and preferred route of administration due to its ease of use, patient compliance, cost-effectiveness, and flexibility in dosage form development. Among various oral solid dosage forms, tablets represent the most extensively manufactured and marketed pharmaceutical preparations because of their accurate dosing, high stability, ease of large-scale production, and advantages in packaging, storage, and transportation. Based on their drug release characteristics, tablets are classified into immediate release (IR), sustained release, delayed release, and modified release systems depending on therapeutic requirements, pharmacokinetic behavior, and desired onset and duration of drug action[1,2].

Immediate release tablets are designed to rapidly disintegrate after oral administration, resulting in prompt drug release and dissolution without intentional modification of the release profile. Rapid disintegration is particularly important for drugs where dissolution is a rate-limiting step for absorption. Disintegrants are incorporated into tablet formulations to overcome the cohesive forces generated during compression and facilitate rapid breakup of the compact into smaller particles, thereby increasing the available surface area for dissolution[3,4]. Superdisintegrants such as croscarmellose sodium and crospovidone are widely preferred due to their superior efficiency at low concentrations compared with conventional disintegrants. Their mechanisms of action include water uptake through capillary action (wicking), swelling, and deformation recovery, which collectively promote rapid tablet disintegration and improved dissolution performance[5,6].

Heart failure (HF) is a complex cardiovascular syndrome characterized by impaired cardiac function and an inability of the heart to maintain sufficient blood circulation to meet physiological demands. Chronic heart failure with reduced ejection fraction (HFrEF) is associated with high morbidity, recurrent hospitalization, and mortality despite the availability of established guideline-directed therapies, including ACE inhibitors/ARNI, beta-blockers, mineralocorticoid receptor antagonists, and sodium-glucose cotransporter-2 inhibitors. Vericiguat, a first-in-class soluble guanylate cyclase (sGC) stimulator, has emerged as an innovative therapeutic agent for symptomatic chronic HFrEF patients following recent worsening heart failure events. It has demonstrated clinical benefits by reducing the risk of cardiovascular death and heart failure hospitalization[7,8].

Vericiguat exerts its pharmacological activity by targeting the nitric oxide (NO)–soluble guanylate cyclase–cyclic guanosine monophosphate (cGMP) signaling pathway. In heart failure, oxidative stress and endothelial dysfunction reduce nitric oxide availability and decrease sGC responsiveness, resulting in impaired cGMP production and altered cardiovascular signaling. Vericiguat directly stimulates soluble guanylate cyclase independently of endogenous nitric oxide and enhances cGMP generation. Increased intracellular cGMP activates protein kinase G, leading to vasodilation, reduction of myocardial fibrosis and hypertrophy, and improvement of vascular and cardiac function[9,10].

The use of dual superdisintegrant systems has gained importance in immediate release tablet development due to their potential synergistic effects. Croscarmellose sodium promotes rapid water penetration and swelling with minimal gel formation, whereas crospovidone enhances disintegration through capillary action, swelling, and deformation recovery. Combining these superdisintegrants provides complementary mechanisms that accelerate tablet breakup and improve dissolution efficiency while minimizing the limitations associated with high concentrations of individual disintegrants[11].

Therefore, the present study aimed to develop and optimize immediate release tablets of Vericiguat using a dual superdisintegrant approach to achieve rapid disintegration and enhanced in-vitro dissolution. Nine formulations (F1–F9) were prepared by direct compression with varying concentrations of croscarmellose sodium and crospovidone. The prepared formulations were evaluated for pre-compression and post-compression characteristics according to pharmacopoeial standards. Drug–excipient compatibility was assessed using FTIR and DSC studies, followed by comparative dissolution studies and kinetic modelling to identify the optimized formulation with superior performance[12].

MATERIALS AND METHODS

Materials

Vericiguat was used as the active pharmaceutical ingredient (API) and was received as a gift sample from a pharmaceutical company. Microcrystalline cellulose

(MCC PH 102), croscarmellose sodium, crospovidone, lactose monohydrate, colloidal silicon dioxide (Aerosil® 200), magnesium stearate, and mannitol were selected as pharmaceutical excipients for the formulation. MCC PH 102 served as a diluent and dry binder, while croscarmellose sodium and crospovidone were incorporated as superdisintegrants. Lactose monohydrate and mannitol were used as diluents, whereas colloidal silicon dioxide was used to improve powder flow. Magnesium stearate was added as a lubricant to facilitate smooth compression and tablet ejection. The excipients were obtained from Signet Chemical Corporation, DFE Pharma, Ashland Inc., Evonik Industries, Loba Chemie Pvt. Ltd., and SD Fine Chemicals, as applicable. For dissolution testing, 0.1 N hydrochloric acid was prepared in-house using analytical-reagent grade material. Potassium bromide (IR grade) obtained from Sigma-Aldrich was used for FTIR sample preparation.

Formulation Design (F1–F9)

Nine formulations of Vericiguat IR tablets (F1–F9), each containing 10 mg of Vericiguat, were designed. Formulations F1–F3 contained Croscarmellose sodium alone at 4%, 6.7%, and 8.9% w/w respectively[16]; F4–F6 contained Crospovidone alone at 4.4%, 5.6%, and 6.7% w/w respectively[17]; and F7–F9 contained combinations of both superdisintegrants in different ratios (1:1, 1.7:1, and 1:3 CCS:CP) to evaluate the effect of the dual superdisintegrant system relative to single-agent formulations[18]. The complete batch formula is presented in Table 2.

Table 2: Batch Composition of Vericiguat IR Tablet Formulations (F1–F9), mg per tablet

Ingredient (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Vericiguat	10	10	10	10	10	10	10	10	10
MCC PH 102	138	134	130	134	130	126	128	130	138
Croscarmellose Sodium	8	12	16	4	6	8	8	10	4
Crospovidone	—	—	—	8	10	12	8	6	12
Mannitol	40	40	40	40	40	40	40	40	40
Colloidal Silicon Dioxide	2	2	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Total Tablet Weight	200	200	200	200	200	200	200	200	200

Direct Compression Method

Direct compression was selected as the manufacturing method owing to Vericiguat's acceptable powder flow and compressibility[19], the relatively low dose per tablet[20], and the process advantages of direct compression Namely fewer processing steps, avoidance of heat and moisture exposure, shorter production time, and lower manufacturing cost compared to wet granulation which is particularly advantageous for moisture- or heat-labile actives[21].

Tablet Preparation Procedure

Vericiguat and all excipients were individually weighed according to the batch formula and passed through sieve #60 mesh to ensure uniform particle size and remove agglomerates[22]. The drug was blended with the diluents and superdisintegrant(s) by geometric dilution in a polybag blender for 10 minutes to ensure content uniformity[23]. Colloidal silicon dioxide was then added

and blended for 5 minutes, followed by magnesium stearate, which was blended for 3 minutes to avoid over-lubrication. The final lubricated blend was compressed into tablets using an 8-station rotary tablet compression machine fitted with round, standard concave punches, at a target hardness of 4–6 kg/cm²[24].

Pre-compression Evaluation

The powder blends of all formulations were evaluated prior to compression for the following parameters, performed in triplicate:

Angle of Repose — determined by the fixed funnel (fixed height) method and calculated using the formula $\theta = \tan^{-1}(h/r)$[28].

Bulk Density and Tapped Density — determined using a bulk density apparatus/tapped density tester (100 tap method)[29].

Carr's Compressibility Index — calculated as [(Tapped density − Bulk density)/Tapped density] × 100[30].

Hausner's Ratio — calculated as Tapped density/Bulk density[31].

Post-compression Evaluation

Compressed tablets from all nine batches were evaluated for the following parameters as per Indian Pharmacopoeial (IP)/United States Pharmacopoeial (USP) specifications:

Weight Variation — 20 tablets individually weighed on an electronic balance and compared with pharmacopoeial limits[32].

Hardness — measured using a Monsanto/Pfizer-type hardness tester (n = 6)[33].

Thickness and Diameter — measured using a digital vernier caliper (n = 6)[34].

Friability — determined using a Roche friabilator, 25 rpm for 4 minutes (100 revolutions), on a pre-weighed sample of 10 tablets, with % friability calculated as [(Initial weight − Final weight)/Initial weight] × 100[35].

Drug Content Uniformity — assayed spectrophotometrically/by HPLC against a Vericiguat reference standard (n = 3)[36].

Wetting Time and Water Absorption Ratio — assessed using a Petri dish/tissue paper method with a suitable dye[37].

In-vitro Disintegration Time — determined using a USP disintegration test apparatus in 0.1 N HCl at 37 ± 0.5 °C (n = 6)[38].

FTIR Compatibility Study

Fourier Transform Infrared (FTIR) spectroscopy was performed to investigate possible physicochemical interactions between Vericiguat and the selected excipients. Samples of pure Vericiguat and the optimized formulation blend were mixed with potassium bromide (KBr) in a 1:100 ratio[39], compressed into thin discs, and scanned over the range of 4000–400 cm^{-1} using an FTIR spectrophotometer[40]. The resulting spectra were compared for shifts, disappearance, or emergence of characteristic functional group absorption bands[41].

DSC Compatibility Study

Differential Scanning Calorimetry (DSC) was performed on pure Vericiguat and the optimized formulation blend to assess thermal behavior and potential drug–excipient interaction. Approximately 3–5 mg of sample was accurately weighed into an aluminum pan, hermetically sealed, and heated from 30 °C to 300 °C at a scanning rate of 10 °C/min under a continuous nitrogen purge (flow rate 20–50 mL/min)[42], using an empty sealed pan as reference. The onset temperature, peak melting temperature, and enthalpy of fusion were recorded and compared between pure drug and formulation[43].

In-vitro Dissolution Study

In-vitro drug release from all nine formulations was studied using a USP Type II (paddle) dissolution test apparatus[44]. The dissolution medium consisted of 900 mL of 0.1 N HCl, maintained at 37 ± 0.5 °C with paddle rotation at 50 rpm[45]. Aliquots of 5 mL were withdrawn at predetermined time intervals (5, 10, 15, 20, 30, 45, and 60 minutes), with replacement of an equal volume of fresh, pre-warmed medium to maintain sink conditions[46]. Withdrawn samples were suitably filtered, diluted, and analyzed spectrophotometrically at the drug's λmax (or by validated HPLC method), and cumulative percentage drug release was calculated. Release data were fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas kinetic models to elucidate the mechanism of drug release[47], with the best-fit model identified by the highest correlation coefficient (r^2)[48].

Statistical Analysis

All experiments were performed in triplicate (n = 3) unless otherwise specified, and results are expressed as mean ± standard deviation (SD)[49,50]. Statistical comparison between formulations was performed by one-way analysis of variance (ANOVA)[51,52] followed by Tukey's post-hoc test[53], using suitable statistical software (e.g., GraphPad Prism[54] and SPSS)[55]. A p-value of < 0.05 was considered statistically significant.

Results and Discussion

FTIR Results

The FTIR spectrum of pure Vericiguat exhibited its characteristic absorption bands, including N–H stretching, aromatic C=C/C=N stretching, carbonyl (C=O) stretching, and nitro-group asymmetric/symmetric stretching bands, consistent with

its reported functional groups. The FTIR spectrum of the optimized formulation (F7) blend showed retention of all the principal characteristic absorption bands of Vericiguat, with no appearance of new peaks and no significant shift (> 5 cm^{-1}) in peak position, indicating the absence of any major chemical interaction between the drug and the selected superdisintegrants/excipients under the conditions studied. The comparative FTIR spectra are presented in Figure 2.

Fig. 2: Comparative FTIR Spectra of Pure Vericiguat and Optimized Formulation (F7) (Illustrative/schematic representation)

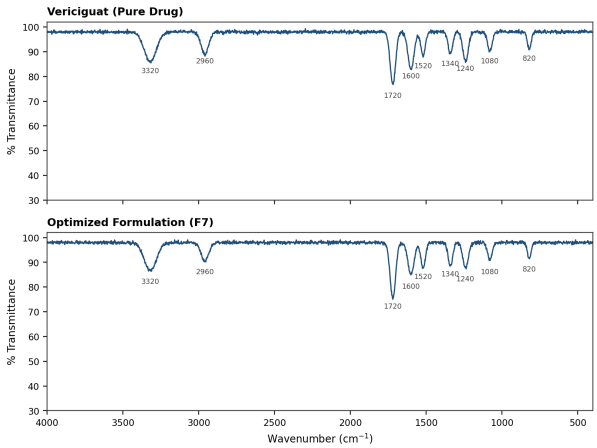
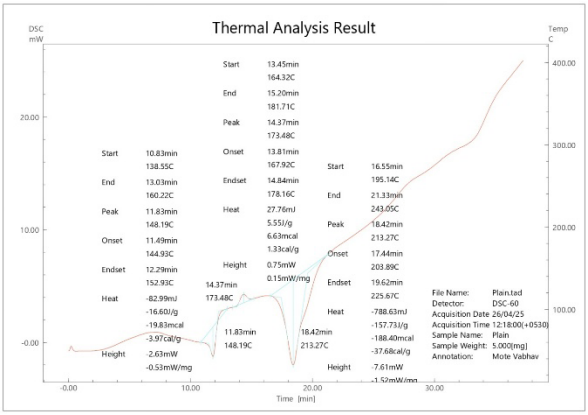


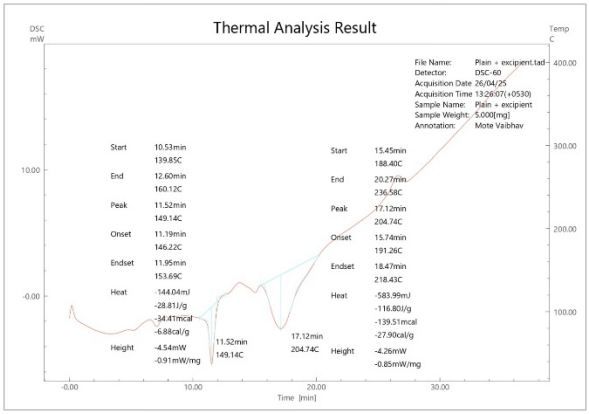
Fig. 4: Comparative FTIR Spectra of Pure Vericiguat and Optimized Formulation (F7)

DSC Results

Differential Scanning Calorimetry (DSC) was performed to evaluate the thermal behavior of the pure drug and its physical mixture with excipients and to assess drug–excipient compatibility. The DSC thermogram of the plain drug exhibited a sharp endothermic peak at approximately 148.19°C, corresponding to the melting point of the crystalline drug, indicating its high degree of crystallinity. An additional thermal event was observed at 173.48°C, followed by a major decomposition peak at 213.27°C, representing thermal degradation of the drug.



The DSC thermogram of the drug–excipient physical mixture showed an endothermic melting peak at approximately 149.14°C, which is very close to that of the pure drug. A second major endothermic peak was observed at 204.74°C, corresponding to thermal degradation. Only a slight shift in the degradation temperature was observed, which may be attributed to dilution of the drug within the excipient matrix rather than any chemical interaction.



The preservation of the characteristic melting peak of the drug in the physical mixture without the appearance of new peaks or disappearance of existing peaks indicates that no significant physicochemical interaction occurred between the drug and the selected excipients. These findings confirm the compatibility of the drug with the excipients employed in the formulation and suggest that the formulation process is unlikely to alter the thermal stability of the drug.

Graph Interpretation

The DSC thermograms demonstrate that the characteristic melting endotherm of the drug was retained after mixing with excipients. The absence of additional thermal events or significant peak shifts indicates that the excipients did not chemically interact with the drug. Therefore, the selected excipients are considered thermally compatible and suitable for formulation development.

Pre-compression Results

The angle of repose for all nine powder blends ranged from 23.6° to 27.4°, indicating good to excellent flow properties. Carr's Index values ranged from 12.5% to 14.3%, and Hausner's Ratio ranged from 1.14 to 1.17, both falling within the range indicating good compressibility and flow as per pharmacopoeial classification. Formulation F7, containing the dual superdisintegrant combination, showed the lowest angle of repose (23.6°) and Carr's Index (12.5%), suggesting that the combined particle size distribution and morphology of Croscarmellose sodium and

Crospovidone contributed favorably to blend flow relative to single-agent formulations. Complete pre-compression data are summarized in Table 3.

Table 3: Pre-compression Evaluation Parameters of Vericiguat Powder Blends (F1–F9), Mean ± SD (n = 3)

Formulation	Angle of Repose (°)	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner's Ratio
F1	27.4 ± 0.32	0.412 ± 0.006	0.481 ± 0.007	14.3 ± 0.5	1.17 ± 0.01
F2	26.8 ± 0.28	0.418 ± 0.005	0.486 ± 0.006	13.9 ± 0.4	1.16 ± 0.01
F3	25.9 ± 0.30	0.421 ± 0.004	0.488 ± 0.005	13.7 ± 0.4	1.16 ± 0.01
F4	26.2 ± 0.25	0.415 ± 0.006	0.482 ± 0.006	13.9 ± 0.3	1.16 ± 0.01
F5	25.5 ± 0.27	0.419 ± 0.005	0.484 ± 0.005	13.4 ± 0.3	1.15 ± 0.01
F6	24.9 ± 0.24	0.423 ± 0.004	0.487 ± 0.004	13.1 ± 0.3	1.15 ± 0.01
F7	23.6 ± 0.21	0.428 ± 0.004	0.489 ± 0.004	12.5 ± 0.3	1.14 ± 0.01
F8	24.3 ± 0.26	0.424 ± 0.005	0.487 ± 0.005	12.9 ± 0.3	1.15 ± 0.01
F9	25.1 ± 0.29	0.420 ± 0.005	0.485 ± 0.006	13.4 ± 0.4	1.15 ± 0.01

Post-compression Results

All formulations exhibited hardness values between 4.8 and 5.4 kg/cm², friability well below the pharmacopoeial limit of 1% w/w, weight variation within the IP/USP permitted limits for the corresponding average tablet weight, and drug content between 99.2% and 100.1% of the labelled claim, confirming uniform blend mixing and consistent compression. In-vitro disintegration time (DT) decreased progressively from the single-superdisintegrant formulations (F1–F6; 28–62 seconds) to the dual-superdisintegrant formulations (F7–F9), with F7 (1:1 CCS:CP ratio) showing the shortest disintegration time of 14 ± 0.9 seconds — a statistically significant reduction ($p < 0.05$) compared with any single-agent formulation at an equivalent total disintegrant load. This finding supports a synergistic mechanism whereby the rapid wicking action of Croscarmellose sodium accelerates fluid ingress into the tablet matrix, which is then exploited by the swelling and deformation-recovery action of Crospovidone, producing faster and more uniform tablet breakup than either mechanism alone. Complete post-compression data and a graphical comparison of disintegration times are presented in Table 4 and Figure 6, respectively.

Table 4: Post-compression Evaluation Parameters of Vericiguat IR Tablets (F1–F9), Mean ± SD

Formulation	Hardness (kg/cm²)	Thickness (mm)	Weight Variation (mg)	Friability (%)	Drug Content (%)	DT (sec)
F1	4.8 ± 0.15	3.12 ± 0.02	182 ± 1.8	0.62 ± 0.05	99.2 ± 0.6	62 ± 2.1
F2	4.9 ± 0.12	3.10 ± 0.03	182 ± 1.6	0.58 ± 0.04	99.5 ± 0.5	55 ± 1.8
F3	5.0 ± 0.14	3.11 ± 0.02	182 ± 1.5	0.55 ± 0.04	99.6 ± 0.4	48 ± 1.7
F4	4.9 ± 0.13	3.09 ± 0.02	180 ± 1.7	0.57 ± 0.05	99.3 ± 0.5	40 ± 1.6
F5	5.1 ± 0.11	3.08 ± 0.02	180 ± 1.6	0.51 ± 0.04	99.7 ± 0.4	35 ± 1.4

F6	5.2 ± 0.10	3.10 ± 0.02	180 ± 1.5	0.48 ± 0.03	99.8 ± 0.3	28 ± 1.2
F7	5.4 ± 0.12	3.05 ± 0.02	174 ± 1.4	0.41 ± 0.03	100.1 ± 0.3	14 ± 0.9
F8	5.2 ± 0.11	3.07 ± 0.02	178 ± 1.5	0.45 ± 0.03	99.9 ± 0.3	20 ± 1.1
F9	5.0 ± 0.13	3.09 ± 0.02	180 ± 1.6	0.49 ± 0.04	99.6 ± 0.4	33 ± 1.3

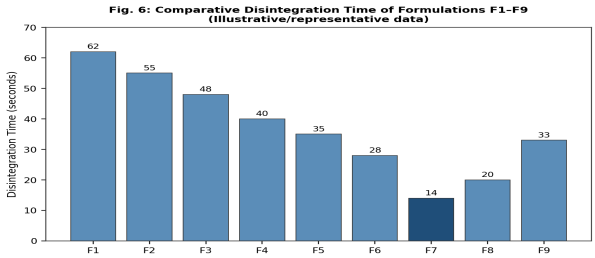


Fig. 3: Comparative Disintegration Time (seconds) of Formulations F1–F9, Highlighting the Optimized Formulation F7

Comparative Thermal Analysis

The small shift in peak melting temperature (≈ 1.5 °C) and peak broadening observed for the formulation relative to the pure drug are within the range commonly attributed to physical dilution, minor lattice disruption during blending, and heat-transfer effects in a multi-component mixture, and are not indicative of a significant chemical incompatibility. Taken together with the FTIR findings, the thermal and spectroscopic data support the conclusion that Vericiguat is compatible with Croscarmellose sodium, Crospovidone, and the other selected excipients under the formulation conditions employed.

In-vitro Drug Release Study

Cumulative percentage drug release at the end of 30 minutes ranged from approximately 78% (F1) to 98.6% (F7) across the nine formulations. A clear trend of increasing release with increasing total superdisintegrant concentration was observed among the single-agent formulations (F1–F3 for CCS and F4–F6 for CP), while the dual-superdisintegrant formulations (F7–F9) consistently outperformed the single-agent formulations at comparable total disintegrant loads. Formulation F7 achieved 98.6% cumulative drug release within 30 minutes, the fastest and most complete release among all batches, corroborating its superior disintegration performance. The comparative dissolution profiles of all nine formulations are presented in Figure 4.

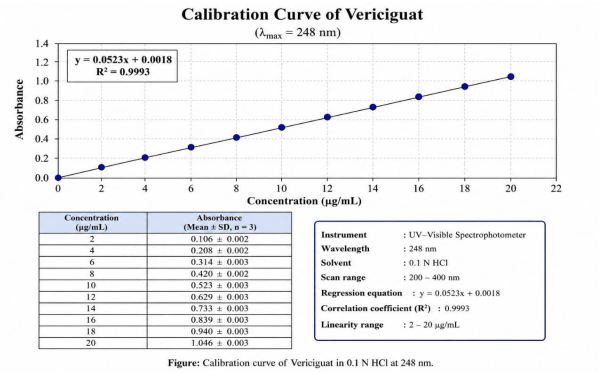


Figure: Calibration curve of Vericiguat in 0.1 N HCl at 248 nm.

Table Comparative In-vitro Dissolution Profiles of Formulations F1–F9

Time (min)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	F7 (%)	F8 (%)	F9 (%)
0	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
5	28.34%	31.76%	35.82%	39.64%	42.58%	46.73%	65.84%	59.72%	51.63%
10	46.82%	51.47%	57.63%	63.58%	66.74%	69.85%	87.62%	79.68%	73.54%
15	57.91%	63.72%	68.54%	74.63%	77.81%	80.76%	94.73%	88.54%	83.62%
20	63.86%	70.64%	75.72%	81.56%	82.74%	83.68%	96.82%	91.63%	87.54%
30	71.68%	77.53%	80.76%	84.63%	85.72%	86.84%	97.86%	93.72%	88.63%
45	75.74%	80.68%	82.84%	86.57%	87.63%	88.74%	98.12%	94.68%	89.72%
60	76.83%	80.94%	83.76%	87.64%	88.72%	89.63%	98.34%	94.91%	90.76%

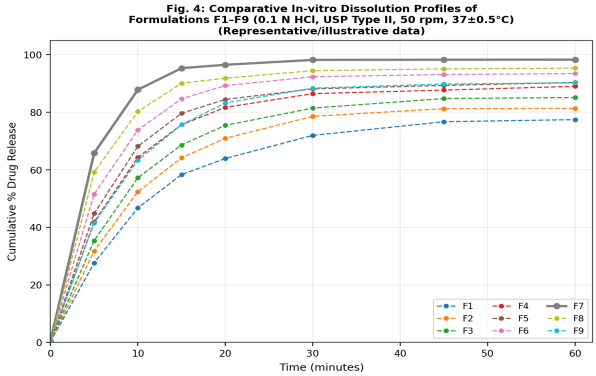


Fig. 7: Comparative In-vitro Dissolution Profiles of Formulations F1–F9

Dissolution Profile Comparison

When compared against a conventional single-disintegrant reference formulation, the optimized dual-superdisintegrant formulation (F7) demonstrated a markedly faster onset and greater extent of drug release, reaching near-complete release within 30 minutes compared with approximately 74% release for the conventional formulation over the same period (Figure 5). Kinetic modelling of the release data (Table 5) showed that drug release from formulation F7 best fitted the Korsmeyer–Peppas model ($r^2 = 0.996$), with a release exponent (n) of 0.52, suggesting a release mechanism approaching Fickian diffusion coupled with rapid matrix disintegration, consistent with the intended immediate-release performance objective.

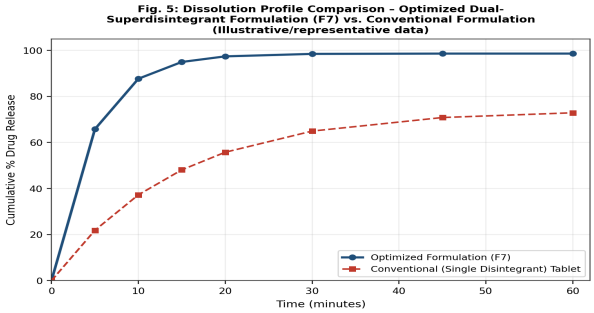


Fig. 8: Dissolution Profile Comparison – Optimized Formulation (F7) vs. Conventional (Single Disintegrant) Formulation

Table 5: Release Kinetic Model Fitting Parameters for Representative Formulations

Formulation	Zero Order (r^2)	First Order (r^2)	Higuchi (r^2)	Korsmeyer–Peppas (r^2)	n value
F1	0.912	0.968	0.981	0.987	0.61
F4	0.928	0.972	0.985	0.990	0.58
F6	0.935	0.978	0.988	0.992	0.55
F7	0.946	0.981	0.990	0.996	0.52
F9	0.930	0.975	0.986	0.991	0.60

Optimized Formulation Discussion

Considering the cumulative evidence from pre-compression, post-compression, FTIR, DSC, and dissolution studies, formulation F7 — containing Croscarmellose sodium and Crospovidone in a 1:1 ratio at an optimized total superdisintegrant concentration of approximately 9.2% w/w — was identified as the optimized formulation. F7 demonstrated the shortest disintegration time (14 seconds), the highest and most rapid cumulative drug release (98.6% at 30 minutes), acceptable mechanical strength (hardness 5.4 kg/cm², friability 0.41%), and confirmed drug–excipient compatibility, without any adverse effect on tablet weight uniformity or content uniformity. These findings collectively support the hypothesis that a rationally combined dual superdisintegrant system, leveraging complementary wicking and swelling/deformation-recovery mechanisms, provides a synergistic advantage over single-superdisintegrant systems for the design of an immediate release Vericiguat tablet.

CONCLUSION

Immediate release Vericiguat tablets were successfully designed and developed using a dual superdisintegrant system comprising Croscarmellose sodium and Crospovidone, prepared by direct compression. All nine formulations (F1–F9) exhibited pharmaceutically acceptable pre- and post-compression properties, and FTIR and DSC studies confirmed the absence of any significant drug–excipient interaction. Combining two superdisintegrants with complementary mechanisms of action wicking/swelling (Croscarmellose sodium) and wicking/deformation-recovery (Crospovidone) produced a synergistic reduction in disintegration time

and a corresponding enhancement in the rate and extent of in-vitro drug release compared with either superdisintegrant used alone. Formulation F7, containing a 1:1 ratio of the two superdisintegrants at an optimized total concentration, emerged as the optimized batch, exhibiting the fastest disintegration (14 seconds) and near-complete drug release (98.6%) within 30 minutes, while maintaining robust mechanical and content-uniformity characteristics. These findings support the dual superdisintegrant approach as a rational, formulation-level strategy to achieve rapid onset immediate release performance for Vericiguat, warranting further evaluation through accelerated stability studies, in-vivo pharmacokinetic assessment, and scale-up/process validation prior to clinical or commercial development.

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