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Research article

Optimized Formulation of Sitagliptin Fast Dissolving Tablets Using Statistical Design Techniques

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ABSTRACT

The study focused on developing and statistically optimizing sitagliptin-loaded fast-dissolving tablets (FDTs) utilizing a systematic DoE-based approach to enhance oral drug delivery and patient compliance in type 2 diabetes management. FDTs were prepared via direct compression with varying concentrations of variable excipients, crospovidone (superdisintegrant) and Avicel 102 (binder) as part of a 3^2 full factorial design. The study assessed their impact on formulation attributes, specifically hardness and disintegration time, alongside pre- and post-compression characteristics, dissolution performance, and stability over time. All developed formulations met pharmacopoeial standards. The optimized batch (B7) disintegrated in 34 ± 3 seconds with adequate hardness of 4.5 ± 0.09 kg/cm^2 and achieved 99.11% drug release within 30 minutes. Statistical analysis confirmed significant effects of both excipients, with crospovidone having a greater influence on disintegration. Stability studies over three months indicated no significant changes in key parameters. The results demonstrated a robust, cost-effective sitagliptin FDT with improved dissolution properties, particularly beneficial for those with dysphagia or requiring immediate pharmacological response.

Introduction

The oral pathway remains predominant in pharmacotherapy, largely because of its convenience, safety, and broad patient acceptance. Despite their advantages, traditional oral formulations may be unsuitable for geriatric and pediatric populations, as well as for patients experiencing dysphagia or lacking immediate access to water during medication intake.[1] Fast-dissolving tablets (FDTs) have been developed as a patient-friendly alternative that rapidly disintegrates in the oral cavity-usually within a minute, and requires no water for swallowing, ensuring rapid availability of the API, thereby enhancing convenience as well as treatment adherence.[2,3]

Numerous studies have validated the efficacy of FDTs in enhancing bioavailability and therapeutic outcomes. For example, Basu *et al.* formulated cinnarizine FDTs using superdisintegrants and sublimation techniques to achieve faster onset of action.[4] Similarly, Sharma *et al.* developed salbutamol FDTs for respiratory disorders, demonstrating improved disintegration and absorption rates.[5] Satpute *et al.* also successfully formulated metoprolol tartrate FDTs and emphasized their advantages in terms of patient compliance and faster drug action. [6] These studies collectively highlight the growing interest in FDTs as a viable approach to enhance drug delivery for conditions requiring rapid therapeutic response.

Sitagliptin, a DPP-4 inhibitor, facilitates glycemic regulation by augmenting insulin secretion and inhibiting glucagon release, both of which are dependent on blood glucose concentrations. It is commonly prescribed for type 2 diabetes and is often used in combination with lifestyle interventions to achieve glycemic control.[7,8] Despite its clinical effectiveness, sitagliptin's conventional tablet form may not be ideal for all patients, particularly the elderly, who often face swallowing difficulties. Additionally,

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enhancing the dissolution rate of sitagliptin can potentially improve its bioavailability and therapeutic onset, especially in controlling postprandial hyperglycemia.

Responding to the need for patient-centric drug delivery systems, particularly for chronic conditions like type 2 diabetes, this investigation utilized a systematic DoE framework to design and optimize sitagliptin-loaded FDTs. Their rapid disintegration and dissolution facilitate faster drug absorption, mitigating postprandial hyperglycemia as well, improving therapeutic effectiveness.[9]

To achieve a robust, cost-effective formulation with improved disintegration and mechanical properties, the study employed Quality by Design (QbD) principles. [10] A 3^2 full factorial design was adopted to systematically investigate the effects of crospovidone (as a superdisintegrant) and Avicel 102 (as a binder) on critical quality attributes, including tablet hardness and disintegration time. This structured approach ensured a better understanding of formulation behavior and enhanced reproducibility [11], ultimately supporting the development of an effective sitagliptin FDT for improved diabetes management.

Materials and Methods

Materials

A complimentary sample of sitagliptin was supplied, and all other excipients of pharmaceutical grade, including Avicel 102, crospovidone, lactose, magnesium stearate, mannitol, talc, and aspartame, were sourced from Amishi Drugs and Chemicals Pvt. Ltd., Ahmedabad.

Methods

API characterization and compatibility analysis

Preformulation assessment examined the physicochemical characteristics of the API and its compatibility with selected excipients, serving as the initial step in dosage form development.

Organoleptic properties

Organoleptic properties, including color, odor, appearance, and melting point, were evaluated as part of physical and chemical characterization. [12]

Calibration Curve

To obtain standard solutions of concentrations 1000 µg/mL, 10 mg of sitagliptin was accurately dissolved in 10 mL of phosphate buffer (pH 6.8). A 100 µg/mL solution was prepared by diluting 2 mL of this stock to 20 mL. Further dilutions (1–5 mL) of this intermediate were made up to 10 mL to produce final concentrations of 10 to 50 µg/mL and assessed at 267 nm.

Compatibility assessment

Compatibility testing of the API with excipients represents a critical phase in the formulation development of pharmaceutical products. Excipients, although pharmacologically inactive, can interact chemically and physically with APIs. Compatibility tests determine the suitability of excipients for use in pharmaceutical formulations. In this study, the API was blended with individual excipients (crospovidone, Avicel 102, talc, aspartame, mannitol, magnesium stearate, and lactose) in a 1:1 (*w/w*) ratio. The mixtures were uniformly blended, screened (40# mesh), and filled into glass vials, closed with grey rubber stoppers and aluminum seals. These samples underwent accelerated conditions of 40 ± 2°C/75 ± 5% RH as per ICH guidelines. [13]

Development and Evaluation of FDTs

Sitagliptin FDTs were developed employing the direct compression method, as detailed in Table 1. Sitagliptin, crospovidone, Avicel 102, lactose, talc, aspartame, mannitol, and magnesium were individually sieved using a 60-mesh sieve to ensure consistent particle size distribution. A drug-excipient mixture was created by uniformly mixing sitagliptin, mannitol, and lactose using gentle trituration with a mortar and pestle. Crospovidone,

Table 1: Formulation composition

Sr. No.	*Ingredients*	*Quantity (mg)*								
		B1	*B2*	*B3*	*B4*	*B5*	*B6*	*B7*	*B8*	*B9*
1.	Sitagliptin	100	100	100	100	100	100	100	100	100
2.	Crospovidone	12.5	12.5	12.5	18.75	18.75	18.75	25	25	25
3.	Avicel 102	37.5	43.75	50	37.5	43.75	50	37.5	43.75	50
4.	Lactose	45	38.75	32.5	38.75	32.5	26.25	32.5	26.25	20
5.	Mannitol	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5
6.	Aspartame	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
7.	Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
8.	Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Total weight of tablet		250 mg								

Avicel 102, and aspartame were then added according to the formulation and mixed with the initial mixture. The resulting blend was further homogenized for 30 minutes using a rapid mixer granulator operated at a speed of 150 rpm to ensure uniform blending. Magnesium stearate, as well as talc, was subsequently incorporated as lubricants and blended with the mixture for an additional 5 minutes to ensure uniform distribution. Tablets weighing 250 mg with a convex surface were manufactured using a 9 mm punch on a 10-station rotary tablet press fitted with 'B' type tooling. [13,14]

Pre and post-compression evaluation

The powder mixture was assessed for flowability characteristics, including density indices, Hausner's ratio, Carr's index, and angle of repose,[12,15,16] whereas post-compression evaluation of the formulated FDTs comprised tests for hardness, diameter, thickness, weight variation, friability, drug content, and disintegration time. [17-20]

Dissolution Profiling

The dissolution profiling of sitagliptin-loaded FDTs was conducted employing a USP Type II (paddle) apparatus. The speed of the rotation of the paddle was 50 rpm. Dissolution flask contains 900 mL dissolution medium (phosphate buffer-pH 6.8) kept at 37 ± 0.5°C. At specified time points (every 5 minutes up to 30 minutes), 10 mL samples were taken out, filtered, and assessed at 267 nm. Fresh buffer was immediately added to maintain sink conditions.[21] The cumulative percentage of drug release was calculated and plotted against time to assess the release profile.

Experimental design

A 3^2 factorial experimental design was utilized to investigate how varying levels of crospovidone (X_1) - Avicel 102 (X_2) influence disintegration time (Y_1) - tablet hardness (Y_2), aiming to develop an FDT demonstrating optimal performance. Table 2 outlines the factor levels along with their respective coded values. [22] The study's approach of pre-selecting the levels of Crospovidone and Avicel 102 based on preliminary studies ensured that the experimental design started with factor levels most likely to achieve desirable results. This strategy facilitated the efficient development of an FDT that balanced both quick disintegration and adequate hardness, optimizing the formulation for effective delivery and patient convenience.

Table 2: Optimization design strategy

Symbol	*Independent variables*	*Level*		
		Low (-1)	*Medium (0)*	*High (+1)*
X_1	Crospovidone (%)	5	7.5	10
X_2	Avicel 102 (%)	15	17.5	20

Stability assessment

Following the ICH stability testing protocol, the optimized formulation of sitagliptin FDTs underwent accelerated conditions of 40 ± 2°C/75 ± 5% RH for three months. [23] Triplicate measurements were obtained for each parameter, followed by statistical assessment using one-way ANOVA, taking $p < 0.05$ as the threshold for statistical significance. Stability under accelerated conditions was assessed by comparing results over time with initial values.

Statistical assessment

The experimental layout and subsequent statistical interpretation were carried out using Design-Expert version 7.0. DoE approach was utilized to optimize the formulation by evaluating the impact of formulation variables on key responses. Model validation was assessed through ANOVA and, and the regression model's strength was confirmed by R^2 value, indicating adequacy and predictability of the models.

Results and Discussion

Preformulation Studies

Organoleptic properties

Sitagliptin in its original form is presented as a white, finely powdered substance, exuding an odorless characteristic.

Calibration curve of sitagliptin

The UV absorbance profile of sitagliptin at various concentrations in a phosphate buffer (6.8 pH) is graphically depicted in Fig. 1. The absorbance versus concentration graph for sitagliptin showed a linear relationship between 10 to 50 µg/mL. The correlation coefficient values (R^2) were 0.9929, indicating excellent linearity of the data.

Compatibility assessment

The results of the compatibility assessment indicated no observable color change, precipitation, or odor, and

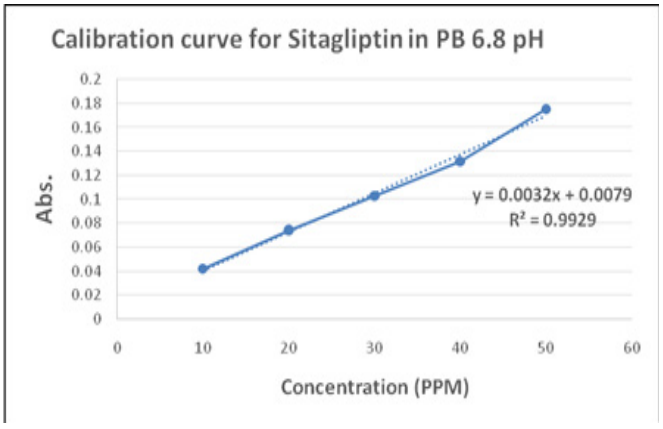

Fig. 1: Calibration curve for sitagliptin

no significant shifts in physical state were detected. Moreover, there was no evidence of drug degradation or incompatibility upon visual inspection, suggesting that sitagliptin maintained its stability with the selected excipients under stress conditions. These findings confirm the suitability of the excipients for use in the formulation of FDTs of sitagliptin.

Pre-compression parameters

All powder blends of the trial batches (B1–B9) were subjected to pre-compression parameters testing, and all were observed within predefined acceptable ranges.

Formulations exhibited bulk densities (0.609 ± 0.001-0.641 ± 0.001 g/cm^3) as well as tapped densities (0.691 ± 0.001-0.731 ± 0.001 g/cm^3) across all formulations. The Carr's index values (11.05 ± 0.05-13.95 ± 0.05%) confirmed good powder flow, which was supported by Hausner's ratios (1.12 ± 0.01-1.16 ± 0.01), falling within an acceptable limit for good flowability (<1.25).

The formulations demonstrated angle of repose values from 23.04 ± 0.02° to 26.13 ± 0.03°, falling within the 20°–30° range typically associated with desirable flow properties. [24] These observations confirm that the prepared blends exhibited favorable flow and compressibility characteristics, rendering them appropriate for direct compression in tablet production. [14] **Table 3:** The findings in the following manner.

Development and evaluation of FDTs

The direct compression method was used to develop FDTs due to its simplicity and benefits. Post-compression evaluations showed all nine batches (B1–B9) complied with pharmacopoeial standards. Tablet dimensions, measured with a vernier caliper, were: thickness 4.51 ± 0.02 to 4.55 ± 0.05 mm, and diameter 8.80 ± 0.02 to 8.85 ± 0.02 mm, indicating uniformity in die fill and compression. Hardness ranged from 4.0 ± 0.13 to 5.5 ± 0.08 kg/cm^2, reflecting enough mechanical durability suitable for handling and packaging. Friability remained below the acceptable limit of 1% in all batches, ranging from 0.40 ± 0.01 to 0.84 ± 0.02%, suggesting sufficient tablet integrity (Table 4A).

Weight variation analysis revealed that all tablets were within the acceptable limits, with observed

Table 3: Assessment of flow property

Batches	*Bulk density*	*Tapped density*	*Hausner's ratio*	*Carr's index*	*Angle of repose*
B1	0.641 ± 0.001	0.721 ± 0.001	1.12 ± 0.01	11.10 ± 0.10	23.23 ± 0.03
B2	0.631 ± 0.001	0.721 ± 0.020	1.14 ± 0.01	12.48 ± 0.08	24.34 ± 0.04
B3	0.629 ± 0.001	0.731 ± 0.001	1.16 ± 0.01	13.95 ± 0.05	24.87 ± 0.02
B4	0.630 ± 0.050	0.727 ± 0.020	1.15 ± 0.01	13.34 ± 0.04	23.23 ± 0.02
B5	0.618 ± 0.001	0.718 ± 0.001	1.16 ± 0.01	13.93 ± 0.03	23.04 ± 0.02
B6	0.609 ± 0.001	0.691 ± 0.001	1.13 ± 0.01	11.87 ± 0.07	24.09 ± 0.02
B7	0.620 ± 0.001	0.697 ± 0.030	1.12 ± 0.01	11.05 ± 0.05	26.13 ± 0.03
B8	0.617 ± 0.001	0.701 ± 0.030	1.14 ± 0.01	11.98 ± 0.08	25.25 ± 0.02
B9	0.627 ± 0.050	0.711 ± 0.001	1.13 ± 0.01	11.81 ± 0.06	24.63 ± 0.02

*Results reported as mean ± SD, using triplicate observations.

Table 4A: Assessment of tablet quality attributes

Batches	***Thickness (mm)***	***Diameter (mm)***	***Hardness (kg/cm^2)***	***Friability (%)***
B1	4.55 ± 0.01	8.81 ± 0.01	4.0 ± 0.13	0.40 ± 0.01
B2	4.55 ± 0.05	8.84 ± 0.03	4.5 ± 0.16	0.42 ± 0.01
B3	4.50 ± 0.05	8.85 ± 0.02	5.0 ± 0.13	0.81 ± 0.03
B4	4.52 ± 0.02	8.80 ± 0.02	4.5 ± 0.18	0.41 ± 0.01
B5	4.52 ± 0.01	8.83 ± 0.02	4.5 ± 0.09	0.84 ± 0.02
B6	4.50 ± 0.01	8.85 ± 0.02	5.0 ± 0.05	0.42 ± 0.01
B7	4.53 ± 0.05	8.83 ± 0.02	4.5 ± 0.09	0.41 ± 0.01
B8	4.53 ± 0.05	8.85 ± 0.02	5.0 ± 0.03	0.40 ± 0.01
B9	4.54 ± 0.02	8.83 ± 0.02	5.5 ± 0.08	0.40 ± 0.01

*Results reported as mean ± SD, using triplicate observations.

Table 4B: Assessment of tablet quality attributes

Batches	Drug content	Weight variation		Disintegration time* (s)
		Weight* (mg)	Weight variation (5 %)	
B1	100.15	258 ± 3	Passes	48 ± 2
B2	98.61	245 ± 2	Passes	52 ± 3
B3	99.74	255 ± 5	Passes	58 ± 4
B4	99.89	250 ± 7	Passes	38 ± 2
B5	100.65	245 ± 4	Passes	46 ± 2
B6	101.28	244 ± 6	Passes	50 ± 4
B7	100.5	252 ± 6	Passes	34 ± 1
B8	100.41	249 ± 5	Passes	37 ± 4
B9	100.45	240 ± 8	Passes	39 ± 3

* Results reported as mean ± SD, using triplicate observations.

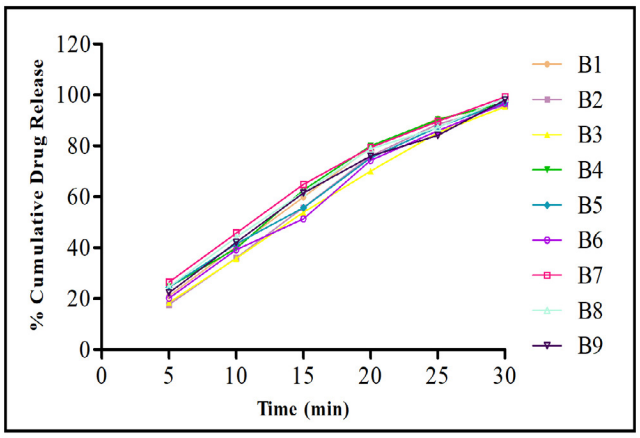

Fig. 2: Assessment of dissolution characteristics of FDTs

weights ranging from 240 to 258 mg, complying with pharmacopoeial specifications for ± 5% deviation. Drug content uniformity for all batches met specifications, ranging from 98 to 101%, ensuring dose accuracy (Table 4B).

Disintegration time ranged from 34 ± 1 to 58 ± 4 seconds. The inverse relationship between crospovidone concentration and disintegration time observed in this study is well-supported by superdisintegrant theory, where water uptake and particle swelling disrupt tablet cohesion. In contrast, increasing concentrations of Avicel 102, a directly compressible binder with moderate disintegration capacity, increased hardness but also delayed disintegration. This indicates that excessive binder content can reduce porosity and water penetration, thus slowing tablet breakup.[25]

Notably, batch B7 exhibited the most desirable balance-rapid disintegration (34 ± 1 s) and adequate hardness (4.5 ± 0.09 kg/cm^2)-demonstrating that higher concentrations of crospovidone effectively reduced disintegration time without compromising tablet integrity. This aligns with previous findings that crospovidone, due to its capillary action and swelling mechanism, rapidly draws water into the tablet matrix, promoting quick disintegration.[26]

Dissolution Profiling

All sitagliptin FDT batches (B1–B9) demonstrated rapid and complete drug release within the specified time (Fig. 2). The percentage cumulative drug release ranged between 95.21 and 99.11% at 30 minutes, depending on the formulation composition.

Notably, batches B7, B8, and B9 exhibited superior dissolution profiles, with drug release exceeding 99% within 30 minutes. Among them, Batch B7 achieved 99.11% drug release, which is indicative of excellent dissolution behavior. This enhanced dissolution rate is attributed to the synergistic effects of high crospovidone concentration, which promotes rapid disintegration and increased surface area, and the optimized level of Avicel 102, which ensures adequate porosity and compressibility.

The dissolution performance aligns with the disintegration data and confirms the effectiveness of the selected formulation variables in enhancing the drug release kinetics of sitagliptin from FDTs.

Optimization of FDT

The experimental design for the optimization of sitagliptin FDTs generated a total of nine formulation runs, as presented in Table 5. Design-Expert® 7.0 was employed for model generation, regression analysis, and response surface methodology. The software suggested and tested suitable models (Linear, 2FI, Quadratic, and Cubic) using ANOVA statistical analysis.

Table 5: Experimental configuration for DoE

Runs	Factor		Response	
	X_1	X_2	Y_1	Y_2
	Crospovidone (%)	Avicel 102 (%)	Disintegration time (s)	Tablet hardness (kg/cm^2)
1	7.5	15	38	4.5
2	10	15	34	4.5
3	10	20	39	5.5
4	10	17.5	37	5
5	5	17.5	52	4.5
6	5	20	58	5
7	7.5	17.5	46	4.5
8	7.5	20	50	5
9	5	15	48	4

Effect of formulation variables on disintegration time

Interaction between Crospovidone and Avicel 102 on disintegration rate is illustrated in Fig. 3. FDT batches exhibited disintegration times ranging from 34 to 58 s. A minimum disintegration time was observed in the batch with a Crospovidone: Avicel 102 ratio of 10:15%.

Formulation percentages of Crospovidone and Avicel 102 significantly impact drug disintegration time. Crospovidone (X_1) showed a strong negative effect on disintegration time, significantly reducing it as concentration increased (*p <0.0001*).

Design-Expert software's fit summary suggested a "Linear vs Mean" model after data input for the disintegration time effect (Table 6).

The ANOVA results, as presented in Table 7, identified both formulation factors as statistically significant contributors to disintegration time. The model exhibited a high F-value of 91.91 (*p <0.0001*), indicating that the model's predictive capability is not a result of random error. Variables exhibiting Prob > F value below 0.05 were identified as significant contributors, confirming that both factors significantly influenced the response variable. These findings support the robustness and predictive reliability of the fitted model.

Fit statistics summarized in Table 8 further support the reliability of the disintegration time model. The model exhibited a strong goodness of fit, as reflected by an R^2 (0.9684) and an adjusted R^2 (0.9579). The predicted R^2 value (0.9194) confirms its strong predictive performance.

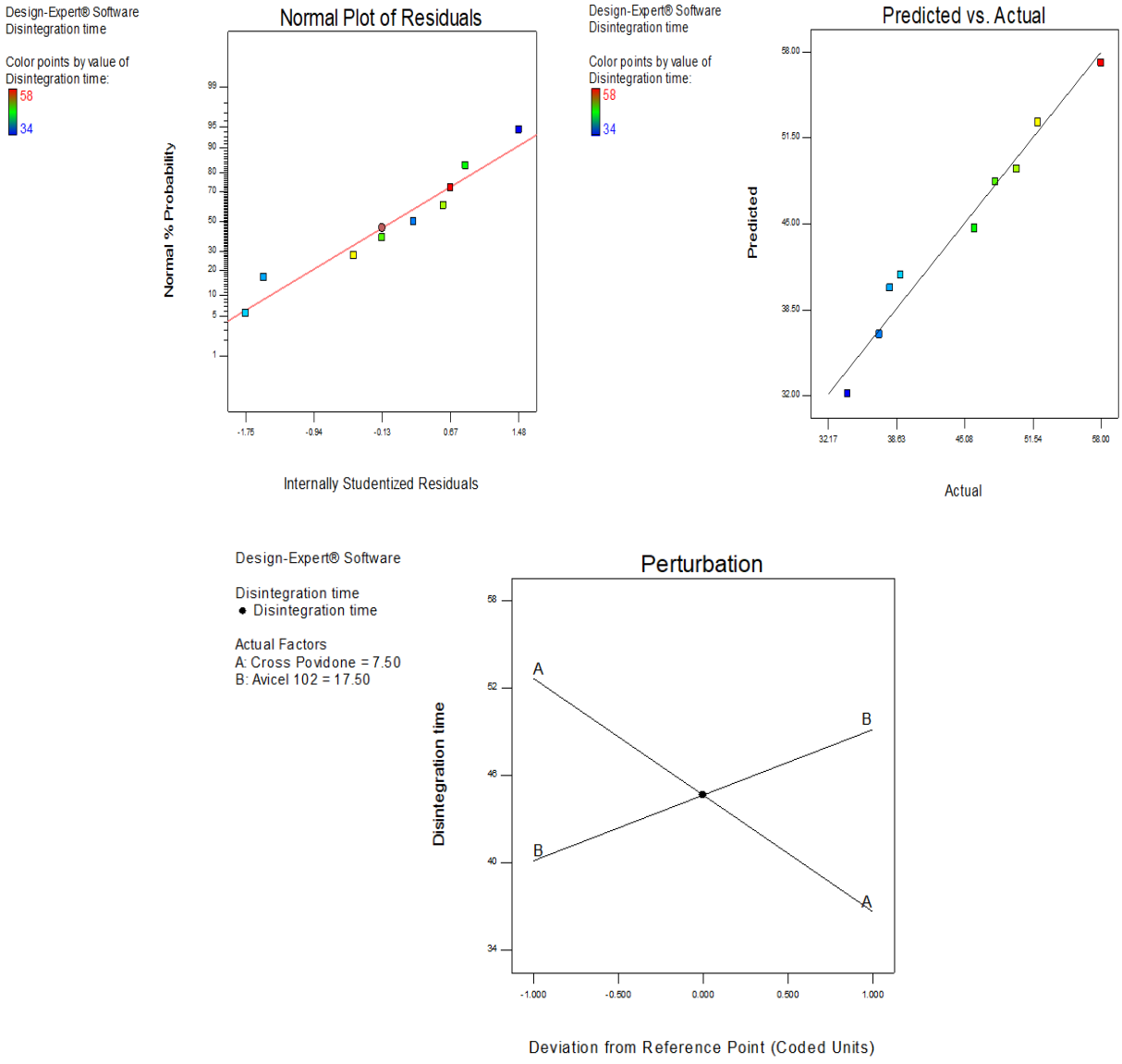

Fig. 3: Interaction plot for crospovidone and Avicel 102 influencing the disintegration time of the formulation

Table 6: Regression fit statistics for disintegration time

Source	*SS*	*df*	*MS*	*F-statistic*	**p-value** *Prob > F*	*Remarks*
Mean vs Total	17956	1	17956			
Linear vs Mean	505.5	2	252.75	91.90909	< 0.0001	Suggested
2FI vs Linear	6.25	1	6.25	3.04878	0.1412	
Quadratic vs 2FI	0.5	2	0.25	0.076923	0.9277	
Cubic vs Quadratic	7.5	2	3.75	1.666667	0.4804	Aliased
Residual	2.25	1	2.25			
Total	18478	9	2053.111			

Table 7: ANOVA results for the disintegration time response variable

Source	*SS*	*df*	*MS*	*F-statistic*	*p-value Prob > F*	*Remarks*
Regression	505.5	2	252.75	91.90909	< 0.0001	Significant
Crospovidone	384	1	384	139.6364	< 0.0001	
Avicel 102	121.5	1	121.5	44.18182	0.0006	
Unexplained Variation	16.5	6	2.75			
Corrected Total	522	8				

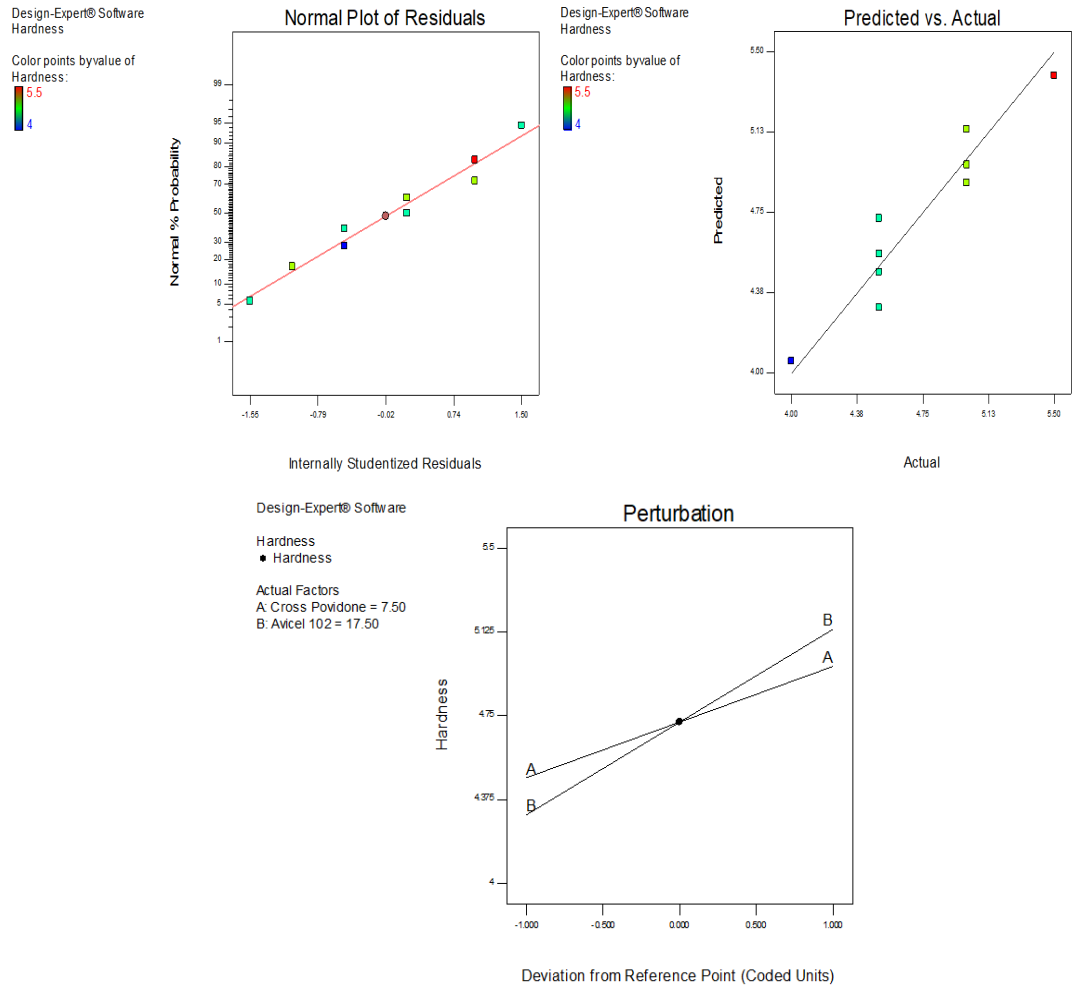

Fig. 4: Interaction plot for Crospovidone and Avicel 102 influencing the hardness of formulation

Table 8: Statistical significance and model fit of disintegration time

SD	*1.66*	*R^2*	*0.9684*
Mean	44.67	Adj R^2	0.9579
CV %	3.71	Pred R^2	0.9194
PRESS	42.09	Adeq Precision	26.112

A low CV of 3.71% further validates the model's precision, and an adequate precision of 26.112 confirms a strong signal relative to noise, making the model appropriate for navigating the response surface.

Effect of formulation variables on tablet hardness

Fig. 4 illustrates the interaction between Crospovidone and Avicel 102 on hardness. FDT batches exhibited hardness ranging from 4 to 5.5 kg/cm^2. A maximum hardness was observed in the batch with a Crospovidone: Avicel 102 ratio of 10:20%.

Percentages of Crospovidone and Avicel 102 significantly impact on hardness of FDTs. Hardness increases with increasing Crospovidone and Avicel 102 concentration. Avicel 102 has a greater impact on the hardness of FDTs than Crospovidone, evidenced by its significantly lower p-value.

Design-Expert software suggested "Linear vs Mean" as a fit summary model after data input for the disintegration time effect (Table 9).

As shown in Table 10, ANOVA analysis for the response variable 'hardness' revealed that both independent variables had statistically significant effects on tablet hardness. The model demonstrated F-value-30.6 (*p = 0.0007*), indicating that the observed variation is highly significant and not attributable to random error. Both factors exhibited 'Prob > F' values well below the 0.05 threshold, affirming their substantial influence on tablet mechanical integrity. The results affirm that the linear model is both adequate and dependable for predicting hardness as a function of formulation variables.

Fit statistics in Table 11 confirm the adequacy and reliability of the model developed for tablet hardness. With an R^2 (0.9107), adjusted R^2 (0.8810), and predicted R^2 (0.8233), the model showed strong fit and predictive validity. Additionally, the low CV (3.22%) and an adequate signal-to-noise ratio of 15.179 (adequate precision) highlight minimal variability, making the model appropriate for navigating the response surface.

The optimization study effectively demonstrated that crospovidone had a more dominant influence on disintegration time, while Avicel 102 played a key role in ensuring tablet integrity. High R^2 values and adequate precision confirmed the model's predictability and reliability. The factorial design approach enabled efficient screening and fine-tuning of excipient levels, leading to a robust and patient-compliant formulation. Based on pre-

Table 9: Regression fit statistics for hardness

Source	*SS*	*df*	*MS*	*F-statistic*	*p-value Prob > F*	*Remarks*
Mean vs Total	200.6944	1	200.6944			
Linear vs Mean	1.416667	2	0.708333	30.6	0.0007	Suggested
2FI vs Linear	0	1	0	0	1.0000	
Quadratic vs 2FI	0.027778	2	0.013889	0.375	0.7155	
Cubic vs Quadratic	0.083333	2	0.041667	1.5	0.5000	Aliased
Unexplained Variation	0.027778	1	0.027778			
Total	202.25	9	22.47222			

Table 10: ANOVA results for the hardness response variable

Source	*SS*	*df*	*MS*	*F-statistic*	*p-value Prob > F*	*Remarks*
Regression	1.416667	2	0.708333	30.6	0.0007	significant
Crospovidone	0.375	1	0.375	16.2	0.0069	
Avicel 102	1.041667	1	1.041667	45	0.0005	
Unexplained Variation	0.138889	6	0.023148			
Corrected Total	1.555556	8				

Table 11: Statistical significance and model fit for hardness

SD	*0.15*	*R^2*	*0.9107*
Mean	4.72	Adj R^2	0.8810
CV %	3.22	Pred R^2	0.8233
PRESS	0.27	Adeq Precision	15.179

Table 12: Stability assessment

Evaluation parameters	*Hardness (kg/cm²)*	*Friability (%)*	*Disintegration Time (s)*	*Drug Content (%)*
0 Month	4.50 ± 0.09	0.41 ± 0.01	34.00 ± 1.00	100.50 ± 0.03
1 Month	4.60 ± 0.10	0.48 ± 0.01	37.33 ± 0.58	99.87 ± 0.05
2 Month	4.60 ± 0.10	0.57 ± 0.01	40.00 ± 1.00	99.52 ± 0.05
3 Month	4.70 ± 0.10	0.65 ± 0.01	39.00 ± 1.00	99.33 ± 0.04

*Results reported as mean ± SD, using triplicate observations.

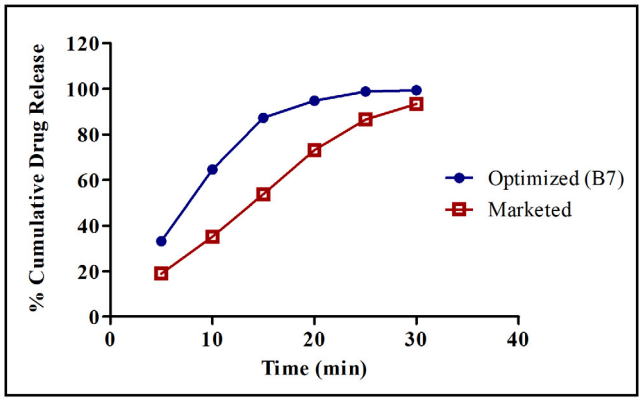

Fig. 5: Comparative analysis of drug release behavior

and post-compression data and factorial design modelling, batch B7- comprising 10% crospovidone and 15% Avicel 102, as the optimal formulation, offering an ideal balance between rapid disintegration (34.00 ± 1.00 seconds) and sufficient mechanical strength (4.50 ± 0.09 kg/cm^2). It also showed 99.11% drug release within 30 minutes, confirming excellent dissolution behavior.

Stability study

The accelerated stability testing under ICH conditions demonstrated that the optimized formulation retained its physicochemical characteristics, including disintegration time, drug content, and hardness (Table 12). The results revealed no statistically significant change in tablet hardness (F = 02.00, $p = 0.1927$), suggesting the formulation retained mechanical integrity throughout the study. However, friability (F=306.00, $p < 0.0001$), disintegration time (F=26.02, $p = 0.0008$), and drug content (F=26.02, $p < 0.0001$) showed statistically significant differences over time. Despite these changes, drug content remained above 99% and disintegration time within acceptable limits, indicating that the formulation exhibited consistent pharmaceutical stability and effectiveness under said circumstances.

The overall results confirm that the optimized FDT formulation retained its physical and chemical integrity over the course of three months under accelerated conditions. The minor variations observed were statistically significant for some parameters, but not pharmaceutically critical, indicating the formulation's robustness and suitability for commercial development.

Comparative study- Dissolution profiling

Dissolution profiling of an optimized sitagliptin 100 mg FDT batch and a marketed formulation was compared using the same controlled conditions of dissolution testing. Aliquots were withdrawn every 5 minutes to quantify the cumulative amount of drug released. After 30 minutes, the optimized formulation released > 99% drug release within 30 minutes, significantly outperforming the marketed formulation (93.41%) (Fig. 5), suggesting improved therapeutic potential.

Conclusion

A sitagliptin-loaded FDT was effectively developed and optimized as part of the present investigation employing a 3^2 full factorial design and QbD principles. Crospovidone, utilized as a superdisintegrant, significantly reduced disintegration time, while Avicel 102 functioned as a compressible binder, ensuring adequate tablet hardness. Statistical analysis confirmed that crospovidone exhibited a more significant role in controlling disintegration time compared to the impact of Avicel 102 on mechanical strength. The optimized batch (B7) demonstrated superior performance, disintegrating in 34.00 ± 1.00 seconds with sufficient mechanical strength (4.50 ± 0.09 kg/cm^2) and 99.11% drug release within 30 minutes. The formulation exhibited acceptable stability under accelerated ICH conditions over three months, maintaining critical quality attributes. These findings affirm the robustness, patient compliance potential, and clinical relevance of the optimized sitagliptin FDT, particularly for populations with dysphagia or requiring rapid therapeutic onset in type 2 diabetes management.

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